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MERCURY IN MEDICINE—ARE WE TAKING UNNECESSARY RISKS?

HEARING

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

ONE HUNDRED SIXTH CONGRESS

SECOND SESSION

JULY 18, 2000

Serial No. 106–232

Printed for the use of the Committee on Government Reform



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CONTENTS

Page

Hearing held on July 18, 2000 1

Statement of:

Redwood, Lyn, Tyrone, GA; Sallie Bernard, Cranford, NJ; Albert Enayati, Pyramus, NJ; Elizabeth Birt, Chicago, IL; Dr. Stephanie Cave, Baton Rouge, LA; Dr. H. Vasken Aposhian, professor of molecular and cellular biology, and pharmacology, University of Arizona; and Dr. Sharon Humiston, Pittsford, NY 12

Trovato, E. Ramona, Director, Office of Children's Health Protection, U.S. Environmental Protection Agency; Dr. William Egan, Acting Office Director, Office of Vaccine Research and Review, Center for Biologics Evaluation and Research [CBER], FDA; Dr. Roger H. Bernier, Associate Director for Science, National Immunization Program, Centers for Disease Control and Prevention; and Dr. Marie Bristol-Power, National Institute of Health and Human Development, National Institute of Health 227

Letters, statements, etc., submitted for the record by:

Aposhian, Dr. H. Vasken, professor of molecular and cellular biology, and pharmacology, University of Arizona, prepared statement of 201

Bernard, Sallie, Cranford, NJ, prepared statement of 21

Bernier, Dr. Roger H., Associate Director for Science, National Immunization Program, Centers for Disease Control and Prevention, prepared statement of 253

Birt, Elizabeth, Chicago, IL, prepared statement of 163

Bristol-Power, Dr. Marie, National Institute of Health and Human Development, National Institute of Health, prepared statement of 270

Cave, Dr. Stephanie, Baton Rouge, LA, prepared statement of 179

Chenoweth-Hage, Hon. Helen, a Representative in Congress from the State of Idaho, prepared statement of 216

Egan, Dr. William, Acting Office Director, Office of Vaccine Research and Review, Center for Biologics Evaluation and Research [CBER], FDA, prepared statement of 236

Gilman, Hon. Benjamin A., a Representative in Congress from the State of New York, prepared statement of 220

Humiston, Dr. Sharon, Pittsford, NY, prepared statement of 209

Morella, Hon. Constance A., a Representative in Congress from the State of Maryland, prepared statement of 8

Redwood, Lyn, Tyrone, GA, article entitled, "Mercury and Autism" 15

Schakowsky, Hon. Janice D., a Representative in Congress from the State of Illinois, prepared statement of 11

Trovato, E. Ramona, Director, Office of Children's Health Protection, U.S. Environmental Protection Agency, prepared statement of 229

MERCURY IN MEDICINE—ARE WE TAKING UNNECESSARY RISKS?

TUESDAY, JULY 18, 2000

HOUSE OF REPRESENTATIVES,
COMMITTEE ON GOVERNMENT REFORM,
Washington, DC.

The committee met, pursuant to notice, at 1 p.m., in room 2154, Rayburn House Office Building, Hon. Dan Burton (chairman of the committee) presiding.

Present: Representatives Burton, Gilman, Morella, Ros-Lehtinen, Chenoweth-Hage, Waxman, Maloney, Norton, Cummings, Kucinich, Davis of Illinois, and Schakowsky.

Also present: Mr. Weldon.

Staff present: Kevin Binger, staff director; David A. Kass, deputy counsel and parliamentarian; S. Elizabeth Clay, Nicole Petrosino, and Nat Weinecke, professional staff members; Robert Briggs, clerk; Robin Butler, office manager; Michael Canty, legislative aide; Toni Lightle, legislative assistant; Leneal Scott, computer systems manager; John Sare, staff assistant; Corinne Zaccagnini, systems administrator; Phil Schiliro, minority staff director; Phil Barnett, minority chief counsel; Sarah Despres, minority counsel; Ellen Rayner, minority chief clerk; and Jean Gosa and Earley Green, minority assistant clerks.

Mr. BURTON. A quorum being present, the Committee on Government Reform will come to order. I ask unanimous consent that all Members and witnesses' written statements be included in the record. Without objection, so ordered. I ask unanimous consent that all articles, exhibits and extraneous or tabular material referred to be included in the record. Without objection, so ordered.

For the last year, the Government Reform Committee has been looking at issues regarding vaccine safety, research and policy. A few people have tried to portray this investigation as anti-vaccine. Nothing could be further from the truth. Safe, effective vaccines save lives. On the other hand, vaccines that have not been thoroughly tested and reviewed can be dangerous. The rotavirus vaccine was a good example. The government and manufacturers ignored the warning signs. A lot of babies were injured and required surgery. One baby died before the vaccine was pulled off the market.

Is it irresponsible to ask questions about why that happened? Of course not.

We have a lot of doctors who serve on Federal advisory committees who have serious conflict of interest problems. They are al-

lowed to vote on vaccines made by companies that they get money from.

Is it irresponsible to ask questions about conflicts of interest? Of course not, especially where public health and safety are concerned.

Today we are holding a hearing about why mercury is put into vaccines that are given to children. Is that irresponsible? Of course not.

If someone holds hearings about mismanagement at the Department of Education, that does not mean they are anti-education. That means they want our educational system to be as well run as possible. That is the way that I feel about our vaccine policies. No area is so sacrosanct that the world will come to an end if we ask some sensible questions and expect to get some sensible answers.

I think this kind of oversight will make our vaccine program stronger not weaker.

This spring we held a hearing about possible connections between autism and the MMR vaccine. We heard lots of testimony on both sides of the issue. After the hearing, I sent a letter to Secretary Shalala. So did Congressman Waxman. We both asked her to put together a panel of the best experts in the field to look at this issue. That was May 16—2 months ago. No response.

That's intolerable. If your position is that we should base our policies on good science and good research, then fine. I agree with you 100 percent. But if you are not willing to do the research, if you're not willing to ask the questions, then we have a real problem on our hands.

I believe that our primary focus on vaccine policy should always be what is best for the children. We need to insure that only vaccines that are truly needed to protect the public health are added to the childhood immunization schedule. At no time should the interests of vaccine developers be a higher priority than our children's health and well-being.

Vaccines are the only drugs that Americans are required by a government agency to take. It is thus imperative that the Federal Government ensures the safety of these mandated vaccines. Each State sets a schedule for the vaccines a child must receive in order to attend school or day care. The States rely on the Federal Government for guidance on which vaccines should be mandated. The Federal Government is also the largest purchaser of vaccines.

That brings us to today's hearing topic—mercury in medicine. This should be a no-brainer. We all know that mercury is a toxic substance. Long-term exposure to low levels of mercury has been linked to mental retardation, cerebral palsy and central nervous system disorders. We assume that the FDA will protect our children from exposure to any level of mercury through drugs. But that hasn't been the case. Thimerosal was first marketed in 1930 and has become the most widely used preservative in vaccines. It is present in over 50 licensed vaccines.

The FDA recently acknowledged that in the first 6 months of life children get more mercury than is considered safe by the EPA. The truth is that sometimes kids go to their doctor's office and get four or five vaccines at the same time. My grandson received vaccines for nine different diseases in 1 day. He may have been exposed to 62.5 micrograms of mercury in 1 day through his vaccines. Accord-

ing to his weight, the maximum safe level of mercury he should have been exposed to in 1 day is 1.5 micrograms, so that is 41 times the amount at which harm can be caused.

How much mercury are kids being exposed to at once? One would think that the FDA would have moved aggressively to remove vaccines that contain mercury from the market immediately. They did not. On July 9, 1999, the American Academy of Pediatrics and the U.S. Public Health Service issued a joint statement recommending the removal of all thimerosal from vaccines. On May 31, 2000, the Food and Drug Administration notified vaccine manufacturers that the review of mercury compounds in drugs and foods concluded that reducing or eliminated thimerosal from vaccines is merited. However, there has been no mandatory action. These vaccines are still in use.

The FDA continues to allow the mercury containing vaccines to remain on the market. Today, over 8,000 children in America may be given a toxic dose of mercury in their vaccines.

Many parents who have contacted the committee are concerned about other ingredients as well, including formaldehyde, MSG, and aluminum. We have also been contacted by many individuals who have concerns about mercury in dental amalgams. While this is not the focus of today's hearing, it certainly warrants discussion as well.

Congress directed the Environmental Protection Agency to contract with the National Research Council to prepare recommendations on the appropriate dose for mercury exposure. That report was released on July 11. While the FDA relies on the Agency for Toxic Substances and Disease Registry's dosing level for mercury of 0.5 micrograms per kilogram of body weight per day, this is significantly higher than the EPA's dose of 0.1 microgram per kilogram of body weight. In that report it was confirmed that the EPA's reference dose is correct. We will hear from Dr. Vasken Aposhian, University of Arizona at Tucson, one of the scientists who worked on this report. Romana Trovato will testify on behalf of the Environmental Protection Agency.

Section 413 of the Food and Drug Administration Modernization Act of 1997 required the FDA to compile a list of drugs and foods that contain internally introduced mercury compounds, and provide a quantitative and qualitative analysis of the mercury compounds in this list. The act also requires the agency to compile the list and provide the analysis within 2 years after the date of its enactment on November 21, 1997. Dr. William Egan will be testifying on behalf of the FDA today.

While thimerosal has previously been ruled by the FDA to fit the "generally recognized as safe" standard, when the FDA conducted their over the counter drug review they changed their minds. The FDA determined that mercury compounds used as active ingredients in over the counter drug products were not found to be generally recognized as safe. Additionally, the FDA has not approved any mercury containing compounds as food additives and does not consider any mercury containing compounds to be generally recognized as safe. On their own Website, the FDA states, "lead, cadmium, and mercury are examples of elements that are toxic when present at relatively low levels."

How is it that mercury is not safe for food additives and over the counter drug products but it is safe in our vaccines and dental amalgams?

Dr. Roger H. Bernier, Associate Director for Science at the National Immunization Program, Centers for Disease Control and Prevention, will testify regarding the recent discussion of the Advisory Committee on Immunization Practices regarding thimerosal.

Autism is a syndrome characterized by impairments in social relatedness and communication, repetitive behaviors, abnormal movements, and sensory dysfunction. Autism may now affect 1 in 150 U.S. children. We will hear from Dr. Marie Bristol-Power of the National Institutes of Health regarding the existing research in autism. The characteristics of autism and of mercury poisoning are strikingly similar.

Dr. Stephanie Cave, a physician from Baton Rogue, LA will be testifying about the mercury toxicity she is seeing in the 200 autistic children she has as patients.

Autism strikes families from a diverse background. We will hear from five parents today. Elizabeth Birt of Chicago, an attorney and mother of an autistic child, will be testifying about the need to remove mercury from all vaccines and a citizens petition that is being presented to the FDA making this request.

Several parents with scientific and medical backgrounds have written a report entitled "Autism: A Unique Type of Mercury Poisoning." Three of these parents will be testifying today. The lead author of the report is Sallie Bernard of Cranford, NJ. Lyn Redwood of Tyrone, GA is a nurse practitioner, and Albert Enayati of Paramus, NJ is a chemist. Dr. Sharon Humiston, a doctor with an autistic child, will also be testifying.

Our children are the future of this country. As a government, we have a responsibility to do everything within our power to protect them from harm, including insuring that vaccines are safe and effective. Every day that these mercury containing vaccines remain on the market is another day we are putting 8,000 children that day at risk.

The record will remain open until August 1, 2000.

Now I will recognize my colleague, Mr. Waxman, for his opening statement.

Mr. WAXMAN. Today we are having another hearing to highlight allegations of the safety of vaccines.

In April this committee held a hearing to publicize the chairman's theory that certain vaccines, particularly the MMR vaccine, cause autism. This theory is based mainly on speculation. As the American Medical Association concluded recently, "Scientific data does not support a causal association between vaccination and autism."

Today we are going to hear testimony about a new theory, that there is a link between autism and the mercury-based vaccine preservative called thimerosal. It should be noted that the MMR vaccine does not contain thimerosal. So this new theory is directed at childhood vaccines other than the measles, mumps and the rubella vaccine.

As I said in April, we must not get ahead of the science or raise false alarms. The best answers come from research that can with-

stand the rigors of the scientific method. These standards have been developed in order to find the truth. But if allegations are raised without scientific evidence, we risk scaring parents into foregoing potentially life saving childhood immunizations.

Regrettably I fear that once again we are proceeding without a sound scientific basis.

This hearing today combines two issues that I have worked on for years, autism and mercury. I have been a strong supporter of research and treatment for autism. I am a current sponsor of autism research and surveillance legislation, H.R. 997 and H.R. 274. I was also a leading supporter and sponsor of the Work Incentives Program Act of 1999, the American Disabilities Act of 1990 and the Developmental Disabilities Assistance and Bill of Rights Act of 1990, which are all laws of tremendous importance to persons with autism.

And in 1993, when I was chairman of the House Commerce Subcommittee on Health and the Environment, I was the lead sponsor of the NIH Revitalization Act, which reauthorized expanded funding for and strengthened NIH research into autism and childhood health.

I have also been very concerned about public exposure to mercury. For example, last year I introduced the Clean Smokestacks Act, H.R. 2900, to reduce methyl mercury emissions from power plants by 90 percent. As a National Academy of Sciences report confirmed only last week, these emissions pose a significant health threat and must be reduced. Methyl mercury contamination has caused 40 States to issue warnings about fish consumption. Human exposure to eating contaminated fish can cause numerous adverse health affects such as losses of sensory or cognitive ability, delays in developmental milestones, birth defects, tremors, convulsions and even death.

Currently, my legislation to reduce mercury emissions has over 100 bipartisan cosponsors, but it hasn't even been called up for a hearing, let alone movement by the leadership of the committee that has jurisdiction. For the last two Congresses, I have also introduced bipartisan legislation to require better public disclosure of mercury pollution. This legislation has over 100 bipartisan cosponsors, and I point this out to illustrate that I take the issue of mercury very seriously. Where we have a reasonable basis for taking action I believe that the Congress and agencies should expeditiously work to protect the public health from mercury exposure.

For this reason I strongly support the efforts by FDA to eliminate the use of thimerosal in vaccines. Thimerosal is a preservative that contains ethyl mercury. Although less is known about the effects of ethyl mercury in thimerosal than about the effect of ethyl mercury from power plant emissions, ethyl mercury may pose similar health risks. It is appropriate, therefore, that thimerosal be phased out of vaccines.

This process is well underway. The maximum exposure to mercury through vaccines today is 60 percent of what it was a year ago. The entire childhood immunization schedule is currently available without thimerosal and FDA expects all vaccines to be thimerosal free by the first quarter of next year.

The question this hearing poses, however, is not whether mercury-containing thimerosal should be in vaccines in the United States. FDA decided a year ago that it should not. Rather, the purpose of this hearing appears to be to publicize the theory that thimerosal is causing autism.

The evidence to support this theory is virtually nonexistent. I fear that once again we are pursuing an anti-vaccine agenda in disregard for the scientific and medical consensus on the safety of vaccines.

The chairman has held a series of hearings on questioning vaccine safety, the public health benefits of childhood immunizations and the integrity of the scientists, health professionals and public servants working to immunize our children. The chairman has promoted allegations that MMR vaccines causes autism. He has provided a forum for allegations that vaccines can cause diabetes, and he has alleged that parents should be skeptical about vaccines because our government is beholden to the drug industry.

Well, this is a backward attitude to take at a time when vaccines promise more than ever to improve human health.

I will read and listen to the testimony of the witnesses today very attentively. I want to thank the parents who are coming here and testifying. It takes a lot of courage to share your personal experiences with Congress.

We have other things going on at the same time as this hearing, which keeps us from being able to attend the hearing in full, and I will be in and out and I want to apologize to those witnesses. The written testimony will be part of the record. I will have a chance to review it. My staff will be here and will have an opportunity to report to me on all of the testimony that is given orally that may supplement the written record as well.

Thank you, Mr. Chairman, for this chance to give an opening statement.

Mr. BURTON. Before we ask any other Members if they would like to make an opening statement, we have Dr. Weldon, Congressman Weldon, who is very interested in this subject, and I would like to ask unanimous consent that he be able to participate in the hearing.

Mr. WAXMAN. Reserving the right to object, I am not going to object to him sitting in and being able to hear the testimony and pursue questions, but that is unusual because usually you have only members of the committee participate and if we allowed all Members to come in, it could delay many hearings to a great extent. But we want to accommodate this request and I certainly want to accommodate Dr. Weldon, for whom I have a great deal of respect.

We have 11 witnesses testifying today, and we on the minority asked for four witnesses and we were only accommodated by getting three. Now, when I say we were accommodated, we asked that the Centers for Disease Control be allowed to testify. We asked for a witness from NIH to testify. It shouldn't be a request of ours, it is no favor to us to have them testify. In any balanced hearing we certainly ought to have these people in to testify as well as those who are going to come in and express a particular point of view. We requested four witnesses and we got three. One more witness would have taken 5 minutes of testimony because that is what we

allow each witness to take in giving oral testimony. Mr. Weldon will have an opportunity to ask questions at least 5 minutes one round——

Mr. WELDON. Would the gentleman yield.

Mr. WAXMAN. In a minute. I welcome that because I think he will bring out information, but it just troubles me that while we try to be accommodating, I find it incomprehensible why the majority of the committee and the chairman of this committee is not accommodating our requests.

And I yield to the gentleman, and I do not object and I welcome you because you have a special interest and expertise.

Mr. WELDON. I thank the gentleman's kindness and I just want to point out that I have another hearing to go to in 30 minutes, so I doubt that I will be able to get in any oral questions.

Mr. WAXMAN. I don't object to you participating and asking questions. I point out the reluctance of the majority to have a fair and full and open hearing and accommodate all of the witnesses who have something to add, even if they may have something to add on a point that the chairman may disagree with. I withdraw my reservation.

Mr. BURTON. Without objection, so ordered. Do any other members have opening statements?

Representative Morella.

Mrs. MORELLA. Mr. Chairman, I just ask the fact that my written statement be included in the record and I just want to comment on the fact that I appreciate your efforts to hold this hearing on mercury and medicine, and I look forward to hearing the testimony of the witnesses. I really want to learn more about mercury and medicine and vaccines specifically.

In Montgomery County, the incidence of autism in our children is alarming, and some do feel that autism may be related to vaccines, but I am concerned about the lack of information and misinformation surrounding the issue of vaccines and its possible relationship to autism, so that I hope that today we can come to a conclusion on what the appropriate steps are for this committee and the government to take.

So with your approval, the rest of my opening statement I would like to have in the record.

Mr. BURTON. Without objection, so ordered.

[The prepared statement of Hon. Constance A. Morella follows:]

Mr. Chairman, I appreciate your efforts to hold this hearing on Mercury in Medicine. I look forward to hearing the testimony of the witnesses.

I come today to learn more about mercury in medicine, in vaccines more specifically. In my district, Montgomery Country, Maryland, the incidence rate of autism in our children is alarming. Some feel autism may be related to vaccines.

I am very concerned about the lack of information and misinformation surrounding the issue of vaccines and its possible relationship to autism. I hope that today we can come to a conclusion on what is the appropriate steps for the this committee and the government to take.

I do believe that for over fifty years, vaccines have been protecting our nation's children from deadly infectious diseases. Vaccines are one of the most significant public health achievements, and can be credited for saving more lives and preventing more illnesses than any medical treatment. We need to continue to ensure that our children are vaccinated with licensed vaccines, and we need to ensure that the vaccines are safe.

With regard to the issue of thimerosal and its use in vaccines, I applaud our Public Health Service for being proactive on this issue. Just one year ago a joint statement was issued by the American Academy of Pediatrics and the Public Health Service which established the goal of removing the vaccine preservative thimerosal as soon as possible from vaccines routinely recommended for infants and children.

The goal of removing thimerosal from vaccines, has also been accompanied by new and ongoing research to better assess the potential health effects of exposure to thimerosal-containing vaccines. The

National Institutes of Health, in collaboration with researchers from the University of Rochester and the Bethesda Navel Hospital, undertook a study to determine how much mercury, if any, could be detected in the blood of infants following exposure to thimerosal-containing vaccines. Preliminary data from the study indicate that the blood levels of mercury produced by exposure to thimerosal Preservative-containing vaccines are below the level that many experts consider as background.

The CDC is using large automated databases that link vaccination and International Classification of Disease codes stored in the medical records in two managed care organizations (i.e., the Vaccine Safety Datalink project) to screen for any possible associations between exposure to thimerosal-containing vaccines and a variety of neurologic, developmental disabilities. In the preliminary screening phase of this investigation, CDC and VSD researchers observed no association between exposure to thimerosal containing vaccines

Mr. Chairman, at the current time, no conclusive data indicate that any vaccine or vaccine-additive increases the risk of developing autism or any other behavior disorder. Nonetheless, given the level of concern among parents and others regarding vaccines and autism, I am committed to investigating this issue to the fullest extent possible based upon using the best scientific research available.

Thank you.

Congresswoman Constance Morella

Mr. BURTON. Ms. Schakowsky.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman. I will not be able to stay for all of today's hearing. I would like unanimous consent to submit some questions for the EPA and to the FDA for the record.

Mr. BURTON. Without objection, so ordered.

[The prepared statement of Ms. Schakowsky follows:]

Government Reform Committee Hearing July 18, 2000

Questions submitted for the Record by Congresswoman Jan Schakowsky (D-IL)

Questions for Panel III:

Dr. Trovato (or appropriate staff at the EPA):

1. Congress has focused on power plants as a significant cause of mercury in the environment. I believe this is an ongoing problem, and I am a cosponsor of HR 2900, legislation introduced by Representative Waxman that deals with this subject. I am also aware that the Environmental Protection Agency has made efforts to reduce mercury emissions from power plants.

   I understand that mercury from dental offices may also be a source of environmental contamination. Can we get estimates from EPA how much of a problem mercury disposal from dental offices causes and what can be done to eliminate mercury waste from this source?

2. I understand that much of today's hearing will focus on mercury in medicine-and I think we clearly should be looking at this issue. I also think we need additional information on where mercury from medical products and procedures ends up. Are we facing a health risk to the public from these sources, other than that of the patients themselves?

3. I understand that fish consumption advisories have been issued for bodies of water all over the country: In my state of Illinois, I believe there are three advisories currently in effect. In Ohio, I understand there is a consumption advisory for every body of water. What can be done to prevent or reduce mercury releases into the environment from medical uses?

4. Under our jurisdiction are a number of federal medical and dental facilities-military, veterans, prisons,-where we have the immediate ability to reduce mercury entering the environment. I would appreciate additional information on what impact there would be from minimizing mercury in the waste from these facilities in terms of the environment. If technology exists to eliminate mercury emissions from dental and other offices, is it being put to use in federal facilities?

For FDA witnesses (or appropriate staff at FDA)

1. What peer-reviewed, published studies prove thimerosal in vaccines is safe at any level for infants, children, adolescents and adults?

Ms. SCHAKOWSKY. I also want to take a moment to welcome all of the witnesses, but particularly Ms. Birt. While not a constituent of mine, we live in neighboring towns and the two of us have exchanged letters in the past. Again, a thank you to all of the witnesses for being here, and I yield back the balance of my time.

Mr. BURTON. Mrs. Maloney.

Mrs. MALONEY. I would like to put my opening statement in the record so we can hear from the witnesses. Thank you.

Mr. BURTON. Without objection, so ordered. We will now welcome our first panel to the witness table, Ms. Redwood, Ms. Bernard, Mr. Enayati, Ms. Birt, Dr. Cave, Dr. Aposhian and Dr. Humiston.

[Witnesses sworn.]

Mr. BURTON. Ms. Redwood, if you can confine your remarks to 5 minutes. Ms. Redwood.

STATEMENTS OF LYN REDWOOD, TYRONE, GA; SALLIE BERNARD, CRANFORD, NJ; ALBERT ENAYATI, PYRAMUS, NJ; ELIZABETH BIRT, CHICAGO, IL; DR. STEPHANIE CAVE, BATON ROUGE, LA; DR. H. VASKEN APOSHIAN, PROFESSOR OF MOLECULAR AND CELLULAR BIOLOGY, AND PHARMACOLOGY, UNIVERSITY OF ARIZONA; AND DR. SHARON HUMISTON, PITTSFORD, NY

Ms. REDWOOD. Chairman Burton, Congressman Waxman and committee members, I want to thank you for holding this hearing today and inviting me to testify on this important issue. My name Lyn Redwood. I reside in Atlanta, GA with my husband Tommy and three children, Hanna, Drew and Will. My husband and I are both health care professionals. My husband is a physician, and I am nurse practitioner. I also hold a master's degree in community health nursing and I am a member of our county's Board of Health and Local Planning Commission.

My son Will weighed in at close to 9 pounds at birth. He was a happy baby who ate and slept well, smiled, cooed, walked and talked all by 1 year of age. Shortly after his first birthday, he experienced multiple infections, lost speech, eye contact and developed a very limited diet and suffered intermittent bouts of diarrhea. He underwent multiple evaluations and was initially diagnosed with a global receptive and expressive speech delay and later with pervasive developmental disorder, a form of autism.

I would never have made a correlation between my son's disability and vaccines until July 1999, when I read that a preservative, thimerosal, utilized in some infant vaccines actually contained 49.6 percent mercury. The report said that the FDA had determined that "infants who received thimerosal-containing vaccines at several visits may be exposed to more mercury than recommended by Federal guidelines for total mercury exposure." As health care providers, my husband and I constantly receive notices that adverse events have been reported with a drug or product safety sheets have been revised, and I was wondering why no such notices were sent out notifying us that thimerosal preservative vaccines were exceeding Federal guidelines for mercury exposure in infants.

It was in light of this information that I reviewed my son's vaccine record and my worse fears were confirmed. All of his early vaccines that could have possibly contained thimerosal, had. From my

research on mercury, I have found it to be a potent human toxin, which is especially damaging to the rapidly developing fetal and infant brain. While acceptable levels for exposure are published by Federal agencies, mercury is a poison at any level.

The dose thought to be safely allowed on a daily basis by EPA is 0.1 micrograms per kilogram of body weight. At 2 months of age my son had received 62.5 micrograms of mercury from three infant vaccines. According to this EPA criteria, his allowable dose was only 0.5 micrograms based upon his weight. He had received 125 times his allowable exposure on that day. These large injected bolus exposures continued at 2 months, 4 months, 12 months and 18 months to a total mercury exposure of 237.5 micrograms. I also discovered that the injections that I received during my pregnancy, the first and third trimesters, and hours after the delivery of my son to prevent RH blood incompatibility disease also contained mercury.

Knowing that the major effect of mercury compounds is neurotoxicity, I questioned if these exposures could account for my son's regression and disability. Since he was now 5½ years old, it would be difficult for me to know what his mercury levels had been at that time. It was then that I remembered having kept a lock of hair from his first haircut at 20 months of age. Heavy metal analysis detected 4.8 parts per million mercury in his hair, the allowable levels being less than 1 part per million. The EPA action level in hair is 1 part per million as well, and 5 parts per million is considered diagnostic for mercury toxicity.

Since my son has never eaten fish nor seafood nor had dental amalgams, I had no other identifiable source for his mercury levels outside of the thimerosal exposure from his vaccines and my RhoGAM injections.

Since last fall I have spent every free moment researching this issue. As a nurse and a member of the Board of Health for our county, I felt an urgency to share my findings and concerns about thimerosal with other professionals. I did research and made phone calls, and I wrote letters and I actually went in person to Washington to meet with FDA and CDC officials to voice my concerns and present data on documented levels of mercury in many other children with developmental delays who were also exposed to thimerosal in their vaccines. All of my efforts seemed to fall on deaf ears.

On June 21, 2000 I attended the Advisory Committee for Immunization Practices meeting held in Atlanta. At that meeting a study was presented that looked at Vaccine Safety Datalink information and thimerosal exposure in over 120,000 children. The key findings of the study were significant associations between thimerosal exposure and ADD, tics, speech and language delay and neurodevelopmental delays in general. A panel of experts who were convened to review the data who concluded, "The findings support a statistically significant, albeit weak association, but that the implications are profound."

Unfortunately, ACIP chose not to give preference to thimerosal free vaccines, even though the vaccine manufacturers present at this meeting assured there was enough supply available to meet vaccine needs the first 6 months of life. From the comments made by ACIP committee members it was apparent that political and

economic concerns for the vaccine program had taken precedence over the health, safety and welfare of the children it is charged to protect. One committee member even remarked that giving preference for thimerosal free vaccines may result in reduced public confidence in vaccine programs. From my own personal perspective, just the opposite has occurred.

You may hear today from some officials that the mercury exposure from medicinal sources is insignificant. The fact is that neurological damage is documented to occur in infants at these levels of exposure. You may also hear that these levels of exposure only exceed EPA guidelines the first 6 months of life. That is because the data was inaccurately averaged over a 6-month period of time. As any independent toxicologist will tell you, mercury has a long half-life and its inherent pharmacokinetics you cannot legitimately calculate the effect of a bolus dose as though it were ingested in small amounts over a long period of time. To make a simple analogy, what FDA is trying to assert is that giving someone two Tylenol a day for 30 days has the same effect of giving them 60 Tylenol all at once in 1 day. This defies common sense, much less sound medical practice.

The truth is vaccines are the single largest source of mercury exposure postnatally in infants, but nowhere in the mercury literature of EPA, FDA, ATSDR are these products even identified as being a source of exposure. When I spoke with one official from EPA, he commented that my son's exposure was very high and was rather sympathetic, but since it was not an environmental exposure, his agency could not get involved. So whom do I turn to for help?

Over 1 year ago the FDA, AAP and the Public Health Service called for the immediate elimination of reduction of thimerosal from vaccines, but the sad truth is that while some progress has been made, infants continue to be injected with one of the most neurotoxic metals on Earth in excess of Federal safety guidelines as I speak here today, and the responsible agencies are unwilling to address this issue.

We are in the midst of an autism epidemic and children diagnosed with learning disabilities continue to increase daily. The statement that there is no evidence of harm does not equate with no harm not having occurred. The truth is that we have not adequately looked or we just refuse to see.

A recent national news article which addressed these concerns reported that some may say we don't have a smoking gun but the truth is the bullets are all over the floor. Millions of children have been needlessly exposed to toxic acts from federally sponsored vaccine programs and have suffered neurological damage. This problem has become so pervasive in our society that few are left untouched, as Chairman Burton well knows. It is time for someone to step forward and acknowledge these facts and provide the science to fully investigate what has happened to our children and what can be done to help them.

Thank you.

[The information referred to follows:]

MERCURY and AUTISM

COINCIDENCE or CAUSE and EFFECT?

By Lyn Redwood RN, MSN, CRNP

Will had been the perfect baby. He was always happy, ate and slept well, smiled, played, walked and talked all by one year. Shortly after his first birthday he developed multiple infections, strep throat, rotovirus and an upper respiratory infection which required hospitalization. It was at this time that he began to regress. He lost speech, interaction and eye contact. Although he was often in his own little world, he remained very affectionate and loving to his family. Will had been through MRI's, sleep study EEG's, ABR's, (brainstem evoked hearing test) chromosome studies, and tympanostomy tube insertion, all without any answers or improvement. When I had asked one doctor what to do next, he said "Why don't you just take your son fishing." Well, I took his advice and we went fishing. Fishing to find some answer as to what had happened to my perfectly normal son, what had taken him away. I felt like I finally had a bite on the line.

I'll never forget the day. I was reading my e-mail and came across a post from FEAT (Families for Early Autism Treatment) that stated the FDA had just determined that "infants who received thimerosal-containing vaccines at several visits may be exposed to more mercury than recommended by Federal guidelines for total mercury exposure." It took months for me to realize the full ramifications of this statement. I still wake up some mornings and think I had been reading a Stephen King novel and that this could not have really happened. Unfortunately, this story is non-fiction.

In 1997 when the FDA Modernization Act was signed into law there was an attached amendment which required the FDA to "compile a list of drugs and food that contain intentionally introduced mercury compounds and...provide a quantitative and qualitative analysis of the mercury compounds in the list...". Interesting. Why had this never been done before now?

Thimerosal has been used as an additive to vaccines and biologics since the 1930's to prevent bacterial contamination. It is present in some, but not all infant vaccines. The problem is that it contains 49.5% mercury by weight. From my research on mercury I found that it is a potent human toxicant which has long been the source of many serious health problems. It is especially toxic to the rapidly developing fetal and infant brain. While acceptable levels for exposure are published by Federal Agencies, mercury is a poi- at any level. The dose thought allowable on a daily basis by A is 0.1mcg per kilogram per day. In the late 1980's and early 1990's the vaccine schedule was amended to include both Hepatitis B and HiB vaccines. Each of these vaccines is administered to infants 3 times during the first six-months of life. Their addition to the vaccine schedule potentially tripled an infant's exposure to mercury, should they receive all thimerosal-containing vaccines.

It is interesting to note that thimerosal was introduced only a few short years before Dr. Leo Kanner described a new mental disorder which differed "markedly and uniquely from anything reported" before. In its early history autism was diagnosed more frequently in affluent families, but became more evenly distributed socioeconomically by the 1970's. This apparent widening in demographics paralleled the increasing availability of vaccines to all children through federally sponsored programs. It has been during this same time period, the 1980's and especially the 1990's, that we have witnessed a tremendous increase in the occurrence of autism spectrum disorders.

Being a member of the Board of Health for our county, my first thought was whether vaccines, administered through the Health Department contained thimerosal. I immediately called and found that only one vaccine, hepititis B, contained thimerosal. The DPT and HiB products given by the county health department were both thimerosal free. Responding to the news that infants had been exposed to mercury in excess of Federal Guidelines, the American Academy of Pediatrics and the US Public Health Service issued a statement on July 7, 1999 calling for the elimination or reduction of thimerosal in vaccines. They also recommended deferral, from birth to six months of age, of the first dose of hepatitis B vaccine for infants born to hepatitis B negative mothers. I was somewhat relieved to know that our county's vaccine program was relatively low risk for mercury exposure. But my mind was already fast-forwarding to an even more alarming question. Since my son had received his vaccines from his pediatrician and not the county health department, had he received thimerosal containing vaccines, and been exposed to excessive levels of mercury?



Initially my husband and I never considered any link between our son's vaccines and his diagnosis of Pervasive Developmental Disorder. It was not until I attended my first Autism Conference and heard Dr. Andrew Wakefield

speak of finding measles virus in the guts of children with autism, that the thought even crossed my mind. Dr. Wakefield's findings were alarming and I immediately shared them with my husband who is a physician. Although we both had never questioned the safety or effectiveness of vaccines based on the information we received in our medical training, we were now concerned. Our son had developed unexplained intermittent bouts of bloody, culture negative diarrhea after his MMR, which correlated with Wakefield's findings, but he had actually started his regression a few months before his MMR vaccine.

When I reviewed my son's vaccine schedule, my worse fears were confirmed. All of his vaccines had contained thimerosal. He had been exposed to the maximum possible amount of mercury! At his two-month well baby visit he had received DT and HiB vaccine which both contained .25 mcg of mercury and a Hepatitis B vaccine which contained another 12.5 mcg. Total mercury exposure: 62.5 mcg. According to EPA guidelines for safe daily mercury exposure based on his weight, his allowable exposure for that day was only .5 mcg. He continued to receive high dose intermittent exposures to mercury in his vaccines. During his first 18 months of life, his mercury exposure was 237.5mcg.

When I shared this information concerning Will's mercury exposure to my husband, he looked at me in disbelief and was sure I had done the math wrong. Additional calculations based on his weight revealed that he had received an exposure to mercury approximately 125% over the EPA's safe allowable daily exposure.

We found it perplexing that the FDA's analysis had approached a child's potential total exposure to mercury over the first six months of life as though children were being exposed on a daily basis. So the daily safe exposure levels of .1mcg per kilogram were multiplied by 180 days, even though only on 3 days out of 180 had the exposures occurred. It is my opinion that calculating mercury exposure this way only serves to falsely minimize the levels of exposure. If one were to look at the mercury in thimerosal from a daily dose perspective, no one vaccine containing thimerosal would be able to meet EPA's guidelines for safe exposure.

At the same time the FDA findings were released, The American Academy of Pediatrics published An Interim Report to Physicians on Thimerosal in Vaccine. In this document the AAP and Public Health Service agreed that the use of thimerosal containing vaccines should be reduced or eliminated, stating that any potential risk was of concern. While the document discussed much of the uncertainty regarding the potential effect of mercury exposure in vaccines, it clearly stated that there was no evidence of harm having occurred from this exposure. What really caught my attention was the recommendation that "Infants and children who have received thimerosal-containing vaccines do not need to have blood, urine, or hair tested for mercury since the concentrations would be quite low and would not require treatment." If no testing for mercury was recommended, then how could one know for a fact that there was no "evidence of harm"?

Knowing that the major effect of mercury compounds was neurotoxicity, I questioned if the level of mercury exposure for my son could account for his regression into autism.

Knowing that the major effect of mercury compounds was neurotoxicity, I questioned if the level of mercury exposure for my son could account for his regression into autism. I immediately called a toxicology lab to find out information about mercury testing. I was told that mercury could only be detected in the blood if the exposure had been recent, in the last 50 to 70 days, or ongoing. They stated that since my son was now 5 1/2 years old, I would not be able to accurately determine his exposure levels now, years later. I remembered reading that hair is often utilized to determine heavy metal exposure. But again, it was only accurate for about one year after the exposure. So a sample now would not provide any information about his levels during his first year of life. I had almost given up when I came across my son's first haircut that I had saved in his baby book. I sat staring at his beautiful brown locks, knowing I would have to give them up to answer this nagging question. With little hesitation, I packed them off to the lab.

A few days later we were on our way to our first DAN (Defeat Autism Now) conference. I knew it would be days before we would return and get the results of the hair analysis. Just in case the test had been completed early, I called the lab on the way out the door. To my surprise the test was complete. They agreed to fax us a copy. As the report slowly crept out of the fax machine, I noticed two metals way out of normal reference range - mercury and aluminum, both present in his early vaccines. I felt anger, anxiety and relief, all at the same time. I had no idea what the levels meant or what if anything could be done. But it had given me a long sought after answer. This was one of only a few test results that had ever returned with a detectable abnormality.

During one of the panel discussions at the DAN conference I asked about mercury and explained how we had just discovered that our son's levels had been almost 5 times the normal range. His hair analysis from when he was 20 months old had revealed 4.8 ppm mercury. A level of 5 ppm was diagnostic for toxicity. The lab had even gone a step further to identify that his exposure was endogenous, from within the body, and not a contaminate. Since at 20 months Will have never eaten any form of seafood or fish and had no dental amalgams, I had no other known source for mercury outside the thimerosal in his vaccines. Dr. Stephanie Cave fielded the question and suggested that we look into chelation therapy for our son. After I sat down another mother came up to me and shared that her son had also just been found to have high mercury levels in his urine after chemet testing. She said that her son's hair levels had been normal for mercury and the metal was only detected after being given chemet, an oral chelating agent. Chelators bind with metals that are stored in the body tissue and pull them out so they can be detected during testing. She went on to say that they had seen almost an immediate improvement in his behavior after the chemet.

I now had a direction and quickly turned to the medical library and internet to find out everything I could about mercury. The more I researched mercury, the more uncertainty I uncovered. The type of mercury in thimerosal is ethyl mercury. All guidelines for mercury exposure address methyl mercury. No guidelines exist for the ethyl compound. Both forms are associated with neurotoxicity in high doses, but data was not available regarding the doses at which developmental effects occur in infants. Safety guidelines had been based on lower daily dose exposures. No one knew what neurological effects occur with intermittent high dose "bolus" exposures.

Recent information from two studies suggests that intermittent large exposures may pose more risk than small daily exposures. In one study, lower scores on memory, attention, language and motor function tests were found years later in children who had been exposed prenatally to intermittent bolus doses of methyl mercury at levels that had been previously thought to be safe. Not only are there many unanswered questions concerning mercury exposure from thimerosal in vaccines, but there appears to be no general consensus as to how best proceed to diagnose, or effectively treat elevated mercury levels in children. The effectiveness of chelating agents in crossing the blood brain barrier has become a topic of scrutiny, as well as the ability to treat a long-standing exposure which occurred during a critical time in development.

Through the Internet I made contact with a group of parents in New Jersey who were also researching the mercury-autism link. On Thanksgiving morning I received a call from Albert Enayti, President of New Jersey CAN. We talked at length about our concerns over the mercury our children had received from vaccines. He had been working with two other parents, Sallie Bernard and Heidi Rogers, collecting research on mercury. We all agreed that the overlap between the symptoms of mercury toxicity and those of autism were too extensive to be just a chance occurrence. I gave thanks that day for having connected with other parents who shared my same concerns.

After months of almost daily communications and conference calls late into the night, we were able to put together a paper reviewing the literature. To further document our concerns, I opened a website and onelist and began collecting reports from parents with similar histories of high levels of mercury in their autistic children. Dr. Woody McGinnis, who has an interest in mercury toxicity, heard of our efforts and contacted me. Together we compiled several case studies of children with autism who had also been found to have elevated mercury levels. Teresa Binstock, a well-respected autism researcher, became actively involved and has helped tremendously in the organization and preparation of our paper. Our goal in preparing the paper was to not only elucidate the correlation between mercury toxicity and autism, but to stimulate further discussion and research into the possibility that some forms of autism may, in fact, be a unique form of mercury poisoning.

Currently there are still 30 vaccine products on the market that contain thimerosal. Parents and pediatricians need to be aware that there are many different vaccine products available, both with and without thimerosal. As Shelly Reynolds, an advocate and parent of a child with autism once said, "I researched the safest car seat and crib for my son, but did not realize I also needed to research the safest vaccines." Thimerosal has been eliminated from latex paints, merthiolate and many other over the counter products because of serious toxic effects in infants from these products. Despite this information, the FDA has only "encouraged" vaccine manufacturers to reduce or eliminate thimerosal. According to the FDA, there are currently enough vaccine products that are thimerosal free to meet the immunization needs in the U.S. Therefore, until there is more research available assuring its safe use in infants, I feel a preference should be given to all thimerosal-free vaccines. Dr. Neal Halsey, at the Institute for Vaccine Safety, Johns Hopkins, summed up this issue best in a recent article on thimerosal published in the Hepatitis Control Report, Summer 1999 issue. "We can say there is no evidence of harm (from thimerosal), but the truth is no one has looked." It is time to look!

Although there are many unanswered questions about excessive mercury exposure in infants who received multiple thimerosal containing vaccines, there are many well-documented facts that support our concerns that mercury is playing a role in the recent epidemic of autism spectrum disorders. These include the facts that:

- **Mercury toxicity is cumulative and occurs when the rate of exposure exceeds the rate of elimination. This results in a delayed neurotoxicity, which can manifest months after the exposure. Many children diagnosed with autism experience normal development and then regress.**
- **The major toxicity of mercury compounds is expressed in the central nervous system, although immune and gastrointestinal systems are also commonly affected. The same abnormalities in these systems have been found in children with autism.**
- **Mercury causes a pervasive disruption in the body by binding to sulfur which causes widespread dysfunction of enzymes, transport mechanisms and structural proteins. Therefore, clinical manifestations involve multiple organ systems with variable features and intensities. The same is true for autism.**
- **Susceptibility to mercury appears to have a genetic component and boys are documented to be more affected than girls. Autism also occurs more frequently in boys than girls.**
- **Mercury toxicity is known to cause speech and hearing deficits, including difficulty speaking and understanding speech. One of the primary features of autism is receptive and expressive language delays.**
- **Sensory disturbances, including numbness in the mouth, hands and feet, sensitivity to loud noises, aversion to touch and over or under response to pain, are common manifestations of mercury toxicity. These same sensory disturbances are also common in children with autism.**
- **Mercury exposure is known to cause cognitive impairment and difficulty with abstract ideas and complex commands, social withdrawal, anxiety and obsessive-compulsive behaviors. These same symptoms are also well documented in children with autism.**
- **Mercury disrupts serotonin, dopamine, glutamate and acetylcholine neurotransmitters. These same abnormalities have been documented in autism.**
- **Mercury in the brain targets the Purkinje cells and granule layer of the cerebellum as well as the amygdala and hippocampus, while other areas are spared. This same pattern of pathology has been found in autistic brains.**
- **Mercury toxicity causes damage to the immune system and triggers autoimmune processes, including shifts in the Th2 lymphocytes. These same autoimmune processes are known to occur in autism.**
- **Mercury poisoning can cause gastrointestinal disturbances and inhibit digestive enzymes and peptides. Many children with autism develop gastrointestinal problems and have difficulty digesting dairy and wheat products.**

If you would like additional information on mercury and autism go to
http://tiredwood.home.mindspring.com
To review the Autism-Mercury paper go to
www.cantoundation.org/newcansite/sciwatch/invest.html
For a list of vaccine products and thimerosal-mercury content go to
www.immunize.org/news.d/thimtabl.htm
For additional information on vaccines go to
www.909shot.com
www.vaccinesafety.edu/Aboutus.htm

Just Released

Dr. William Egan, acting Director of the Center for Biologic Evaluation and Research at FDA, speaking at the Third Annual Conference on Vaccine Research in Washington, DC last month focused his talk on thimerosal in vaccines. He stated that US Food and Drug Administration is moving in the direction of "single dose presentations of vaccines without preservatives." Concerns about the preservative thimerosal stem from the fact that "it contains mercury and mercury is toxic." Although there is "no known risk associated with the level of thimerosal in vaccines, there is concern that we can't detect subtle" neurological damage, Dr. Egan said.
If you would like to see mercury removed from all vaccines now, or feel that research efforts into vaccine safety and autism should be vastly increased, please contact ,...

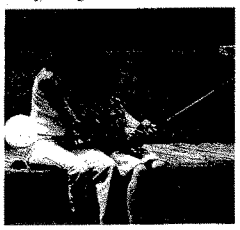
Dr. William Egan, FDA,
(301) 827-0655

Dr. Walter Orenstein, CDC,
(404) 639-8200

Dr. Marie Bristol-Power, NIH,
(301) 496-1383

BIO

...yn Redwood is a Nurse Practitioner. She lives in Tyrone, Georgia with her husband Tommy, who is double boarded as a physician in Family Medicine and Emergency Medicine (he watched too many episodes of ER and changed his speciality). They have three children, Hanna 16, Drew 13, and Will 6, who is somewhere on the spectrum. After years of traditional hospital and clinic based practice, Lyn now works part time in an integrative and holistic medicine practice. She is also a Fayette County Board of Health member and a planning commissioner for the town of Tyrone. In her spare time she moderates an autism-mercury onelist and is an advocate for vaccine safety. She also enjoys scuba diving, stack stone masonry and a new hobby, fishing with her son.



Thimerosal Content in Some U.S. Licensed Vaccines

June 1, 2000 - Adapted from the American Academy of Pediatrics and the Institute for Vaccine Safety at Johns Hopkins University

Vaccine	Brand Name	Manufacturer	% Thimerosal Concentration(1)	Mercury µg/0.5ml
DtaP	Acel-Imune	Lederle Laboratories	.01%	25
	Tripedia	Pasteur Merieux Connaught	.01%	25
	Certiva	North American Vaccine	.01%	25
	Infanrix	SmithKline Beecham	0	0
DTwP	All products		.01%	25
DT	All products		.01%	25
Td	All products		.01%	25
TT	All products		.01%	25
DTwP-Hib	Tetramune	Lederle Laboratories	.01%	25
DtaP-Hib	TriHIBit	Pasteur Merieux Connaught	.01%	25
Hib	HibTITER (multidose)	Lederle Laboratories	.01%	25
	HibTITER (single dose)	Lederle Laboratories	0	0
	ActHIB	Pasteur Merieux Connaught	0	0
	Omni-Hib	SmithKline Beecham	0	0
	PedvaxHIB liquid (2)	Merck	0	0
	ProHIBit (3)	Pasteur Merieux Connaught	.01%	25
Hib-Hep B	COMVAX (4)	Merck	0	0
Hepatitis B	Engerix-B	SmithKline Beecham	.005%	12.5
	Engerix-B preservative free	SmithKline Beecham	(5)	0.05
	Recombivax HB	Merck	.005%	12.5
	Recombivax HB infant formulation	Merck	0	0
Influenza	All products		.01%	25

The following Vaccines are Thimerosal Free:

Hepatitis A	Havrix®	SmithKline Beecham
Varicella		Merck
IPV	IPOL	Pasteur Merieux Connaught
OPV	Orimune	Lederle Laboratories
MMR	MMR-II	Merck
Varicella	Varivax	Merck
Rotavirus	Rotashield	Wyeth-Ayerst
Lyme	LYMErix	SmithKline Beecham

Notes:
(1) A concentration of 1:10,000 is equivalent to a 0.01 concentration. Thimerosal is approximately 50% Hg by weight. A 1:10,000 concentration contains 25 micrograms of Hg per 0.5 ml.
(2) A previously marketed lyophilized preparation contained .005% thimerosal.
(3) ProHIBit is recommend by the American Academy of Pediatrics only for children 12 months of age and older.
(4) COMVAX is not approved for use under 6 weeks of age because of decreased response to the Hib component.
(5) The new Engerix-B contains only trace amounts of thimerosal (< 1 mcg) which "have no clinically relevant effect making it equivalent to a thimerosal-free produce," according to IVS director Dr. Neal Halsey.

Adapted from the website of the Immunization Action Coalition, 1573 Selby Avenue, St. Paul, MN 55104; Tel: 651.647.9009 Web: http://www.immunize.org/

Mr. BURTON. Ms. Bernard.

Ms. BERNARD. I have some slides.

Mr. BURTON. We will put those up on the screen as you speak.

Ms. BERNARD. Chairman Burton, Congressman Waxman and other distinguished members of this committee, thank you for holding this hearing to examine the possible role of mercury and thimerosal in causing neurodevelopmental disorders.

My name is Sallie Bernard. I live in New Jersey. I am the mother of triplets, age 12, Fred, Jimmy and Billy. After meeting all of his developmental milestones on schedule and receiving unremarkable pediatric reports up to age 2½, Billy began to exhibit slower word acquisition than his brothers, articulation difficulties and attentional problems. At 3½ he was diagnosed with language dysphasia and attention deficit hyperactivity disorder. At age 4½ he was diagnosed with autism.

Anyone familiar with the signs of mercury toxicity in children will recognize language difficulties and ADHD traits as common features. But in fact, research conducted by me and others has shown that the characteristics of autism itself are identical to those arising from mercury exposure.

This chart that I have up here shows only some of the similarities between autism and mercury poisoning. This shows some of the behavioral characteristics of autism and mercury poisoning. They include social withdrawal, repetitive and compulsive behaviors, language difficulties, sensory disturbance, movement disorders, cognitive deficits and unusual behaviors like head banging.

Next slide. This slide shows physiological aspects of mercury poisoning and autism. We see the same similarities, damage to the same brain areas, EEG patterns, and so forth.

The next slide. On the population characteristics, males more affected than females for both disorders and the presence of a strong genetic component. We feel that these similarities are too close to have occurred by chance. We are not alone in our thinking. The just released congressionally mandated mercury report by the National Academy of Sciences links methyl mercury and the environment to neurological deficits in children, and we know from researchers such as Suzuki and Magos that the ethyl mercury found in thimerosal is as toxic as methyl mercury. The latest issue of Environmental Health Perspectives also notes that an association has been found between exposure to toxic chemicals and various neurodevelopmental disorders such as learning disabilities, intellectual retardation, attention deficit, hyperactivity disorder, autism and propensity to violence.

It is well-recognized by autism researchers, as reviewed by Dr. Bristol-Power and others, that autism is caused by an interaction of environmental and genetics factors. Based on epidemiological and other data we have proposed that this environmental factor is thimerosal from vaccinations acting alone or synergistically with other toxins. This is why we believe this to be true.

Next slide. This chart shows the prevalence of autism and vaccine history. Thimerosal was first introduced into vaccines in the 1930's and autism was first discovered by Leo Kanner in the early 1940's among children born in the 1930's. Studies prior to 1970 estimated autism to occur in 1 in 2,000 children while studies after

1970 showed the prevalence at about 1 in 1,000. This was also a period of increased immunization of American children. In 1996 the NIH has estimated the rate of autism to be higher at 1 in 500, and just this year the CDC has found 1 in 250 children affected with classic autism. This dramatic increase in the past decade coincides with the introduction and spread of two new thimerosal containing vaccines, the HIB and the hepatitis B.

Another observation is that autistic symptoms emerge within a short time after vaccination, generally following a period of normal development. Importantly, the amount of mercury injected with each vaccine given as a bolus or spike does greatly exceeds EPA and safety guidelines and thus is highly likely to be neurotoxic and injurious.

Last, as Lyn noted, a recent CDC study has found a statistically significant association between thimerosal and vaccines specifically, and attention deficit disorders, speech delay, motor tics and neurodevelopmental disorders in general.

Thus, we see the symptoms of autism and mercury poisoning are the same and the epidemiological and exposure data are highly supportive of a thimerosal etiology. Since thimerosal is not a necessary component of vaccines and every child can be fully immunized today with a non-thimerosal alternative, thimerosal should no longer be allowed in vaccines.

Congress, again listening to the needs of citizens, passed legislation in 1997 requiring government agencies to review thimerosal content in products. In response, the FDA investigated thimerosal in vaccines and found that no safety studies had ever been conducted on this substance.

As a parent, this is very disconcerting indeed. Vaccines are recognized as the crown jewels of the U.S. Public Health Service and their effectiveness relies on the willingness of parents to bring their children in to be immunized. By not conducting safety studies and then not taking immediate steps to ban thimerosal once its potential for harm was publicly recognized, this program has been put at great risk. What parent will want their baby injected repeatedly with a known neurotoxin? How much confidence will parents have that our national vaccine program really cares about safety? Parents like me already have their doubts that it does.

I hope that Congress will respond once again with effective action to ensure the safety and well-being of all our children in light of the information now presented. Thank you.

[The prepared statement of Ms. Bernard follows:]

AUTISM: A UNIQUE TYPE OF MERCURY POISONING

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ABSTRACT

Autism is a syndrome characterized by impairments in social relatedness, language and communication, a need for routine and sameness, abnormal movements, and sensory dysfunction. Mercury (Hg) is a toxic metal that can exist as a pure element or in a variety of inorganic and organic forms and can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autism. Thimerosal, a preservative frequently added to childhood vaccines, has become a major source of Hg in human infants and toddlers. According to the FDA and the American Academy of Pediatricians, fully vaccinated children now receive, within their first two years, Hg levels that exceed safety limits established by the FDA and other supervisory agencies. A thorough review of medical literature and U.S. government data indicates (i) that many and perhaps most cases of idiopathic autism, in which an extended period of developmental normalcy is followed by an emergence of symptoms, are induced by early exposure to Hg; (ii) that this type of autism represents a unique form of Hg poisoning (HgP); (iii) that excessive Hg exposure from thimerosal in vaccine injections is an etiological mechanism for causing the traits of autism; (iv) that certain genetic and non-genetic factors establish a predisposition whereby thimerosal's adverse effects occur only in some children; and (v) that vaccinal Hg in thimerosal is causing a heretofore unrecognized mercurial syndrome.

SYNOPSIS

A review of medical literature indicates that the characteristics of autism and of mercury poisoning (HgP) are strikingly similar. Traits defining or associated with both disorders are summarized in *Table A* immediately following the *Table of Contents* and are discussed and cited in the body of this document. The parallels between the two diseases are so thorough as to suggest, based on total Hg injected into U.S. children, that many cases of autism are a form of mercury poisoning.

For these children, the exposure route is childhood vaccines, most of which contain thimerosal, a preservative which is 49.6% ethylmercury by weight. The amount of mercury a typical child under two years receives from vaccinations equates to 237.5 micrograms, or 3.53×10^{17} molecules (353,000,000,000,000,000 molecules). Most such vaccinal Hg may not be excreted and instead migrates to the brain.

The total amount injected into infants and toddlers (i) is known to exceed Federal safety standards, (ii) is officially considered to be a "low" level; whereby (iii) only a small percentage of exposed individuals exhibit symptoms of toxicity. In fact, children who develop Hg-related autism are likely to have had a predisposition derived from genetic and non-genetic factors.

Importantly, the timings of vaccinal Hg-exposure and its latency period coincide with the emergence of autistic-symptoms in specific children. Moreover, excessive mercury has been detected in urine, hair, and blood samples from autistic children; and parental reports, though limited at this date, indicate significant improvement in symptoms subsequent to heavy-metal chelation therapy.

The HgP phenotype is diverse and depends upon a number of factors – including type of Hg, route of entry into the body, rate and level of dose, individual genotype, and the age and immune status of the patient. Historically, variation among these factors has caused slightly different manifestations of mercurialism; Mad Hatter's disease, Minamata disease, acrodynia, and industrial exposures provide examples.

The pathology arising from the mercury-related variables involved in autism – intermittent bolus doses of ethylmercury injected into susceptible infants and toddlers – is heretofore undescribed in medical literature. Therefore, in accord with existing HgP data and HgP's ability to induce virtually all the traits defining or associated with autism spectrum disorders, we hypothesize that many and perhaps most cases of autism represent a unique form of mercury poisoning.

This conclusion and its supporting data have important implications for the affected population of autistic individuals and their families, for other unexplained disorders with symptoms similar to those of heavy metal intoxication, for vaccine content, and for childhood vaccination programs. Due to its high potential for neurotoxicity, thimerosal should be removed immediately from all vaccine products designated for infants and toddlers.

Table of Contents

Page

ABSTRACT & SYNOPSIS i
TABLE OF CONTENTS iii
AUTISM-MERCURIALISM COMPARISONS iv

INTRODUCTION
Autism 1
Mercury 1
Diagnosing Mercury Poisoning in Autism 2

I. SYMPTOM COMPARISON
a. Affect/Psychological Presentation 5
b. Language & Hearing 10
c. Sensory Perception 12
d. Movement/Motor Function 13
e. Cognition/Mental Function 15
f. Behaviors 18
g. Vision 19
h. Physical Presentations 20
j. Gastrointestinal Function 22

II. COMPARISON OF BIOLOGICAL ABNORMALITIES
a. Biochemistry 24
b. Immune System 25
c. CNS Structure 29
d. Neurons & Neurochemicals 33
e. EEG Activity/Epilepsy 36

III. MECHANISMS, SOURCES & EPIDEMIOLOGY OF EXPOSURE
a. Exposure Mechanism 38
b. Population Susceptibility 39
c. Sex Ratio 40
d. Exposure Levels & Autism Prevalence 40
e. Genetic Factors 41
f. Course of Disease 42
g. Thimerosal Interaction with Vaccines 44

IV. DETECTION OF MERCURY IN AUTISTIC CHILDREN
Case Studies 47
Discussion 52

DISCUSSION
Diagnostic Criteria Are Met 54
Unique Form Would be Expected, Implicates Vaccinal Thimerosal 54
Historical Precedent Exists 55
Barriers Preventing Earlier Discovery Are Removed 56

MEDICAL & SOCIETAL IMPLICATIONS
Affected Population 57
Other Disorders 57
Vaccination Programs 57

Summary Comparison of Characteristics of Autism & Mercury Poisoning

	Mercury Poisoning	Autism
Psychiatric Disturbances	Social deficits, shyness, social withdrawal	Social deficits, social withdrawal, shyness
	Depression, mood swings; mask face	Depressive traits, mood swings; flat affect
	Anxiety	Anxiety
	Schizoid tendencies, OCD traits	Schizophrenic & OCD traits; repetitiveness
	Lacks eye contact, hesitant to engage others	Lack of eye contact, avoids conversation
	Irrational fears	Irrational fears
	Irritability, aggression, temper tantrums	Irritability, aggression, temper tantrums
	Impaired face recognition	Impaired face recognition
Speech, Language & Hearing Deficits	Loss of speech, failure to develop speech	Delayed language, failure to develop speech
	Dysarthria; articulation problems	Dysarthria; articulation problems
	Speech comprehension deficits	Speech comprehension deficits
	Verbalizing & word retrieval problems	Echolalia; word use & pragmatic errors
	Sound sensitivity	Sound sensitivity
	Hearing loss; deafness in very high doses	Mild to profound hearing loss
	Poor performance on language IQ tests	Poor performance on verbal IQ tests
Sensory Abnormalities	Abnormal sensation in mouth & extremities	Abnormal sensation in mouth & extremities
	Sound sensitivity	Sound sensitivity
	Abnormal touch sensations; touch aversion	Abnormal touch sensations; touch aversion
	Vestibular abnormalities	Vestibular abnormalities
Motor Disorders	Involuntary jerking movements – arm flapping, ankle jerks, myoclonal jerks, choreiform movements, circling, rocking	Stereotyped movements - arm flapping, jumping, circling, spinning, rocking; myoclonal jerks; choreiform movements
	Deficits in eye-hand coordination; limb apraxia; intention tremors	Poor eye-hand coordination; limb apraxia; problems with intentional movements
	Gait impairment; ataxia – from incoordination & clumsiness to inability to walk, stand, or sit; loss of motor control	Abnormal gait and posture, clumsiness and incoordination; difficulties sitting, lying, crawling, and walking
	Difficulty in chewing or swallowing	Difficulty chewing or swallowing
	Unusual postures; toe walking	Unusual postures; toe walking
Cognitive Impairments	Borderline intelligence, mental retardation - some cases reversible	Borderline intelligence, mental retardation - sometimes "recovered"
	Poor concentration, attention, response inhibition	Poor concentration, attention, shifting attention
	Uneven performance on IQ subtests	Uneven performance on IQ subtests
	Verbal IQ higher than performance IQ	Verbal IQ higher than performance IQ
	Poor short term, verbal, & auditory memory	Poor short term, auditory & verbal memory
	Poor visual and perceptual motor skills, impairment in simple reaction time	Poor visual and perceptual motor skills, lower performance on timed tests
	Difficulty carrying out complex commands	Difficulty carrying out multiple commands
	Word-comprehension difficulties	Word-comprehension difficulties
	Deficits in understanding-abstract ideas & symbolism; degeneration of higher mental powers	Deficits in abstract thinking & symbolism, understanding other's mental states, sequencing, planning & organizing

Unusual Behaviors	Stereotyped sniffing (rats)	Stereotyped, repetitive behaviors
	ADHD traits	ADHD traits
	Agitation, unprovoked crying, grimacing, staring spells	Agitation, unprovoked crying, grimacing, staring spells
	Sleep difficulties	Sleep difficulties
	Eating disorders, feeding problems	Eating disorders, feeding problems
	Self injurious behavior, e.g. head banging	Self injurious behavior, e.g. head banging
Visual Impairments	Poor eye contact, impaired visual fixation	Poor eye contact, problems in joint attention
	"Visual impairments," blindness, near-sightedness, decreased visual acuity	"Visual impairments"; inaccurate/slow saccades; decreased rod functioning
	Light sensitivity, photophobia	Over-sensitivity to light
	Blurred or hazy vision	Blurred vision
	Constricted visual fields	Not described
Physical Disturbances	Increase in cerebral palsy; hyper- or hypo-tonia; abnormal reflexes; decreased muscle strength, especially upper body; incontinence; problems chewing, swallowing, salivating	Increase in cerebral palsy; hyper- or hypotonia; decreased muscle strength, especially upper body; incontinence; problems chewing and swallowing
	Rashes, dermatitis/dry skin, itching; burning	Rashes, dermatitis, eczema, itching
	Autonomic disturbance: excessive sweating, poor circulation, elevated heart rate	Autonomic disturbance: unusual sweating, poor circulation, elevated heart rate
Gastro-intestinal Disturbances	Gastroenteritis, diarrhea; abdominal pain, constipation, "colitis"	Diarrhea, constipation, gaseousness, abdominal discomfort, colitis
	Anorexia, weight loss, nausea, poor appetite	Anorexia; feeding problems/vomiting
	Lesions of ileum & colon; increased gut permeability	Leaky gut syndrome
	Inhibits dipeptidyl peptidase IV, which cleaves casomorphin	Inadequate endopeptidase enzymes needed for breakdown of casein & gluten
Abnormal Biochemistry	Binds -SH groups; blocks sulfate transporter in intestines, kidneys	Low sulfate levels
	Has special affinity for purines & pyrimidines	Purine & pyrimidine metabolism errors lead to autistic features
	Reduces availability of glutathione, needed in neurons, cells & liver to detoxify heavy metals	Low levels of glutathione; decreased ability of liver to detoxify heavy metals
	Causes significant reduction in glutathione peroxidase and glutathione reductase	Abnormal glutathione peroxidase activities in erythrocytes
	Disrupts mitochondrial activities, especially in brain	Mitochondrial dysfunction, especially in brain
Immune Dysfunction	Sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies, asthma, autoimmune-like symptoms, especially rheumatoid-like ones	More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies
	Can produce an immune response in CNS	On-going immune response in CNS
	Causes brain/MBP autoantibodies	Brain/MBP autoantibodies present
	Causes overproduction of Th2 subset; kills/inhibits lymphocytes, T-cells, and monocytes; decreases NK T-cell activity;	Skewed immune-cell subset in the Th2 direction; decreased responses to T-cell mitogens; reduced NK T-cell function;

	induces or suppresses IFNg & IL-2	increased IFNg & IL-12

(v)

CNS Structural Pathology	Selectively targets brain areas unable to detoxify or reduce Hg-induced oxidative stress	Specific areas of brain pathology; many functions spared
	Damage to Purkinje and granular cells	Damage to Purkinje and granular cells
	Accummulates in amygdala and hippocampus	Pathology in amygdala and hippocampus
	Causes abnormal neuronal cytoarchitecture; disrupts neuronal migration & cell division; reduces NCAMs	Neuronal disorganization; increased neuronal cell replication, increased glial cells; depressed expression of NCAMs
	Progressive microcephaly	Progressive microcephaly and macrocephaly
	Brain stem defects in some cases	Brain stem defects in some cases
Abnormalities in Neuro-chemistry	Prevents presynaptic serotonin release & inhibits serotonin transport; causes calcium disruptions	Decreased serotonin synthesis in children; abnormal calcium metabolism
	Alters dopamine systems; peroxidine deficiency in rats resembles mercurialism in humans	Possibly high or low dopamine levels; positive response to peroxidine (lowers dopamine levels)
	Elevates epinephrine & norepinephrine levels by blocking enzyme that degrades epinephrine	Elevated norepinephrine and epinephrine
	Elevates glutamate	Elevated glutamate and aspartate
	Leads to cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus & cerebellum	Cortical acetylcholine deficiency; reduced muscarinic receptor binding in hippocampus
	Causes demyelinating neuropathy	Demyelination in brain
EEG Abnormalities/ Epilepsy	Causes abnormal EEGs, epileptiform activity	Abnormal EEGs, epileptiform activity
	Causes seizures, convulsions	Seizures; epilepsy
	Causes subtle, low amplitude seizure activity	Subtle, low amplitude seizure activities
Population Charact-eristics	Effects more males than females	Male:female ratio estimated at 4:1
	At low doses, only affects those geneticially susceptible	High heritability - concordance for MZ twins is 90%
	First added to childhood vaccines in 1930s	First "discovered" among children born in 1930s
	Exposure levels steadily increased since 1930s with rate of vaccination, number of vaccines	Prevalence of autism has steadily increased from 1 in 2000 (pre1970) to 1 in 500 (early 1990s), higher in 2000.
	Exposure occurs at 0 - 15 months; clinical silent stage means symptom emergence delayed; symptoms emerge gradually, starting with movement & sensation	Symptoms emerge from 4 months to 2 years old; symptoms emerge gradually, starting with movement & sensation

AUTISM: A UNIQUE TYPE OF MERCURY POISONING

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ABSTRACT

Autism is a neurodevelopmental syndrome characterized by impairments in social relatedness, language, and communication, a need for routine and sameness, abnormal movements, and sensory dysfunction. Mercury is a toxic metal that can exist as a pure element or in a variety of inorganic and organic forms and can cause immune, sensory, neurological, motor, and other behavioral dysfunctions.

The characteristics of autism and mercury poisoning, derived from a review of medical literature, have been found, upon comparison, to be strikingly similar. The characteristics of both disorders are summarized in the following table and fully elucidated in the body of this document. The parallels between the two diseases are so close that it would be unreasonable to assume that the similarities occur by chance.

We claim that autism is a form of mercury poisoning, based on similarities of characteristics and on the known exposure to mercury of the majority of US children. The exposure route is childhood vaccines, most of which contain thimerosal, a preservative comprised of 50% ethylmercury by weight. The amount of mercury a typical child under two years receives from vaccinations equates to 237.5 micrograms, or 3.53×10^{17} molecules (353,000,000,000,000,000 molecules), most of which is not excreted and goes directly to the brain. The amount is known to exceed Federal safety standards, but is still considered a "low" level, such that only a small percentage of exposed individuals will exhibit signs of toxicity. Affected individuals are those genetically prone to mercury sensitivity, which is consistent with the observed high heritability rate of autism. Furthermore, the timing of mercury exposure via vaccines coincides with the emergence of autistic symptoms. Moreover, mercury has been detected in urine, hair, and blood samples from autistic children, and parental reports, though limited at this date, indicate significant improvement in symptoms with administration of standard heavy metal chelators. Thus, the four agreed-upon criteria used by clinicians to diagnose mercury poisoning – i.e., observable symptoms, known exposure at the time of symptom onset, detectable levels in biologic samples, and improvement with chelation - have been met for autism.

The phenotypic expression of mercury poisoning varies by a host of factors – including type of mercury given, method of administration, rate and level of dose, individual genotype, and age of patient – so that each variation in factors has created in the past a slightly different manifestation of the disease – Mad Hatter's disease, Minamata disease, and acrodynia, for example. The pathology arising from the set of mercury-related variables involved in autism – intermittent bolus doses of ethylmercury injected into genetically susceptible infants and toddlers – has never been reported before in medical literature. Thus we argue that autism represents a unique form of mercury poisoning not heretofore described. Our findings have widespread implications for the affected population of autistic individuals, for other unexplained disorders with symptoms similar to heavy metal intoxication, and for childhood vaccination programs.

Table of Contents

Page

ABSTRACT i

Summary Chart of Comparisons ii

INTRODUCTION

Autism 1

Mercury 1

Diagnosing Mercury Poisoning in Autism 2

I. SYMPTOM COMPARISON

a. Affect/Psychological Presentation 5
b. Language and Hearing 10
c. Sensory Perception 12
d. Movement/Motor Function 13
e. Cognition/Mental Function 15
f. Behaviors 18
g. Vision 19
h. Physical Presentations 20
j. Gastrointestinal Function 22

II. BIOLOGICAL ABNORMALITIES

a. Biochemistry 24
b. Immune System 25
c. CNS Structure 29
d. Neurons & Neurochemicals 33
e. EEG Activity/Epilepsy 36

III. MECHANISMS, SOURCES & EPIDEMIOLOGY OF EXPOSURE

a. Exposure Mechanism 38
b. Population Susceptibility 39
c. Sex Ratio 40
d. Exposure Levels & Autism Prevalence 40
e. Genetic Factors 41
f. Course of Disease 42
g. Thimerosal Interaction with Vaccines 44

IV. DETECTION OF MERCURY IN AUTISTIC CHILDREN

Case Studies 47
Discussion 52

DISCUSSION

Diagnostic Criteria Are Met 54
Unique Form Would be Expected, Implicates Vaccinal Thimerosal 54
Historical Precedent Exists 55
Barriers Preventing Earlier Discovery Are Removed 56

MEDICAL & SOCIETAL IMPLICATIONS
Affected Population 57
Other Disorders 57
Vaccination Programs 57

# of Autism & Mercury Poisoning

	Mercury Poisoning	Autism
Psychiatric Disturbances	Social deficits, shyness, social withdrawal	Social deficits, social withdrawal, shyness
	Depression, mood swings; mask face	Depressive traits, mood swings; flat affect
	Anxiety	Anxiety
	Schizoid tendencies, OCD traits	Schizophrenic & OCD traits; repetitiveness
	Lacks eye contact, hesitant to engage others	Lack of eye contact, avoids conversation
	Irrational fears	Irrational fears
	Irritability, aggression, temper tantrums	Irritability, aggression, temper tantrums
	Impaired face recognition	Impaired face recognition
Speech, Language & Hearing Deficits	Loss of speech, failure to develop speech	Delayed language, failure to develop speech
	Dysarthria; articulation problems	Dysarthria; articulation problems
	Speech comprehension deficits	Speech comprehension deficits
	Verbalizing & word retrieval problems	Echolalia; word use & pragmatic errors
	Sound sensitivity	Sound sensitivity
	Hearing loss; deafness in very high doses	Mild to profound hearing loss
	Poor performance on language IQ tests	Poor performance on verbal IQ tests
Sensory Abnormalities	Abnormal sensation in mouth & extremities	Abnormal sensation in mouth & extremities
	Sound sensitivity	Sound sensitivity
	Abnormal touch sensations; touch aversion	Abnormal touch sensations; touch aversion
	Vestibular abnormalities	Vestibular abnormalities
Motor Disorders	Involuntary jerking movements - arm flapping, ankle jerks, myoclonal jerks, choreiform movements, circling, rocking	Stereotyped movements - arm flapping, jumping, circling, spinning, rocking; myoclonal jerks; choreiform movements
	Deficits in eye-hand coordination; limb apraxia; intention tremors	Poor eye-hand coordination; limb apraxia; problems with intentional movements
	Gait impairment; ataxia – from incoordination & clumsiness to inability to walk, stand, or sit; loss of motor control	Abnormal gait and posture, clumsiness and incoordination; difficulties sitting, lying, crawling, and walking
	Difficulty in chewing or swallowing	Difficulty chewing or swallowing
	Unusual postures	Unusual postures
Cognitive Impairments	Borderline intelligence, mental retardation - some cases reversible	Borderline intelligence, mental retardation - sometimes "recovered"
	Poor concentration, attention, response inhibition	Poor concentration, attention, shifting attention
	Uneven performance on IQ subtests	Uneven performance on IQ subtests
	Verbal IQ higher than performance IQ	Verbal IQ higher than performance IQ
	Poor short term, verbal, & auditory memory	Poor short term, auditory & verbal memory
	Poor visual and perceptual motor skills, impairment in simple reaction time	Poor visual and perceptual motor skills, lower performance on timed tests
	Difficulty carrying out complex commands	Difficulty carrying out multiple commands
	Alexia (inability to comprehend the meaning of written words)	Hyperlexia (ability to decode words while lacking word comprehension)
	Deficits in understanding abstract ideas & symbolism; degeneration of higher mental powers	Deficits in abstract thinking & symbolism, understanding other's mental states, sequencing, planning & organizing

Unusual Behaviors	Stereotyped sniffing (rats)	Stereotyped, repetitive behaviors
	ADHD traits	ADHD traits
	Agitation, unprovoked crying, grimacing, staring spells	Agitation, unprovoked crying, grimacing, staring spells
	Sleep difficulties	Sleep difficulties
	Eating disorders, feeding problems	Eating disorders, feeding problems
	Self injurious behavior, e.g. head banging	Self injurious behavior, e.g. head banging
Visual Impairments	Poor eye contact, impaired visual fixation	Poor eye contact, problems in joint attention
	"Visual impairments," blindness, near-sightedness, decreased visual acuity	"Visual impairments"; inaccurate/slow saccades; decreased rod functioning
	Light sensitivity, photophobia	Over-sensitivity to light
	Blurred or hazy vision	Blurred vision
	Constricted visual fields	Not described
Physical Disturbances	Increase in cerebral palsy; hyper- or hypo-tonia; abnormal reflexes; decreased muscle strength, especially upper body; incontinence; problems chewing, swallowing, salivating	Increase in cerebral palsy; hyper- or hypotonia; decreased muscle strength, especially upper body; incontinence; problems chewing and swallowing
	Rashes, dermatitis/dry skin, itching; burning	Rashes, dermatitis, eczema, itching
	Autonomic disturbance: excessive sweating, poor circulation, elevated heart rate	Autonomic disturbance: unusual sweating, poor circulation, elevated heart rate
Gastro-intestinal Disturbances	Gastroenteritis, diarrhea; abdominal pain, constipation, "colitis"	Diarrhea, constipation, gaseousness, abdominal discomfort, colitis
	Anorexia, weight loss, nausea, poor appetite	Anorexia; feeding problems/vomiting
	Lesions of ileum & colon; increases gut permeability	Leaky gut syndrome
	Inhibits dipeptidyl peptidase IV, which cleaves casomorphin	Inadequate endopeptidase enzymes needed for breakdown of casein & gluten
Abnormal Biochemistry	Ties up -SH groups; blocks sulfate transporter in intestines, kidneys	Low sulfate levels
	Has special affinity for purines & pyrimidines	Purine & pyrimidine metabolism errors lead to autistic features
	Reduces availability of glutathione, needed in cells & liver to detoxify heavy metals	Low levels of glutathione; decreased ability of liver to detoxify heavy metals
	Causes significant reduction in glutathione peroxidase and glutathione reductase	Abnormal glutathione peroxidase activities in erythrocytes
	Disrupts mitochondrial activities, especially in brain	Mitochondrial dysfunction, especially in brain
Immune Dysfunction	Sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies, asthma, autoimmune-like symptoms, especially rheumatoid-like ones	More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies
	Can produce an immune response in CNS	On-going immune response in CNS
	Causes brain/MBP autoantibodies	Brain/MBP autoantibodies present
	Causes overproduction of Th2 subset; kills/inhibits lymphocytes, T-cells, and monocytes; decreases NK T-cell activity; induces or suppresses IFNg & IL-2	Skewed immune-cell subset in the Th2 direction; decreased responses to T-cell mitogens; reduced NK T-cell function; increased IFNg & IL-12

CNS Structural Pathology	Selectively targets brain areas unable to detoxify or reduce Hg-induced oxidative stress	Specific areas of brain pathology; many functions spared
	Damage to Purkinje and granular cells	Damage to Purkinje and granular cells
	Accummulates in amygdala and hippocampus	Pathology in amygdala and hippocampus
	Causes abnormal neuronal cytoarchitecture; disrupts neuronal migration & cell division; reduces NCAMs	Neuronal disorganization; increased neuronal cell replication, increased glial cells; depressed expression of NCAMs
	Progressive microcephaly	Progressive microcephaly and macrocephaly
	Brain stem defects in some cases	Brain stem defects in some cases
Abnormalities in Neuro-chemistry	Prevents presynaptic serotonin release & inhibits serotonin transport; causes calcium disruptions	Decreased serotonin synthesis in children; abnormal calcium metabolism
	Alters dopamine systems; peroxidine deficiency in rats resembles mercurialism in humans	Possibly high or low dopamine levels; positive response to peroxidine (lowers dopamine levels)
	Elevates epinephrine & norepinephrine levels by blocking enzyme that degrades epinephrine	Elevated norepinephrine and epinephrine
	Elevates glutamate	Elevated glutamate and aspartate
	Leads to cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus & cerebellum	Cortical acetylcholine deficiency; reduced muscarinic receptor binding in hippocampus
	Causes demyelating neuropathy	Demyelation in brain
EEG Abnormalities/ Epilepsy	Causes abnormal EEGs, epileptiform activity	Abnormal EEGs, epileptiform activity
	Causes seizures, convulsions	Seizures; epilepsy
	Causes subtle, low amplitude seizure activity	Subtle, low amplitude seizure activities
Population Charact-eristics	Effects more males than females	Male:female ratio estimated at 4:1
	At low doses, only affects those geneticially susceptible	High heritability - concordance for MZ twins is 90%
	First added to childhood vaccines in 1930s	First "discovered" among children born in 1930s
	Exposure levels steadily increased since 1930s with rate of vaccination, number of vaccines	Prevalence of autism has steadily increased from 1 in 2000 (1940s) to 1 in 500 (1990s)
	Exposure occurs at 0 - 15 months; clinical silent stage means symptom emergence delayed; symptoms emerge gradually, starting with movement & sensation	Symptoms emerge from 4 months to 2 years old; symptoms emerge gradually, starting with movement & sensation

Autism

Autism, or Autistic Spectrum Disorder (ASD), is considered a neurodevelopmental syndrome, emerging early in life and exhibiting a constellation of seemingly unrelated features and a wide variation in symptom expression and level of severity by individual (Filipek et al, 1999; Bailey et al, 1996). The diagnostic criteria for autism are qualitative impairments in social relatedness, deficits in verbal and nonverbal communication, and the presence of repetitive and restricted behaviors or interests (APA, 1994). As will be cited below, other traits associated with autism are movement disorder, sensory dysfunction, and cognitive impairments as well as gastrointestinal difficulties and immune abnormalities (Gillberg & Coleman, 1992; Warren et al, 1990; Horvath et al, 1999). Onset must occur before age 36 months (APA, 1994); although in some instances deficits are apparent at birth, in the great majority of cases there are at least several months of normal development followed by clear regression or failure to progress normally (Gillberg & Coleman, 1992; Filipek et al, 1999; Bailey et al, 1996). Formerly regarded as a rare disease, autism is now said to affect one in 500 children (Bristol et al, 1996), with some estimates suggesting one in 100 for a broader phenotype often labeled as the "autism-spectrum" of disorders and which includes both higher and lower functioning individuals (Arvidsson et al, 1997; Wing, 1996).

Autism and autistic symptoms can arise from a number of known disorders, most notably tuberous sclerosis, Rhett syndrome, Landau-Kleffner syndrome, Fragile X, Phenylketonuria, purine autism, and other purine metabolic diseases such as PRPP synthetase defects and 5'-nucleotidase superactivity. The etiology and pathogenesis of the vast majority of autism cases – 70% - 90% (Gillberg and Coleman, 1992; Bailey et al, 1996) – remain unexplained, however, despite ASD being "one of the most extensively studied disorders in child psychiatry today" (Malhotra and Gupta, 1999). Nevertheless, there is general agreement that most cases of autism arise "from the interaction of an early environmental insult and a genetic predisposition" (Trottier et al, 1999; Bristol et al, 1996).

Mercury

A heavy metal, mercury (Hg) is widely considered one of the most toxic substances on earth (Clarkson, 1997). Instances of Hg poisoning or "mercurialism" have been described since Roman times. The Mad Hatter in *Alice in Wonderland* was a victim of occupational exposure to mercury vapor, referred to as "Mad Hatter's Disease." Further human data has been derived from instances of widespread poisonings during the 20th Century. These misfortunes include an outbreak in Minamata, Japan, caused by consumption of contaminated fish and resulting in "Minamata Disease;" outbreaks in Iraq, Guatemala and Russia due to ingestion of contaminated seed grains; and, in the first half of the century, poisoning of infants and toddlers by mercury in teething powders, leading to acrodynia or Pink Disease. Besides these epidemics, numerous instances of individual or small group cases of Hg intoxication and subsequent phenotype are described in the literature.

The constellation of mercury-induced symptoms varies enormously from individual to individual. The diversity of disease manifestations derives from a number of interacting

an individual's age, the total dosage, dose rate, duration of exposure, type of mercury, routes of exposure such as inhaled, subcutaneous, oral, or intramuscular, and, most importantly, by individual sensitivity arising from immune and genetic factors (Dales, 1972; Koos and Longo, 1976; Matheson et al, 1980; Eto et al, 1999; Feldman, 1982; Warkany and Hubbard, 1953).

Table I: Summary of Mercury Exposure Variables Leading to Diverse & Non-Specific Symptomatology

Variable	Level of Variable
Exposure Amount	Ranges from high doses, leading to death or near death with severe impairments, to low "safe" doses, leading to subtle neurological and other physical impairments
Duration of exposure	One time vs. multiple times over the course of weeks, months, or years
Dose rate	Bolus dose, daily dose
Individual sensitivity	A function of (a) the age at which exposure occurs, that is, prenatal, infant, child, adolescent, or adult, (b) genetically determined reactivity to mercury, and (c) gender
Common types of mercury	The organic alkyl forms – methylmercury and ethylmercury; and inorganic forms - metallic mercury, elemental (liquid) mercury, and ionic mercury/mercuric salt
Primary routes of exposure	Inhalation of mercury vapors, orally through the intestinal tract, subcutaneous and intramuscular injections, topically through ear drops, teething powders, skin creams and ointments, and intravenously during medical treatments

While these variations in exposure, individual status, and genotype give rise to a diverse clinical phenotype, there are nevertheless obvious commonalities across all mercury-caused disorders. Thus, for example, victims will almost always develop a movement disorder, but in some individuals this may manifest as mere clumsiness, while others will develop severe involuntary jerking movements. Likewise, psychological disturbances are usually present, but in some individuals these might manifest as anxiety while in others it might present as aggression or irritability.

Diagnosing Mercury Poisoning in Autism

Mercury poisoning can be difficult to diagnose and is often interpreted by clinicians as a psychiatric disorder, especially if exposure is not suspected (Diner and Brenner, 1998; Frackelton and Christensen, 1998). The difficulty in diagnosis derives primarily from two notable characteristics of this heavy metal. First, there can be a long latent period between time of exposure and onset of overt symptoms, so that the connection between the two events is often overlooked. The latency period is discussed in more detail below. Second, the diverse manifestations of the disease make it difficult for the clinician to find a precise match of his particular patient's symptoms with those described in other case reports (Adams et al, 1983, Kark et al, 1971; Florentine and Sanfilippo, 1991; Matheson et al, 1980; Frackelton and Christensen, 1998; Warkany & Hubbard, 1953).

Due to the difficulty of diagnosing mercurialism based on presentation of non-specific symptoms alone, clinicians have come to rely on the following criteria (Warkany & Hubbard, 1953; Vroom and Greer, 1972).

1. Observation of impairments in many but not all of the following domains: (a) movement/motor disorder, (b) sensory abnormalities, (c) psychological and behavioral disturbances, (d) neurological and cognitive deficits, (e) impairments in language, hearing, and vision, and (f) miscellaneous physical presentations such as rashes or unusual reflexes (Adams et al, 1983; Snyder, 1972; Vroom & Greer, 1972).

2. Known exposure to Hg (a) at a level that has been documenting as causing impairment in similar individuals under similar circumstances, and (b) at approximately the same time as the symptoms emerge, with allowances given for the latency period (Ross et al, 1977; Amin-Zaki et al, 1978). It should be noted that the dose which is considered "toxic" vs. "safe" is unresolved among toxicologists; some researchers feel that any amount of exposure is "unsafe" (see EPA, 1997, pp.6-47 to 6-59, for dose discussion).

3. Detectable levels of mercury in urine, blood, or hair (Florentine and Sanfilippo, 1991; Frackelton and Christensen, 1998; EPA, 1997, p.ES-2). Importantly, because mercury can clear from biologic samples before the patient feels symptoms or is tested, the lack of detectable mercury is not cause for ruling out mercury poisoning; and conversely, detectable levels have been observed in unaffected individuals (Adams et al, 1983; Warkany & Hubbard, 1953; Cloarec, 1995).

4. Improvement in symptoms after chelation. While many patients' symptoms resolve with chelation, some clearly poisoned individuals do not improve. Other exposed subjects have also been known to improve without intervention (Vroom & Greer, 1972; Warkany & Hubbard, 1953).

Thus, none of these criteria is sufficient on its own for a certain diagnosis. Rather, observed effects within two or three domains are generally required. This paper, which reviews and compares the extensive literature available on both ASD and mercury, provides citations documenting that, based on these four diagnostic criteria, many if not most cases of autism meet the requirements for mercury poisoning. In fact, this review and its citations (i) delineate a single mechanism for inducing all of the primary domains of impairment and biological abnormalities in autism, including its genetic component, prevalence levels, and sex ratios; and (ii) identify that mechanism as arising from the "environmental insult" of early childhood exposure to mercury. Furthermore, the route of exposure is thimerosal, which is 50% ethylmercury by weight and which is a preservative used in many childhood vaccines.

We are not suggesting that the previous reports of mercurialism described in the literature are in fact cases of autism; rather, we claim that autism represents its own unique form of

Hg poisoning, just like acrodynia, Minamata disease, and Mad Hatter's disease represent distinct yet closely related presentations of mercurialism. A unique expression would be expected in cases of autism, given that the effects of repeated vaccinal administration of ethylmercury to infants and toddlers have never been described before in mercury-related literature. We maintain that the diverse phenotype that is autism matches the diverse phenotype that is mercurialism to a far greater degree that could reasonably be expected to occur by chance. Given the known exposure to mercury via vaccination of autistic children and the presence of mercury found in biologic samples from a number of autistic subjects, also described here, we are confident that our claim is substantiated. Our paper discusses some important medical and societal ramifications of this conclusion.

I. SYMPTOM COMPARISON

The overt symptoms of ASD and mercury poisoning, described in the literature and presented here, are strikingly similar. Summary tables have been provided after each section to aid in symptom comparisons.

a. Affect/Psychological Presentation

Since its initial description in 1943 by Leo Kanner, a psychiatrist, autism has been defined primarily as a psychiatric condition. One of the three requirements for diagnosis is a severe deficit in social interactions (APA, 1994). Self and parental reports describe children and adults who prefer to be alone and who will withdraw to their rooms if given the chance (MAAP, 1996-1999). Even high functioning autistics tend to be aloof, have poor social skills, are unable to make friends, and find conversation difficult (Tonge et al, 1999; Capps et al, 1998). Face recognition and what psychologists call "theory of mind" are impaired (Klin et al, 1999, Baron-Cohen et al, 1993). Poor eye contact or gaze avoidance is present in most cases, especially in infancy and childhood (Bernabei et al, 1998).

The second psychobehavioral diagnostic characteristic of autism is the presence of repetitive, stereotyped activities and the need for sameness (APA, 1994). Traits in this domain strongly resemble obsessive-compulsive tendencies in both thought and behavior (Lewis, 1996; Gillberg & Coleman, 1992, p.27), especially as the individual becomes more high functioning (Roux et al, 1998): "it [is] very difficult...to distinguish between obsessive ideation and the bizarre preoccupations so commonly seen in autistic individuals" (Howlin, 2000). Serotonin uptake inhibitors known to be effective for OCD also reduce repetitive behaviors in some autistic patients (Lewis, 1996). Most autistic subjects - 84% in one study - show high levels of anxiety and meet diagnostic criteria for anxiety disorder (Muris et al, 1998).

ASD has been linked to depression, based on symptoms, familial history of depression and the positive response to SSRIs among many autistics (Clarke et al, 1999; DeLong, 1999; Piven and Palmer, 1999). One subset of autistics has been described as "passive", with flat affect, "absence of facial expression," lack of initiative, and diminished outward emotional reactions. Some autistics have a strong family history of manic depression and mood swings, and, among those who are verbal, psychotic talk is frequently observed (Plioplys, 1989). Autism is also said to strongly resemble childhood schizophrenia. In the past it was often misdiagnosed as such (Gillberg & Coleman, 1992, p.100), and there are a number of instances of dual ASD-schizophrenia diagnoses in the literature (Clarke et al, 1999). Furthermore, irrational fears, aggressive behaviors, and severe temper tantrums are common (Muris et al, 1998; McDougle et al, 1994), as are chronic hyperarousal and irritability (Jaselskis et al, 1992). "Inexplicable changes of mood can occur, with giggling and laughing or crying for no apparent reason" (Wing & Attwood, 1987).

Mercury poisoning, when undetected, is often initially diagnosed as a psychiatric disorder in both children and adults (Fagala and Wigg, 1992). Common psychiatric symptoms are (a) depression, including "lack of interest" and "mental confusion;" (b) "extreme

shyness," indifference to others, active avoidance of others or "a desire to be alone"; (c) irritability in adults and tantrums in children; and (d) anxiety and fearfulness. Neurosis, including schizoid and obsessive-compulsive traits, has been reported in a number of cases (Fagala and Wigg, 1992; Kark et al, 1971; O'Carroll et al, 1995; Florentine and Sanfilippo, 1991; Amin-Zaki, 1974 and 1979; Matheson et al, 1980; Joselow et al, 1972; Smith, 1972; Lowell, 1996; Tuthill, 1899; Clarkson, 1997; Camerino et al, 1981; Grandjean et al, 1997; Piikivi et al, 1984; Rice, 1996; Vroom & Greer, 1972; Adams et al, 1973; Hua et al, 1996).

Juvenile monkeys prenatally exposed to mercury exhibit decreased social play and increased passive behavior (Gunderson et al, 1986, 1988), as well as impaired face recognition (Rice, 1996). Humans exposed to mercury vapor also perform poorly on face recognition tests and may present with a "mask face" (Vroom & Greer, 1972); emotional instability can occur in children and adults exposed to Hg. For instance, Iraqi children poisoned by methylmercury had a tendency "to cry, laugh, or smile without obvious provocation" (Amin-Zaki et al, 1974 & 1979), like the autistic group described by Wing and Attwood (1987).

Table II: Summary of Psychiatric Disturbances Found in Autism & Mercury Poisoning

Mercury Poisoning	Autism
Extreme shyness, social withdrawal, feeling overly sensitive, introversion	Social deficits, social withdrawal, self reports of extreme shyness, aloofness
Mood swings; flat affect; mask face; laughing or crying without provocation; episodes of hysteria	Mood swings; flat affect in some; no facial expression; laughing or crying without reason
Anxiety; nervousness; tremulousness; somatization of anxious feelings	Anxiety, nervousness; anxiety disorder
Schizoid tendencies, neurosis, obsessive-compulsive traits, repetitive dreams	Schizophrenic traits; OCD traits; repetitive behaviors and thoughts
Lack of eye contact; being less talkative; hesitancy to engage others	Lack of eye contact, gaze avoidance; avoids conversation
Depression, lack of interest in life, lassitude, fatigue, apathy; feelings of hopelessness; melancholy	Association with depression; lack of initiative, diminished outward emotions
On the one hand, less overtly active, unwilling to go outside or be with others; on the other hand, increased restlessness	Tendency to withdraw, especially to own rooms, prefer to be alone; hyperactivity
Irrational fears	Irrational fears
Irritability, anger, and aggression; in children this may manifest as frequent and severe temper tantrums	Irritability and aggression; severe temper tantrums in children
Psychotic episodes; hallucinations, hearing voices; paranoid thoughts	Psychotic talk, paranoid thoughts
Impaired face recognition	Impaired face recognition

Since traditionally autism has been characterized and studied by researchers primarily in psychiatric terms, providing case studies illustrating the psychiatric aspects of ASD and of mercurialism are necessary in establishing the similarities of the two disorders on this critical domain. Also included is a comparison of "Lenny," an autistic adult described by Rhea Paul (1987), and the Mad Hatter from *Alice in Wonderland*, considered to be an accurate portrayal of victims of the disease. Of particular relevance in all these cases are social withdrawal and deficits in social communication, traits (i) always prominent in autism and (ii) clearly associated with mercurialism.

Case Studies: Autism

"I am 18 years old. My parents found out I was autistic when I was 18 months old. My parents said I banged my head a lot when I got frustrated when I was young. Head banging motions help me deal with nervousness. I also take 2 medications to help me cope with stress. I have very few friends. It is also somewhat painful for me to look people in the eye. This sometimes makes people think I am not paying attention" (The MAAP, Vol. II, 1997).

"I have a high-functioning autistic eight-year-old boy. My mistake was putting him in the second grade with a teacher who was determined to 'socialize' him. After three months, the anxiety proved to be too great for him. He spent a lot of time crying, withdrawing to his room, becoming compulsive and belligerent. In another era, he would have been seen as having a 'nervous breakdown'" (The MAAP, Vol. II, 1997).

"I am writing regarding our 25 year old son who was diagnosed only a few months ago as having Asperger's Syndrome. All his life he displayed the 'classic' symptoms of Asperger's (lack of social skills, disorganization, anxiety, etc.). A few months ago, he became clinically depressed, phobic about being around people for fear of more rejection or being laughed at. He now has obsessive thoughts that our home is electronically 'bugged' and all his actions are being observed and belittled" (The MAAP, Vol. II, 1997).

"Several people have asked me what it's like to have Asperger's Syndrome. Today, I still prefer to work on my computer or with electronics rather than socialize. I've never been able to tolerate any kind of physical contact or intimacy. I like wrestling and rough-housing, but I hate being caressed or held." (The MAAP, Vol. II, 1997).

"My son Brian is a 6-year-old with high functioning autism. Our main problem now is his rigidity and obsessive/compulsive behaviors. He gets extremely upset when activities don't go as he thinks they should. He first gets mad, screaming and yelling, then begins to obsessively talk about how he can remedy the situation, then often begins to cry uncontrollably. These tantrums can go on for hours" (The MAAP, Vol. IV, 1996).

"[I'm] age 12½. I have Autism/PDD. I don't really know any real social skills, though my brother Isaiah says I am a social outcast. I do have trouble making new friends because I get real shy and nervous" (The MAAP, Vol. IV, 1997).

"I am the mother of three autistic boys. Nate was considered very shy. Poor eye contact but very smart and doing well in school. Nate was also diagnosed with Hypotonia of the face (which answered all the mumbling he did wasn't just shyness) and extremities" (The MAAP, Vol. III, 1999)

"I spent many hours sitting in the trees or under the bed or in a dark closet. I had a loud flat voice. Socialization has always been beyond me" (The MAAP, Vol. II, 1998).

"I sit in my room a prisoner to my autism. Mom and sis doing their loving best to get me out. I wanted to get out – really get out. I wanted to love, to feel, to connect. But, I couldn't. I was stuck. I was slowly dying. There were days I truly wanted to end it all. If any days were good, I didn't deserve it. I shouldn't be happy. Autism teaches you that – because it's a life sentence" (The MAAP, Vol. VI, 1996).

Case Studies: Mercury Poisoning

A 12 year old girl with recent mercury vapor poisoning was initially diagnosed as having a psychiatric disturbance. Her behavior was more normal when she was unaware of being watched. She became upset when people were around, was reluctant to speak when others were present, spoke in a soft, mumbling voice, lacked eye contact, had a flat affect, was sometimes tearful, experienced auditory hallucinations of voices laughing at her, wished to stay alone in her room with the lights off and her head covered, and had frequent temper tantrums (Fagala and Wigg, 1992).

Sufferers of Mad Hatter's disease, arising from prolonged mercury vapor exposure, were known to suffer from depression, lassitude, acute anxiety, and irrational fears. They also became nervous, timid, and shy. They blushed readily, were embarrassed in social situations, objected to being watched, and sought to avoid people. They felt a constant impulse to return home. They were easily upset, and were prone to agitation, irritability, anger, and aggressive behavior (O'Carroll et al, 1995).

A survey on an Internet site of adult acrodynia victims, which compared the symptoms of adults who suffered from acrodynia as children with controls, reported the following symptoms as seen to a greater degree in acrodynia sufferers than in controls: dislikes being touched or hugged, is a loner, lacks self confidence, feels nervousness and has a racing heart, has depression and suicidal feelings (Farnesworth, 1997). One acrodynia victim described his own situation: "not having learnt normal social skills I spent a lot of my time alone...Gradually by age 11 or so, I was becoming 'normal'...But, I have never overcome the headache problem, irritability, shyness with real people, not wanting to be touched, depression, fear of doctors, great anxiety..." (Neville's Recollection, Pink Disease site)

A doctor from the 19th century described several cases of mercury poisoning from dental amalgams: "There is mental excitability as well as mental depression; perplexing events cause the highest degree of excitement, ordinary conversation sometimes causes complete confusion, headache, palpitation,

intense solicitude, and anxiety, without reason for it. Such are some of the symptoms attending these cases." As an example he cites the case of a young woman who "had come to be melancholic and to withdraw herself from her family and friends, seeking the seclusion of her room -- refusing to go out or to associate with others, or even with the members of her own household." (Tuthill, 1899)

Nearly a century later, initial questioning of a 28 year old woman, subsequently found to have mercury vapor poisoning, "elicited the fact that she had become increasingly withdrawn from social activities and had felt most uncomfortable when with strangers. She also felt that her friends had turned against her. She had a repetitive disturbing dream of electric fire around the frames of the windows in her bedroom." (Ross et al, 1977)

Lenny and The Mad Hatter

(a) Rigid literal interpretation of word meaning; word meaning and pragmatic errors which interfere with social communication

Lenny -

"He was very literal minded, and words spoken to him became matters of immutable fact. For example, he was trying on new shoes. His mother asked him if they slipped up and down. He said they didn't, and when asked again if he were sure, he replied, 'No, they don't slip up and down; they slip down and *then* they slip up.' "

The Mad Hatter -

"Take some more tea," the March Hare said to Alice, very earnestly.

"I've had nothing yet," Alice replied in an offended tone: "so I ca'n't take more."

"You mean you ca'n't take *less*," said the Hatter: "It's very easy to take *more* than nothing."

(b) Social deficits, inability to interpret social rules, leading to perceived rude behavior

Lenny -

"Although he tried working in his father's business for a time, his immaturity, self-centered behavior, and lack of social judgment required his return to a sheltered setting."

The Mad Hatter -

"Your hair wants cutting," said the Hatter. He had been looking at Alice for some time with great curiosity, and this was his first speech.

"You should learn not to make personal remarks," Alice said with some severity: "it's very rude."

The Hatter opened his eyes wide upon hearing this; but all he said was "Why is a raven like a writing desk?"

(c) Inability to engage in meaningful social conversation; poor conversational interpretation skills; perseverative thoughts

Lenny -
"During one interview he engaged in a 20 minute monologue about a broken washing mashine. The interviewer momentarily dozed off. Upon rousing, the interviewer exclaimed, 'Oh, Lenny, I'm sorry!' 'It's all right,' Lenny replied calmly, 'the washing machine got fixed."

The Mad Hatter (who talks obsessively/perseveratively about Time for a good portion of the chapter) -
"What a funny watch!" she remarked. "It tells the day of the month, and doesn't tell what o'clock it is!"

"Why should it?" muttered the Hatter. "Does *your* watch tell you what year it is?"

"Of course not, " Alice replied very readily: "but that's because it stays the same year for such a long time altogether."

"Which is just the case with *mine*," said the Hatter.

Alice felt dreadfully puzzled. The Hatter's remark seemed to her to have no sort of meaning in it, and yet it was certainly plain English.

b. Language and Hearing

The third diagnostic criterion for autism is a qualitative impairment in communication (APA, 1994), and such impairment is a primary feature of mercury poisoning.

Delayed language onset is often among the first overt signs of ASD (Eisenmajer et al, 1998). Historically, half of those with classic autism failed to develop meaningful speech (Gillberg & Coleman, 1992; Prizant, 1996); and oral-motor deficits (e.g. chewing, swallowing) are often present (Filipek et al, 1999). When speech develops, there may be "specific neuromotor speech disorders," including verbal dyspraxia, a dysfunction in the ability to plan the coordinated movements to produce intelligible sequences of speech sounds, or dysarthria, a weakness or lack of control of the oral musculature" leading to articulation problems (Filipek et al, 1999). Echolalic speech and pronoun reversals are typically found in younger children. Many ASD subjects show poorer performance on tests of verbal IQ relative to performance IQ (Dawson, 1996; Filipek at al, 1999). Higher functioning individuals, such as those with Asperger's Syndrome, may have language fluency but still exhibit semantic (word meaning) and pragmatic (use of language to communicate) errors (Filipek et al, 1999).

Auditory impairment is also common. Two separate studies, for example, both found that 24% of autistic subjects have a hearing deficit (Gillberg & Coleman, 1992). More recently Rosenhall et al (1999) have diagnosed hearing loss ranging from mild to profound, as well as hyperacusis, otitis media, and conductive hearing loss, in a minority of ASD subjects, and these traits were independent of IQ status. Among the earliest signs of autism noted by mothers were strange reactions to sound and abnormal babble (Gillberg & Coleman, 1992), and many ASD children are tested for deafness before receiving a formal autism diagnosis (Vostanis et al, 1998). "Delayed or prompted response to name" differentiates 9-12 months old toddlers, later diagnosed with autism,

from mentally retarded and typical controls (Baranek, 1999). In fact, "bizarre responses" to auditory stimuli are nearly universal in autism and may present as "either a lack of responsiveness or an exaggerated reaction to auditory stimuli" (Roux et al, 1998), possibly due to sound sensitivity (Grandin, 1996). Kanner noted an aversion to certain types of sounds, such as vacuum cleaners (Kanner, 1943). Severe deficits in language comprehension are often present (Filipek et al, 1999). Difficulties in picking out conversational speech from background noise are commonly reported by high functioning ASD individuals (Grandin, 1995; MAAP, 1997-1998).

In regard to language and auditory phenomena, autism's parallels to mercurialism are striking. Emerging signs of mercury poisoning are dysarthria (defective articulation in speech due to CNS dysfunction) and then auditory disturbance, leading to deafness in very high doses (Clarkson, 1992). In some cases, hearing impairment manifests as an inability to comprehend speech rather than an inability to hear sound (Dales, 1972). Hg poisoning can also result in aphasia, the inability to understand and/or physically express words (Kark et al, 1971). Speech difficulties may arise from "intention tremor, which can be noticeable about the mouth, tongue, face, and head, as well as in the extremities" (Adams et al, 1983).

Mercury-exposed children especially show a marked difficulty with speech (Pierce et al, 1972; Snyder, 1972; Kark et al, 1971). Even children exposed prenatally to "safe" levels of methylmercury performed less well on standardized language tests than did unexposed controls (Grandjean et al, 1998). Iraqi babies exposed prenatally either failed to develop language or presented with severe language deficits in childhood. They exhibited "exaggerated reaction" to sudden noise and some had reduced hearing (Amin-Zaki, 1974 and 1979). Iraqi children who were postnatally poisoned from bread containing either methyl or ethylmercury developed articulation problems, from slow, slurred word production to the inability to generate meaningful speech. Most had impaired hearing and a few became deaf (Amin-Zaki, 1978). In acrodynia, symptoms of sufferers (vs. controls) include noise sensitivity and hearing problems (Farnesworth, 1997).

Adults also exhibit these same Hg-induced impairments. There is slurred or explosive speech (Dales, 1972), as well as difficulty in picking out one voice from a group (Joselow et al, 1972). Poisoned Iraqi adults developed articulation problems (Amin-Zaki, 1974). A 25 year old man with elemental mercury poisoning had reduced hearing at all frequencies (Kark et al, 1971). Thimerosal injected into a 44 year old man initially led to difficulty verbalizing, even though his abilities in written expression were uncompromised; he then progressed to slow and slurred speech, although he could still comprehend verbal language; and he finally lost speech altogether (Lowell et al, 1996). In Mad Hatter's disease, there were word retrieval and articulation difficulties (O'Carroll et al, 1995). A scientist who recently died from dimethylmercury poisoning demonstrated an inability to understand speech despite having good hearing sensitivity for pure tones (Musiek and Hanlon, 1999). Workers exposed to mercury vapor showed decreased verbal intelligence relative to performance IQ (Piikivi et al, 1984; Vroom and Greer, 1972).

Table III: Summary of Speech, Language & Hearing Deficits in Autism & Mercury Poisoning

Mercury Poisoning	Autism
Complete loss of speech in adults or children; failure to develop speech in infants	Delayed language onset; failure to develop speech
Dysarthria; speech difficulties from intention tremor; slow and slurred speech	Dysarthria; dyspraxia and oral-motor planning difficulties; unintelligible speech
Aphasia, the inability to use or understand words, inability to comprehend speech although ability to hear sound is intact	Speech comprehension deficits, although ability to hear sound is intact
Difficulties verbalizing; word retrieval problems	Echolalia; pronoun reversals, word meaning and pragmatic errors; limited speech production
Auditory disturbance; difficulties differentiating voices in a crowd	Difficulties following conversational speech with background noise
Sound sensitivity	Sound sensitivity
Hearing loss; deafness in very high doses	Mild to profound hearing loss
Poor performance on standardized language tests	Poor performance on verbal IQ tests

*c. **Sensory Perception***

Sensory impairment is considered by many researchers to be a defining characteristic of autism (Gillberg and Coleman, 1992; Williams, 1996). Baranek (1999) detected sensory-motor problems - touch aversion, poor non-social visual attention, excessive mouthing of objects, and delayed response to name - in 9-12 month old infants later diagnosed with autism, and suggests that these impairments both underlie later social deficits and serve to differentiate ASD from mental retardation and typical controls. Besides sensitivity to sound, as previously noted, ASD often involves insensitivity to pain, even to a burning stove (Gillberg & Coleman, 1992), while on the other hand there may be an overreaction to stimuli, so that even light to moderate touches are painful. Pinprick tests are usually normal. Children with autism have been described as "stiff to hold," and one of the earliest signs reported by mothers is an aversion to being touched (Gillberg & Coleman, 1992). Abnormal sensation in the extremities and mouth are common. Toe-walking is frequently seen. Oral sensitivity often results in feeding difficulties (Gillberg & Coleman, 1992, p.31). Autistic children frequently have vestibular impairments and difficulty orienting themselves in space (Grandin, 1996; Ornitz, 1987).

As in ASD, sensory issues are reported in nearly all cases of mercury toxicity, and serve to demonstrate the similarities between the two conditions. Paresthesia, or abnormal sensation, tingling, and numbness around the mouth and in the extremities, is the most common sensory disturbance in Hg poisoning, and is usually the first sign of toxicity (Fagala and Wigg, 1992; Joselow et al, 1972; Matheson et al, 1980; Amin-Zaki, 1979). In Japanese who ate contaminated fish, there was numbness in the extremities, face and tongue (Snyder, 1972; Tokuomi et al, 1982). Iraqi children who ate bread experienced sensory changes including numbness in the mouth, hands and feet, and a feeling that there were "ants crawling under the skin." These children could still feel a pinprick (Amin-Zaki, 1978). Loss of position in space has also been noted (Dales, 1972). Acrodynia sufferers describe excessive pain when bumping limbs, numbness, and poor circulation (Farnesworth, 1997). One adult acrodynia victim described himself as a boy as "shying away from people wanting to touch me" due to extreme touch sensitivity (Neville Recollection, Pink Disease Support Group). Iraqi babies exposed to mercury prenatally showed excessive crying, irritability, and exaggerated reaction to stimulation such as sudden noise or when touched (Amin-Zaki et al, 1974 and 1979).

Table IV: Summary of Sensory Abnormalities in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Abnormal sensation or numbness around mouth and extremities (paresthesia); burning feet	Abnormal sensation in mouth and extremities; excessive mouthing of objects (infants); toe walking; difficulty grasping objects
Sound sensitivity	Sound sensitivity
Excessive pain when bumping; abnormal touch sensations; touch aversion	Insensitivity or overreaction to pain and touch; touch aversion; stiff to hold
Loss of position in space	Vestibular system abnormalities; difficulty orienting self in space
Normal pinprick tests	Normal pinprick tests

d. Movement/Motor Function

Nearly all cases of autism include disorders of physical movement. Movement disturbances have been detected in infants as young as four to six months old who were later diagnosed as autistic: Teitelbaum et al (1998) have observed that these children do not lie, roll over, sit up or crawl like normal infants; impairment in motor control sometimes caused these babies to fall over while sitting, consistently to avoid using one of their arms, or to rest on their elbows for stability while crawling. Later, when trying to walk their gait was abnormal, and some degree of asymmetry, mostly right-sided, was present in all cases studied. Kanner noted in several of his subjects the absence of crawling and a failure to assume an anticipatory posture preparatory to being picked up in infancy (Kanner, 1943). Arm flapping, abnormal posture, jumping, and hand-finger mannerisms (choreiform movements) are common (Tsai, 1996). Many individuals with Asperger's syndrome are typically characterized as uncoordinated or clumsy (Kugler, 1998). Other autism movement disorders include praxis (problems with intentional

movement), stereotypies, circling or spinning, rocking, myoclonal jerks, difficulty swallowing and chewing, difficulty writing with or even holding a pen, limb apraxia, and poor eye-hand coordination (Caesaroni and Garber, 1991; Gillberg and Coleman, 1992; Filipek et al, 1999).

Like ASD, movement disorders have been a feature of virtually all descriptions of mercury poisoning in humans (Snyder, 1972). Even children prenatally exposed to "safe" levels of methylmercury had deficits in motor function (Grandjean et al, 1998). The movement-related behaviors are extremely diverse: Iraqi infants and children exposed postnatally, for example, developed ataxia that ranged from clumsiness and gait disturbances to an "inability to stand or even sit" (Amin-Zaki et al, 1978). The various movement behaviors are listed more fully in Table VI (Adams et al, 1983; Kark et al, 1971; Pierce et al, 1972; Snyder, 1972; O'Carroll et al, 1995; Tokuomi et al, 1982; Amin-Zaki, 1979; Florentine and Sanfilippo, 1991; Rohyans et al, 1984; Fagala and Wigg, 1992; Smith, 1977; Grandjean et al, 1998; Farnesworth, 1997; Dales, 1972; Matheson et al, 1980; Lowell et al, 1996; O'Kusky et al, 1988; Vroom and Greer, 1972; Warkany and Hubbard, 1953).

Noteworthy because of similarities to movement disorders in autism are reports in the Hg literature of (a) an infant with "peculiar tremulous movements of the extremities which were principally proximal and can best be described as flapping in nature" (Pierce et al, 1972; Snyder, 1972); (b) "jerking movements of the upper extremities" in a man injected with thimerosal (Lowell et al, 1996); (c) "constant choreiform movements affecting the fingers and face" in mercury vapor intoxication (Kark et al, 1971); (d) myoclonal jerks, associated with epilepsy (Amin-Zaki et al, 1978); (e) poor coordination and clumsiness among victims of acrodynia (Farnesworth, 1997); (f) rocking among infants with acrodynia (Warkany and Hubbard, 1953); and (g) unusual postures observed in both acrodynia and mercury vapor poisoning (Vroom and Greer, 1972; Warkany and Hubbard, 1953). In animal studies, cats exposed to mercury by eating fish developed circling movements" (Snyder, 1972), and subcutaneous administration of methylmercury to rats during postnatal development has resulted in postural disorders (O'Kusky et al, 1988). As summarized in Table V, movement similarities in autism and Hg poisoning are clear.

Table V: Summary of Motor Disorder Behaviors in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Involuntary jerking movements, e.g., arm flapping, ankle jerks, myoclonal jerks; choreiform movements; circling (cats); rocking; purposeless movement of extremities; twitching, shaking; muscular spasticity	Stereotyped movements such as arm flapping, jumping, circling, spinning, rocking; myoclonal jerks; choreiform movements
Unsteadiness in handwriting or an inability to hold a pen; deficits in eye-hand coordination; limb apraxia; intention tremors; loss of fine motor skills	Difficulty in writing with or holding a pen; poor eye-hand coordination; limb apraxia; problems carrying out intentional movements (praxia)
Ataxia: gait impairment; severity ranging from mild incoordination, clumsiness to complete inability to walk, stand, or sit; staggering, stumbling; loss of motor control	Abnormal gait and posture, clumsiness and incoordination; difficulties sitting, lying, crawling, and walking in infants and toddlers
Difficulty in chewing or swallowing	Difficulty chewing or swallowing
Unusual postures	Unusual postures
Areflexia	None described
Tremors in general, tremors of the face and tongue, hand tremors	None described

e. Cognition/Mental Function

Nearly all autistic individuals show impairment in some aspects of mental function, even as other cognitive abilities remain intact. Most individuals may test in the retarded range, while others have normal to above average IQs. These characteristics are true in mercurialism. Moreover, the specific areas of impairment are similar in the two disorders.

The impaired areas in autism are generally in (a) short term or working memory and auditory and verbal memory; (b) concentration and attention, particularly attention shifting; (c) visual motor and perceptual motor skills, including eye-hand coordination; (d) language/verbal expression and comprehension; and (e) using visually presented information when constraints are placed on processing time. Relatively unimpaired areas include rote memory skills, pattern recognition, matching, perceptual organization, and stimuli discrimination. Higher level mental skills requiring complex processing are typically deficient; these include (a) processing and filtering of multiple stimuli; (b) following multiple step commands; (c) sequencing, planning and organizing; and (d) abstract/conceptual thinking and symbolic understanding (Rumsey & Hamburger, 1988; Plioplys, 1989; Bailey et al, 1996; Filipek et al, 1999; Rumsey, 1985; Dawson, 1996; Schuler, 1995; Grandin, 1995; Sigman et al, 1987). Younger or more mentally impaired children may have difficulties with symbolic play and understanding object permanence or the mental state of others (Bailey et al, 1996). Some autistic children are hyperlexic, showing superior decoding skills while lacking comprehension of the words being read

(Prizant, 1996). As mentioned before, for most autistic individuals verbal IQ is lower than performance IQ.

As in autism, Hg exposure causes some level of impairment primarily in (a) short term memory and auditory and verbal memory; (b) concentration and attention, including response inhibition; (c) visual motor and perceptual motor skills, including eye-hand coordination; (d) language/verbal expression and comprehension; and (e) simple reaction time. Hg-affected individuals may present as "forgetful" or "confused." Performance IQ may be higher than verbal IQ. "Degeneration of higher mental powers" has resulted in (a) difficulty carrying out complex commands; (b) impairment in abstract and symbolic thinking; and (c) deficits in constructional skills and conceptual abstraction. One study mentions alexia, the inability to comprehend the meaning of words, although reading of the words is intact (Yeates & Mortensen, 1994; O'Carroll et al, 1995; Pierce et al, 1972; Snyder, 1972; Adams et al, 1983; Kark et al, 1971; Amin-Zaki, 1974 and 1979; Davis et al, 1994; Grandjean et al, 1997 & 1998; Myers & Davidson, 1998; Gilbert & Grant-Webster 1995; Dales, 1972; Fagala and Wigg, 1992; Farnesworth, 1997; Tuthill, 1899; Joselow et al, 1972; Rice, 1997; Piikivi et al, 1984; Vroom and Greer, 1972). Even children exposed prenatally to "safe" levels of methylmercury show lower scores on selective subtests of cognition, especially in the domains of memory and attention, relative to unexposed controls (Grandjean et al, 1998). In exposed juvenile monkeys, tests have revealed delays in the development of object permanence, or the ability to conceptualize the existence of a hidden object (Rice, 1996).

Research on mental retardation in autism is contradictory (Schuler, 1995). The finding that "mental retardation or borderline intelligence often co-exists with autism" (Filipek et al, 1999) is based on using standard measures of intelligence (Gillberg & Coleman, 1992, p.32; Bryson, 1996); other intelligence tests, designed to circumvent the language and attentional deficits of autistic children, show significantly higher intelligence test scores (Koegel et al, 1997; Russell et al, 1999). One study using such a modified rating instrument has found 20% of autistic children to be mentally retarded (Edelson et al, 1998), rather than the 70%-80% so scored on standard tests. ASD individuals also show "strikingly uneven scores" on IQ subtests, "unlike other disorders involving mental retardation, in which subtest scores seem to be more or less even" (Bailey et al, 1996). Also unlike typical cases of mental retardation, which is nearly always noted in the peri- or neonatal periods, most parents of ASD children report infants of seemingly normal appearance and development who were later characterized as mentally retarded on tests. For example, one study compared early developmental aberrations in mentally retarded children with and without autism. Findings indicated that, whereas nearly all parents of the non-autistic mentally retarded study group were aware of their child's impairment by age 3 months, nearly all parents of the autistic children failed to notice *any* developmental delays or issues until after 12 months of age (Baranek, 1999). Finally, there are several case reports of autistic adults who were labeled mentally retarded as children based on tests, who later "emerged" from their autism and had normal IQs (ARI Newsletter, 1993, review).

As in autism, symptomatic mercury-poisoned victims can present with normal IQs, borderline intelligence, or mental retardation; some may be so impaired as to be

untestable (Vroom and Greer, 1972; Davis et al, 1994). When lowered intelligence is found, it is always reported as an obvious deterioration among previously normally functioning people; this includes children exposed as infants or toddlers (Dale, 1972; Vroom and Greer, 1972; Amin-Zaki, 1978). Once the Hg-exposure source is removed, many (although not all) of these patients "recover" their normal IQ, suggesting that "real" IQ was not affected (Vroom and Greer, 1972; Davis et al, 1994). Infant monkeys given low doses of Hg, while clearly impaired in visual, auditory, and sensory functions, had intact central processing speed, which has been shown to correlate with IQ in humans (Rice, 1997).

Table VI: Summary of Areas of Mental Impairment in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Some aspect of mental impairment in all symptomatic cases	Some aspect of mental impairment in all cases
Borderline intelligence on testing among previously normal individuals; mental retardation occurring in severe cases of pre-/postnatal exposure; some cases of MR reversible; primate studies indicate core intelligence spared with low exposures	Borderline intelligence or mental retardation on standard tests among previously normally appearing infants; some cases of MR "reversible"; indications that normal IQ might be present in MR-labeled individuals
Uneven performance on subtests of intelligence	Uneven performance on subtests of intelligence
Verbal IQ higher than performance IQ; compromised language/verbal expression and comprehension	Verbal IQ higher than performance IQ; compromised language/verbal expression and comprehension
Poor concentration, shortened attention span, general lack of attention; poor response inhibition	Lack of concentration, short attention span, lack of attention, difficulty shifting attention
Forgetfulness, loss of memory, particularly short term, verbal and auditory memory; mental confusion	Poor short term/working memory; poor auditory and verbal memory; lower verbal encoding abilities
Poor visual and perceptual motor skills, poor eye-hand coordination; impairment in simple reaction time	Poor visual and perceptual motor skills, poor eye-hand coordination; lowered performance on timed tests
Not reported as being tested	Difficulty processing multiple stimuli
Difficulty carrying out complex commands	Difficulty carrying out multiple commands
Alexia (inability to comprehend the meaning of written words)	Hyperlexia (ability to decode words while lacking word comprehension)
Deficits in constructional skills, conceptual abstraction, understanding abstract ideas and symbolism; degeneration of higher mental powers	Deficits in abstract/conceptual thinking, symbolism, understanding other's mental states; impairment in sequencing, planning, organizing
Lack of understanding of object permanence (primates)	Deficient understanding of object permanence (children)

f. Behaviors

Autism is associated with difficulties initiating and/or maintaining sleep; hyperactivity and other ADHD traits; and self injurious behavior such as head banging, even in the absence of mental retardation. Agitation, screaming, crying, staring spells, stereotypical behaviors, and grimacing are common (Gaedye, 1992; Gillberg and Coleman, 1992; Plioplys, 1989; Kanner, 1943; Richdale, 1999; Stores & Wiggs, 1998). Kanner (1943) made a point of noting excessive and open masturbation in two of the eleven young children comprising his initial cases. Feeding and suckling problems are typical (Wing, 1980), and restricted diets and narrow food preferences "are the rule rather than the exception" (Gillberg and Coleman, 1992; Clark et al, 1993); some autistics show a preference for salty foods (Shattock, 1997). Kanner, in his 1943 article, noted feeding problems from infancy, including vomiting and a refusal to eat, in six of the eleven autistic children he described. There are case studies of anorexia nervosa occurring in ASD patients, as well as an increased likelihood of this eating disorder in families with ASD (Gillberg & Coleman, 1992, p.99).

Humans and animals exposed to mercury develop unusual, abnormal, and "inappropriate" behaviors (Florentine and Sanfilippo, 1991). Rats exposed to mercury during gestation have exhibited stereotyped sniffing (Cuomo et al, 1984) and hyperactivity (Fredriksson et al, 1996). "Restlessness" has already been noted, and Davis et al (1994) found poor response inhibition in their human subjects; both of these behaviors are closely associated with ADHD in children. Babies and children with Hg poisoning exhibit agitation, crying for no observable reason, grimacing, and insomnia (Pierce et al, 1972; Snyder, 1972; Kark et al, 1971; Amin-Zaki, 1979; Florentine and Sanfilippo, 1991; Aronow and Fleischmann, 1976). An 18 month old toddler with otitis media, exposed to thimerosal in ear drops, had staring spells and unprovoked screaming episodes (Rohyans et al, 1984). Symptoms of acrodynia in babies and toddlers include continuous crying, anorexia and insomnia (Matheson et al, 1980; Aronow and Fleischmann, 1976). These children were said to bang their heads, have difficulty falling asleep, be irritable, and either refuse to eat or only eat a few foods (Neville Recollection, Pink Disease Support Group Site; Farnesworth, 1997). The frequent temper tantrums of a previously normal 12 year old, poisoned by mercury vapor, included hitting herself on the head and screaming; furthermore, she had extreme genital burning and was observed to masturbate even in front of others (Fagala and Wigg, 1992). Similarly, priapism, persistent erection of the penis due to a pathologic condition resulting in pain and tenderness, has been noted in boys with mercury poisoning (Amin-Zaki et al, 1978).

Adults with mercury poisoning present with insomnia, agitation, and poor appetite (Tuthill, 1899; Adams et al, 1983; Fagala and Wigg, 1992). Relative to controls, more adults who had acrodynia in childhood have eating idiosyncrasies, particularly a preference for salty foods to sweet ones (Farnesworth, 1997), possibly because mercury causes excessive sodium excretion, as shown in studies of dental amalgam placed in monkeys and sheep (Lorscheider et al, 1995).

Table VII: Summary of Unusual Behaviors in Mercury-Poisoned Animals and Humans & in Autism

Mercury Poisoning	Autism
Stereotyped sniffing (rats)	Stereotyped, repetitive behaviors
Hyperactivity (rats); poor response inhibition (humans), restlessness	Hyperactivity; ADHD-traits
Agitation (humans)	Agitation
Insomnia; difficulty falling asleep (humans)	Insomnia; difficulty falling or staying asleep
Eating disorders: anorexia, poor appetite, food aversion, narrow food preferences, decided food preferences (salty food) (humans)	Eating disorders: anorexia; restricted diet/narrow food preferences; feeding and suckling problems
Masturbation, priapism (children)	Masturbatory tendencies
Unintelligible cries; continuous crying; unprovoked crying (infants and children)	Unprovoked crying
Self injurious behavior, including head banging and hitting the head (toddlers and children)	Self injurious behavior, including head banging and hitting the head
Grimacing (children)	Grimacing
Staring spells (infants and children)	Staring spells

g. Vision

In autism, one of the earliest signs detected by mothers is a lack of eye contact (Gillberg & Coleman, 1992), and an early diagnostic behavior is failure to engage in joint attention based on the ability to "look where you are pointing" (CHAT, Baron-Cohen et al, 1992). Of 11 autistic children studied, ten had inaccurate or slow visual saccades (Rosenhall et al, 1988). Although some adults with ASD report exceptional visual acuity, visual problems are common, with two separate studies reporting 50% of ASD subjects having some type of unusual visual impairment (Steffenburg, in Gillberg & Coleman, 1992). Ritvo et al (1986) and Creel et al (1989) found decreased function of the rods in a study of autistic people, including a retinal sheen, and noted that many such individuals tend to use peripheral vision because of this. A number of case reports describe over-sensitivity to light and blurred vision (Sperry, 1998; Gillberg & Coleman, 1992, p.29; O'Neill & Jones, 1997).

Mercury can lead to a variety of vision problems, especially in children (Pierce et al, 1972; Snyder, 1972). Children who ate high doses of mercury from contaminated pork developed blindness (Snyder, 1972). In Iraqi babies exposed prenatally there was blindness or impaired vision (Amin-Zaki, 1974 and 1979). Iraqi children exposed postnatally developed visual disturbances, which ranged from blurred or hazy vision to constriction of the visual fields to complete blindness (Amin-Zaki et al, 1978). Two girls with mercury vapor poisoning were found to have visual field defects (Snyder, 1972), and, as previously noted, one child with Hg poisoning developed gaze avoidance (Fagala & Wigg, 1992). Acrodynia sufferers report vision problems, including near-sightedness

and light sensitivity or photophobia (Diner and Brenner, 1998; Neville Recollection, Pink Disease site; Farnesworth, 1997; Matheson et al, 1980; Aronow and Fleischmann, 1976). A 25 year old man with elemental mercury poisoning exhibited decreased visual acuity, difficulty with visual fixation, and constricted visual fields (Kark et al, 1971). In Japanese victims, there was blurred vision as well as constriction of visual fields (Snyder, 1972; Tokuomi et al, 1982). Iraqi mothers exposed to Hg had visual disturbance (Amin-Zaki, 1979).

In dogs exposed to daily doses of methylmercury, distortion of the visual evoked response from the visual cortex was the first sign. Damage occurred in the preclinical silent stage, demonstrating that CNS damage is occurring before overt symptoms appear (Mattsson et al, 1981). Monkeys treated at birth with low level methylmercury exhibited impaired spatial vision and visual acuity at age 3 and 4 years (Rice and Gilbert, 1982). Disturbances caused by methylmercury in rat optic nerves were observed (Kinoshita et al, 1999).

Table VIII: Summary of Visual Impairments Seen in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Lack of eye contact; difficulties with visual fixation	Lack of eye contact; gaze abnormalities; problems in joint attention
"Visual impairments," blindness, near-sightedness, decreased visual acuity	"Visual impairments"; inaccurate or slow saccades; decreased functioning of the rods; retinal sheen
Light sensitivity, photophobia	Over-sensitivity to light
Blurred or hazy vision	Blurred vision
Constricted visual fields	Not described

h. Physical Presentations

There is a much higher rate of autism among children with cerebral palsy than would be expected by chance (Nordin and Gillberg, 1996). Many autistic children have abnormal muscle tone including hyper- and hypotonia, and many are incontinent or have difficulty being toilet trained (Filipek et al, 1999; Church and Coplan, 1995). Several of the infants which Teitelbaum and colleagues (1998) observed showed decreased arm strength, and Schuler (1995) describes greater muscle weakness in the upper than the lower body. Impairments in oral-motor function, including problems chewing and swallowing, are common, as noted previously.

These impairments are seen in mercurialism as well. In the Iraqi and Japanese epidemics, many children developed clinical cerebral palsy (Amin-Zaki, 1979; Myers & Davidson, 1998; Gilbert & Grant-Webster 1995; Dale, 1972). Amin-Zaki et al (1978) reported muscle wasting and lack of motor power and control in most cases, complete paralysis in several cases, and athetotic movements in 2 cases, of postnatally exposed children. In the Iraqi babies and children, some had increased muscle tone, while others had decreased muscle tone. Abnormal reflexes, spasticity, and weakness were common. One child said

"my hands are weak and do not obey me" (Amin-Zaki et al, 1974 and 1978). The 12 year old who inhaled mercury vapor exhibited weakness and decreased muscle strength (Fagala and Wigg, 1992). As in autism, muscle weakness from mercury poisoning is most prominent in the upper body (Adams et al, 1983). Acrodynia, for example, is marked by poor muscle tone in general and loss of arm strength in particular (Farnesworth, 1997). Finally, difficulty in chewing and swallowing, salivation, and drooling are common in children as well as adults; incontinence was observed in children in the Iraqi Hg-crisis (Amin-Zaki, 1974 and 1978; Pierce et al, 1972; Snyder, 1972; Joselow et al, 1972; Smith, 1977).

The presence of rashes and dermatitis is sometimes reported in descriptions of ASD subjects. Whiteley et al (1998) found that 63% of the ASD children had a history of eczema or other skin complaints. "Some children with autism are frequent scratchers. Gentle rubbing and scratching can become a calming self-stimulation; but when it becomes clawing, and there are rashes and open scrapes on the skin, a tactile intolerance can be responsible" (O'Neill, 1999).

Rashes and itching are common disturbances in mercury toxicity as well (Kark et al, 1971). A 4 year old with Hg poisoning developed an itchy, peeling rash on the extremities (Florentine and Sanfilippo, 1991). Mercury vapor inhalation caused a rash and peeling on the palms and soles of a pre-adolescent (Fagala and Wigg, 1992). An acrodynia victim described himself as a child as having severe itching and a constant burning sensation at the extremities, resulting in him rubbing his hands and feet raw (Neville Recollection, Pink Disease Support Group). Acrodynia symptoms in an adult poisoned by ethylmercury injection included pink scaling palms and soles, flushed cheeks, and itching (Matheson et al, 1980). In acrodynia the skin may be rough and dry, and the soles and palms are usually but not necessarily red (Aronow and Fleischmann, 1976). Thimerosal ingested by 44 year old man led to dermatitis (Pfab et al, 1996).

In autism, "signs of autonomic disturbance may be noticed at times, including sweating, irregular breathing, and rapid pulse" (Wing and Attwood, 1987). There may be elevated blood flow and heart rate (Ornitz, 1987). An increased incidence of acrocyanosis has been observed in Asperger's syndrome. Acrocyanosis is an uncommon disorder of poor circulation in which skin on the hands and feet turn red and blue; there is profuse sweating; and the fingers and toes are persistently cold (Carpenter and Morris, 1991).

Sweating and circulatory abnormalities are also common in some forms of mercury poisoning. Acrodynia in adults and children results in excessive sweating, poor circulation, and rapid heart rate (Farnesworth, 1997; Matheson et al, 1980; Cloarec et al, 1995; Warkany and Hubbard, 1953). The 12 year old with mercury vapor poisoning sweated profusely, especially at night (Fagala and Wigg, 1992), and elevated blood pressure has been reported in exposed workers (Vroom and Greer, 1972). Autonomic system abnormalities can be caused by disturbances in acetylcholine levels, known to be deficient in both autism and Hg poisoning (see neurotransmitter section below).

Table IX: Physical Disturbances in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Increase in cerebral palsy; hyper- or hypotonia; paralysis, abnormal reflexes; spasticity; decreased muscle strength and motor power, especially in the upper body; incontinence; problems chewing, swallowing, and salivating	Increase in cerebral palsy; hyper- or hypotonia; decreased muscle strength, especially in the upper body; incontinence/toilet training difficulties; problems chewing and swallowing
Rashes, dermatitis, dry skin, itching; burning sensation	Rashes, dermatitis, eczema; itching
Autonomic disturbances: excessive sweating; poor circulation; elevated heart rate	Autonomic disturbances: sweating abnormalities; poor circulation; elevated heart rate

j. Gastrointestinal Function

Many if not most autistic individuals have gastrointestinal problems, the most common complaints being chronic diarrhea, constipation, gaseousness, and abdominal discomfort and distention (D'Eufemia et al, 1996; Horvath et al, 1999; Whitely et al, 1998). Colitis is not uncommon (Wakefield et al, 1998). As noted previously, anorexia is sometimes associated with ASD (Gillberg & Coleman, 1992). Kanner noted that over half his initial cases had feeding difficulties and excessive vomiting as infants (1943). O'Reilly and Waring (1993) have described sulfur deficiencies in autism, an effect of which can be clumping of proteins on the gut wall, which is lined with sulfated proteins. The clumping can lead to increased intestinal permeability, or leaky gut syndrome (Shattock, 1997), found in many autistic individuals (D'Eufemia, 1996). Some ASD individuals have unusual opioid peptide fragments in urine; these peptides are believed to enter the bloodstream due to a leaky gut and to result from an incomplete breakdown of gluten and casein in the diet possibly arising from "inadequacy of the [endopeptidase] enzyme systems which are responsible for their breakdown" (Shattock, 1997).

Mercury, which binds to sulfur groups (Clarkson, 1992), is known to cause gastroenteritis (Kark et al, 1971). For example, a four year old with diarrhea was initially diagnosed with gastroenteritis (Florentine and Sanfilippo, 1991). A pre-adolescent with mercury vapor poisoning developed nausea, abdominal pain, poor appetite, rectal itching, and diarrhea; she frequently strained to have a bowel movement, and was at one point diagnosed with colitis (Fagala and Wigg, 1992). Acrodynia is marked by both constipation and diarrhea (Diner and Brenner, 1998). Incontinence of urine and stool are observed in infants and children exposed pre- and postnatally in Iraq (Amin-Zaki, 1974 and 1978). In another case, a 28 year old woman with occupational exposure to mercury vapor developed watery stools (Ross et al, 1977). Diarrhea and digestive disturbance were seen in a dentist with measurable mercury levels; there was obesity in another dentist (Smith, 1977). A 44 year old man poisoned with thimerosal given intramuscularly developed gastrointestinal bleeding, which looked like hemorrhaging colitis (Lowell et al, 1996). Intense exposure to mercury vapor can cause abdominal

pain, nausea, and vomiting (Feldman, 1982). Severe constipation, anorexia, weight loss, and other "disturbances of gastrointestinal function" have been noted in other cases (Adams et al, 1983; Joselow et al, 1972). Rats tested with mercuric chloride were observed with "lesions of the ileum and colon with abnormal deposits of IgA in the basement membranes of the intestinal glands and of IgG in the basement membranes of the lamina propria" (Andres, 1984, reviewed in EPA, 1997, p.3-36). In another rat experiment, Hg was found to increase the permeability of intestinal epithelial tissues (Watzl et al, 1999). Mercury also inhibits the peptidase - dipeptidyl peptidase IV - which cleaves, among other substances, casomorphin during the digestive process (Puschel et al, 1982).

There is no reported increase in incidence in kidney problems in autism. Although renal function is commonly impaired from Hg exposure, such impairment would not be expected if the mercury exposure occurred from thimerosal injections, since kidney function may be unaffected when mercury is injected or inhaled (Davis et al, 1994; Fagala and Wigg, 1992). For example, although thimerosal ingested orally by a 44 year old man resulted in renal tubular failure and gingivitis (Pfab et al, 1996), renal function was normal in another 44 year old man injected intramuscularly with thimerosal (Lowell et al, 1996).

Table X: Summary of Gastrointestinal Problems in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Gastroenteritis, diarrhea; abdominal pain, rectal itching, constipation, "colitis"	Diarrhea, constipation, gaseousness, abdominal discomfort, colitis
Anorexia, weight loss, nausea, poor appetite	Anorexia; feeding difficulties, vomiting as infants
Lesions of the ileum and colon; increased intestinal permeability	Leaky gut syndrome from sulfur deficiency
Inhibits dipeptidyl peptidase IV, which cleaves casomorphin	Inadequate endopeptidase enzymes responsible for breakdown of casein and gluten

II. COMPARISON OF BIOLOGICAL ABNORMALITIES

Like the similarities seen in observable symptoms, parallels between autism and mercury poisoning clearly exist even at cellular and subcellular levels. These similarities are summarized in tables after each individual section.

a. Biochemistry

Sulfur: Studies of autistic children with known chemical or food intolerances show a low capacity to oxidize sulfur compounds and low levels of sulfate (O'Reilly & Waring, 1993; Alberti et al, 1999). These findings were interpreted as suggesting that "there may be a fault either in the manufacture of sulfate or that sulfate is being used up dramatically on an unknown toxic substance these children may be producing" (O'Reilly and Waring, 1993). Alternatively, these observations may be linked to mercury, since mercury preferentially forms compounds with molecules rich in sulfhydryl groups (--SH), such as cysteine and glutathione, making them unavailable for normal cellular and enzymatic functions (Clarkson, 1992). Relatedly, mercury may cause low sulfate by its ability to irreversibly inhibit the sulfate transporter Na-Si cotransporter NaSi-1 present in kidneys and intestines, thus preventing sulfate absorption (Markovitch and Knight, 1998).

Among the sulfhydryl groups, or thiols, mercury has special affinity for purines and pyrimidines, as well as other subcellular substances (Clarkson, 1992; Koos and Longo, 1976). Errors in purine or pyrimidine metabolism are known to result in classical autism or autistic features in some cases (Gillberg and Coleman, 1992, p.209; Page et al, 1997; Page & Coleman, 2000; The Purine Research Society), thereby suggesting that mercury's disruption of this pathway might also lead to autistic traits.

Likewise, yeast strains sensitive to Hg are those which have innately low levels of tyrosine synthesis. Mercury can deplete cellular tyrosine by binding to the SH-groups of the tyrosine uptake system, preventing colony growth (Ono et al, 1987), and Hg-depleted tyrosine would be particularly significant in cells known to accumulate mercury (e.g., neurons of the CNS, see below). Similarly, disruptions in tyrosine production in hepatic cells, arising from a genetic condition called Phenylketonuria (PKU), also results in autism (Gillberg & Coleman, 1992, p.203).

Glutathione: Glutathione is one of the primary means through which the cells detoxify heavy metals (Fuchs et al, 1997), and glutathione in the liver is a primary substrate by which body clearance of organic mercury takes place (Clarkson, 1992). Mercury, by preferentially binding with glutathione and/or preventing absorption of sulfate, reduces glutathione bioavailability. Many autistic subjects have low levels of glutathione. O'Reilly and Waring (1993) suggest this is due to an "exotoxin" binding glutathione so it is unavailable for normal biological processes. Edelson and Cantor (1998) have found a decreased ability of the liver in autistic subjects to detoxify heavy metals. Alternatively, low glutathione can be a manifestation of chronic infection (Aukrust et al, 1996, 1995; Jaffe et al, 1993), and infection-induced glutathione deficiency would be more likely in the presence of immune impairments derived from mercury (Shenkar et al, 1998).

Glutathione peroxidase activities were reported to be abnormal in the erythrocytes of autistic children (Golse et al, 1978). Mercury generates reactive oxygen species (ROS) levels in cells, which increases ROS scavenger enzyme content and thus glutathione, to relieve oxidative stress (Hussain et al, 1999). At high enough levels, mercury depletes rat hepatocytes of glutathione (GSH) and causes significant reduction in glutathione peroxidase and glutathione reductase (Ashour et al, 1993).

Mitochondria: Disturbances of brain energy metabolism have prompted autism to be hypothesized as a mitochondrial disorder (Lombard, 1998). There is a frequent association of lactic acidosis and carnitine deficiency in autistic patients, which suggests excessive nitric oxide production in mitochondria (Lombard, 1998; Chugani et al, 1999), and again, mercury may be a participant. Methylmercury accumulates in mitochondria, where it inhibits several mitochondrial enzymes, reduces ATP production and Ca2+ buffering capacity, and disrupts mitochondrial respiration and oxidative phosphorylation (Atchison & Hare, 1994; Rajanna and Hobson, 1985; Faro et al, 1998). Neurons have increased numbers of mitochondria (Fuchs et al, 1997), and since Hg accumulates in neurons of the CNS, an Hg effect upon neuronal mitochondria function seems likely - especially in children having substandard mercury detoxification.

Table XI: Abnormalities in Biochemistry
Arising from Hg Exposure & Present in Autism

Mercury	Autism
Ties up sulfur groups; prevents sulfate absorption	Low sulfate levels
Has special affinity for purines and pyrimidines	Errors in purine and pyrimidine metabolism can lead to autistic features
Depletes cellular tyrosine in yeast	PKU, arising from disruption in tyrosine production, results in autism
Reduces bioavailability of glutathione, necessary in cells and liver for heavy metal detoxification	Low levels of glutathione; decreased ability of liver to detoxify heavy metals
Can cause significant reduction in glutathione peroxidase and glutathione reductase	Abnormal glutathione peroxidase activities in erythrocytes
Disrupts mitochondrial activities, especially in brain	Mitochondrial dysfunction, especially in brain

b. Immune System

A variety of immune alterations are found in autism-spectrum children (Singh et al, 1993; Gupta et al, 1996; Warren et al, 1986 & 1996; Plioplys et al, 1994), and these appear to be etiologically significant in a variety of ways, ranging from autoimmunity to infections and vaccination responses (e.g., Fudenberg, 1996; Stubbs, 1976). Mercury's effects upon immune cell function are well documented and may be due in part to the ability of Hg to reduce the bioavailability of sulfur compounds:

> "It has been known for a long time that thiols are required for optimal primary in vitro antibody response, cytotoxicity, and proliferative response

> to T-cell mitogens of murine lymphoid cell cultures. Glutathione and cysteine are essential components of lymphocyte activation, and their depletion may result in lymphocyte dysfunction. Decreasing glutathione levels profoundly affects early signal transduction events in human T-cells" (Fuchs & Schöfer, 1997).

Allergy, asthma, and arthritis: Individuals with autism are more likely to have allergies and asthma, and autism occurs at a higher than expected rate in families with a history of autoimmune diseases such as rheumatoid arthritis and hypothyroidism (Comi and Zimmerman, 1999; Whitely et al, 1998). Relative to the general population, prevalence of selective IgA deficiency has been found in autism (Warren et al); individuals with selective IgA deficiency are more prone to allergies and autoimmunity (Gupta et al, 1996). Furthermore, lymphocyte subsets of autistic subjects show enhanced expression of HLA-DR antigens and an absence of interleuken-2 receptors, and these findings are associated with autoimmune diseases like rheumatoid arthritis (Warren et al). These observations suggest autoimmune processes are present in ASD (Plioplys, 1989; Warren et al); and this possibility is reinforced by Singh's findings of elevated antibodies against myelin-basic protein (Singh et al, 1993).

Atypical responses to mercury have been ascribed to allergic or autoimmune reactions (Gosselin et al, 1984; Fournier et al, 1988), and genetic predisposition for Hg reaction may explain why sensitivity to this metal varies so widely by individual (Rohyans et al, 1984; Nielsen & Hultman, 1999). Acrodynia can present as a hypersensitivity reaction (Pfab et al, 1996), or it may arise from immune over-reactivity, and "children who incline to allergic reactions have an increased tendency to develop acrodynia" (Warkany & Hubbard, 1953). Those with acrodynia are also more likely to suffer from asthma, to have poor immune system function (Farnesworth, 1997), and to experience intense joint pains suggestive of rheumatism (Clarkson, 1997). Methylmercury has altered thyroid function in rats (Kabuto, 1991).

Rheumatoid arthritis with joint pain has been observed as a familial trait in autism (Zimmerman et al, 1993). A subset of autistic subjects had a higher rate of strep throat and elevated levels of B lymphocyte antigen D8/17, which has expanded expression in rheumatic fever and may be implicated in obsessive-compulsive behaviors (DelGiudice-Asch & Hollander, 1997).

Mercury exposure frequently results in rheumatoid-like symptoms. Iraqi mothers and children developed muscle and joint pain (Amin-Zaki, 1979), and acrodynia is marked by joint pain (Farnesworth, 1997). Sore throat is occasionally a presenting sign in mercury poisoning (Vroom and Greer, 1972). A 12 year old with mercury vapor poisoning, for example, had joint pains as well as a sore throat; she was positive on a streptozyme test, and a diagnosis of rheumatic fever was made; she improved on penicillin (Fagala and Wigg, 1992). Acrodynia, which is almost never seen in adults, was also observed in a 20 year old male with a history of sensitivity reactions and rheumatoid-like arthritis, who received ethylmercury via injection in gammaglobulin (Matheson et al, 1980). One effective chelating agent, penicillamine, is also effective for rheumatoid arthritis (Florentine and Sanfilippo, 1991).

Mercury can induce an autoimmune response in mice and rats, and the response is both dose-dependent and genetically determined. Mice "genetically prone to develop spontaneous autoimmune diseases [are] highly susceptible to mercury-induced immunopathological alterations" (al-Balaghi, 1996). The autoimmune response depends on the H-2 haplotype: if the strain of mice does not have the susceptibility haplotype, there is no autoimmune response; the most sensitive strains show elevated antibody titres at the lowest dose; and the less susceptible strain responds only at a medium dose (Nielsen & Hultman, 1999). Interestingly, Hu et al (1997) were able to induce a high proliferative response in lymphocytes from even low responder mouse strains by washing away excess mercury after pre-treatment, while chronic exposure to mercury induced a response only in high-responder strains.

Autoimmunity and neuronal proteins: Based upon research and clinical findings, Singh has been suggesting for some time an autoimmune component in autism (Singh, Fudenberg et al, 1988). The presence of elevated serum IgG "may suggest the presence of persistent antigenic stimulation" (Gupta et al, 1996). Connolly and colleagues (1999) report higher rates in autistic vs. control groups of elevated antinuclear antibody (ANA) titers, as well as presence of IgG and IgM antibodies to brain endothelial cells. On the one hand, since mercury remains in the brain for years after exposure, autism's persistent symptoms may be due to an on-going autoimmune response to mercury remaining in the brain; on the other hand, activation and continuation of an autoimmune response does not require the continuous presence of mercury ions: in fact, once induced, autoimmune processes in the CNS might remain exacerbated because removal of mercury after an initial exposure can induce a greater proliferative response in lymphocytes than can persistent Hg exposure (Hu et al, 1997).

In sera of male workers exposed to mercury, autoantibodies (primarily IgG) to neuronal cytoskeletal proteins, neurofilaments (NFs), and myelin basic protein (MBP) were prevalent. These findings were confirmed in rats and mice, and there were significant correlations between IgG titers and subclinical deficits in sensorimotor function. These findings suggest that peripheral autoantibodies to neuronal proteins are predictive of neurotoxicity, since histopathological findings were associated with CNS and PNS damage. There was also evidence of astrogliosis (indicative of neuronal CNS damage) and the presence of IgG concentrated along the bbb (El-Fawal et al, 1999). Autoimmune response to mercury has also been shown by the transient presence of antinuclear antibodies (ANA) and antinucleolar antibodies (ANolA) (Nielsen & Hultman, 1999; Hu et al, 1997; Fagala and Wigg, 1992).

A high incidence of anti-cerebellar immunoreactivity which was both IgG and IgM in nature has been found in autism, and there is a higher frequency of circulating antibodies directed against neuronal antigens in autism as compared to controls (Plioplys, 1989; Connolly et al, 1999). Furthermore, Singh and colleagues have found that 50% to 60% of autistic subjects tested positive for the myelin basic protein antibodies (1993) and have hypothesized that autoimmune responses are related to an increase in select cytokines and to elevated serotonin levels in the blood (Singh, 1996; Singh, 1997). Weitzman et al

(1982) have also found evidence of reactivity to MBP in autistic subjects but none in controls.

Since anti-cerebellar antibodies have been detected in autistic blood samples, ongoing damage may arise as these antibodies find and react with neural antigens, thus creating autoimmune processes possibly producing symptoms such as ataxia and tremor. Relatedly, the cellular damage to Purkinje and granule cells noted in autism (see below) may be mediated or exacerbated by antibodies formed in response to neuronal injury (Zimmerman et al, 1993).

T-cells, monocytes, and natural killer cells: Many autistics have skewed immune-cell subsets and abnormal T-cell function, including decreased responses to T-cell mitogins (Warren et al, 1986; Gupta et al, 1996). One recent study reported increased neopterin levels in urine of autistic children, indicating activation of the cellular immune system (Messahel et al, 1998).

Workers exposed to Hg^{o} exhibit diminished capacity to produce the cytokines TNF (alpha) and IL-1 released by monocytes and macrophages (Shenkar et al, 1998). Both high dose and chronic low-level mercury exposure kills lymphocytes, T-cells, and monocytes in humans. This occurs by apoptosis due to perturbation of mitochondrial dysfunction. At low, chronic doses, the depressed immune function may appear asymptomatic, without overt signs of immunotoxicity. Methylmercury exposure would be especially harmful in individuals with already suppressed immune systems (Shenker et al, 1998). Mercury increases cytosolic free calcium levels [Ca2+]i in T lymphocytes, and can cause membrane damage at longer incubation times (Tan et al, 1993). Hg has also been found to cause chromosomal aberrations in human lymphocytes, even at concentrations below those causing overt poisoning (Shenkar et al, 1998; Joselow et al, 1972), and to inhibit rodent lymphocyte proliferation and function in vitro.

Depending on genetic predisposition, mercury causes activation of the immune system, especially Th2 subsets, in susceptible mouse strains (Johansson et al, 1998; Bagenstose et al, 1999; Hu et al, 1999). Many autistic children have an immune portrait shifted in the Th2 direction and have abnormal CD4/CD8 ratios (Gupta et al, 1998; Plioplys, 1989). This may contribute to the fact that many ASD children have persistent or recurrent fungal infections (Romani, 1999).

Many autistic children have reduced natural killer cell function (Warren et al, 1987; Gupta et al, 1996), and many have a sulfation deficiency (Alberti, 1999). Mercury reduces --SH group/sulfate availability, and this has immunological ramifications. As noted previously, decreased levels of glutathione, observed in autistic and mercury poisoned populations, are associated with impaired immunity (Aukrust et al, 1995 and 1996; Fuchs and Schöfer, 1997). Decreases in NK T-cell activity have in fact been detected in animals after methylmercury exposure (Ilback, 1991).

Singh detected elevated IL-12 and IFNg in the plasma of autistic subjects (1996). Chronic mercury exposure induces IFNg and IL-2 production in mice, while intermittent presence of mercury suppresses IFNg and enhances IL-4 production (Hu et al, 1997). Interferon

gamma (IFNg) is crucial to many immune processes and is released by T lymphocytes and NK cells, for example, in response to chemical mitogens and infection; sulfate participates in IFNg release, and "the effector phase of cytotoxic T-cell response and IL-2-dependent functions is inhibited by even a partial depletion of the intracellular glutathione pool" (Fuchs & Schöfer, 1997). A mercury-induced sulfation problem might, therefore, impair responses to viral (and other) infections - via disrupting cell-mediated immunity as well as by impairing NK function (Benito et al, 1998). In animals, Hg exposure has led to decreases in production of antibody-producing cells and in antibody titres in response to inoculation with immune-stimulating agents (EPA, 1997, review, p.3-84).

Table XII: Summary of Immune System Abnormalities in Mercury Exposure & Autism

Mercury	Autism
Individual sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies and asthma, autoimmune-like symptoms, especially rheumatoid-like ones	More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies
Can produce an immune response, even at low levels; can remain in CNS for years	Indications of on-going immune response in CNS
Presence of autoantibodies (IgG) to neuronal cytoskeletal proteins, neurofilaments, and myelin basic protein; astrogliosis; transient ANA and AnolA	Presence of autoantibodies (IgG and IgM) to cerebellar cells, myelin basis protein
Causes overproduction of Th2 subset; diminishes capacity to produce TNF(alpha) and IL-1; kills lymphocytes, T-cells, and monocytes; inhibits lymphocyte production; decreases NK T-cell activity; may induce or suppress IFN(gamma) and IL-2 production	Skewed immune-cell subset in the Th2 direction and abnormal CD4/CD8 ratios; decreased responses to T-cell mitogens; increased neopterin; reduced NK T-cell function; increased IFN(gamma) and IL-12

c. CNS Structure

Autism is primarily a neurological disorder (Minshew, 1996), and mercury preferentially targets nerve cells and nerve fibers (Koos and Longo, 1976). Experimentally, primates have the highest levels in the brain relative to other organs (Clarkson, 1992). Methylmercury easily crosses the blood-brain barrier by binding with cysteine to form a molecule that is nearly identical to methionine. This molecule - methylmercury cysteine - is transported on the Large Neutral Amino Acid across the bbb (Clarkson, 1992).

Once in the CNS, organic mercury is converted to the inorganic form (Vahter et al, 1994). Inorganic mercury is unable to cross back out of the bbb (Pedersen et al, 1999) and is more likely than the organic form to induce an autoimmune response (Hultman and Hansson-Georgiadis, 1999). Furthermore, although most cells respond to mercurial

injury by modulating levels of glutathione, metallothionein, hemoxygenase, and other stress proteins, "with few exceptions, neurons appear to be markedly deficient in these responses" and thus more prone to injury and less able to remove the metal (Sarafian et al, 1996).

While damage has been observed in a number of brain areas in autism, many functions are spared (Dawson, 1996). In mercury exposure, damage is also selective (Ikeda et al, 1999; Clarkson, 1992), and the list of Hg-affected areas is remarkably similar to the neuroanatomy of autism.

Cerebellum, Cerebral Cortex, & Brainstem: Autopsy studies of carefully selected autistic individuals revealed cellular changes in cerebellar Purkinje and granule cells (Bauman and Kemper, 1988; Ritvo et al, 1986). MRI studies by Courchesne and colleagues (1988; reviewed in ARI Newslett, 1994) described cerebellar defects in autistic subjects, including smaller vermal lobules VI and VII and volume loss in the parietal lobes. The defects were present independently of IQ. "No other part of the nervous system has been shown to be so consistently abnormal in autism." Courchesne (1989) notes that the only neurobiological abnormality known to precede the onset of autistic symptomatology is Purkinje neuron loss in the cerebellum. Piven found abnormalities in the cerebral cortex in seven of 13 high-functioning autistic adults using MRI (1990). Although more recent studies have called attention to amygdaloid and temporal lobe irregularities in autism (see below), and cerebellar defects have not been found in all ASD subjects studied (Bailey et al, 1996), the fact remains that many and perhaps most autistic children have structural irregularities within the cerebellum.

Mercury can induce cellular degeneration within the cerebral cortex and leads to similar processes within granule and Purkinje cells of the cerebellum (Koos and Longo, 1976; Faro et al, 1998; Clarkson, 1992; see also Anuradha, 1998; Magos et al, 1985). Furthermore, cerebellar damage is implicated in alterations of coordination, balance, tremors, and sensations (Davis et al, 1994; Tokuomi et al, 1982), and these findings are consistent with Hg-induced disruption in cerebellar synaptic transmission between parallel fibers or climbing fibers and Purkinje cells (Yuan & Atchison, 1999).

MRI studies have documented Hg-effects within visual and sensory cortices, and these findings too are consistent with the observed sensory impairments in victims of mercury poisoning (Clarkson, 1992; Tokuomi et al, 1982). Acrodynia, a syndrome with symptoms similar to autistic traits, is considered a pathology mainly of the CNS arising from degeneration of the cerebral and cerebellar cortex (Matheson et al, 1980). In monkeys, mercury preferentially accumulated in the deepest pyramidal cells and fiber systems.

Mercury causes oxidative stress in neurons. The CNS cells primarily affected are those which are unable to produce high levels of protective metallothionein and glutathione. These substances tend to inhibit lipid peroxidation and thereby suppress mercury toxicity (Fukino et al, 1984). Importantly, granule and Purkinje cells have increased risk for mercury toxicity because they produce low levels of these protective substances (Ikeda et al, 1999; Li et al, 1996). Naturally low production of glutathione, when combined with

mercury's ability to deplete usable glutathione reserves, provides a mechanism whereby mercury is difficult to clear from the cerebellum -- and this is all the more significant because glutathione is a primary detoxicant in brain (Fuchs et al, 1997).

Mercury's induction of cerebellar deterioration is not restricted to high-doses. Micromolar doses of methylmercury cause apoptosis of developing cerebellar granule cells by antagonizing insulin-like growth factor (IGF-I) and increasing expression of the transcription factor c-Jun (Bulleit and Cui, 1998).

Several researchers have found evidence of a brainstem defect in a subset of autistic subjects (Hashimoto et al, 1992 and 1995; McClelland et al, 1985); and MRI studies have revealed brainstem damage in a few cases of mercury poisoning (Davis et al, 1994). The peripheral polyneuropathy examined in Iraqi victims was believed to have resulted from brain stem damage (Von Burg and Rustam, 1974).

Amygdala & Hippocampus: Atypicalities in other brain areas are remarkably similar in ASD and mercury poisoning. Pathology affecting the temporal lobe, particularly the amygdala, hippocampus, and connected areas, is seen in autistic patients and is characterized by increased cell density and reduced neuronal size (Abell et al, 1999; Hoon and Riess, 1992; Otsuka, 1999; Kates et al, 1998; Bauman and Kemper, 1985). The basal ganglia also show lesions in some cases (Sears, 1999), including decreased blood flow (Ryu et al, 1999).

Mercury can accumulate in the hippocampus and amygdala, as well as the striatum and spinal chord (Faro et al, 1998; Lorscheider et al, 1995; Larkfors et al, 1991). One study has shown that areas of hippocampal damage from Hg were those which were unable to synthesize glutathione (Li et al, 1996). A 1994 study in primates found that mercury accumulates in the hippocampus and amygdala, particularly the pyramidal cells, of adults and offspring exposed prenatally (Warfvinge et al, 1994).

The documenting of temporal lobe mercury provides a direct link between autism and mercury because, as cited previously, (i) mercury alters neuronal function, and (ii) the temporal lobe, and the amygdala in particular, are strongly implicated in autism (e.g., Aylward et al, 1999; Bachevalier, 1994; Baron-Cohen, 1999; Bauman & Kemper, 1985; Kates et al, 1998; Nowell et al, 1990; Warfvinge et al, 1994). Bachevalier (1996) has shown that infant monkeys with early damage to the amygdaloid complex exhibit many autistic behaviors, including social avoidance, blank expression, lack of eye contact and play posturing, and motor stereotypies. Hippocampal lesions, when combined with amygdaloid damage, increases the severity of symptoms.

Also noteworthy is the fact that amygdala findings in autism and mercury literatures are paralleled in fragile X syndrome, a genetic disorder wherein many affected individuals have traits worthy of an autism diagnosis. These traits include sensory alterations, emotional lability, appetite dysregulation, social deficits, and eye-contact aversion (Hagerman). Not only are fraX-related proteins (FRM1, FMR2) implicated in amygdaloid function (Binstock, 1995; Yamagata, 1999), but neurons involved in gaze- and eye-contact-aversion have been identified within the primate temporal lobe and

amygdaloid subareas (Rolls 1992, reviewed in Binstock 1995). These various findings in ASD, mercury poisoning, and fragile X suggest that amygdaloid mercury is a mechanism for inducing traits central to or associated with autism and the autism-spectrum of disorders.

Neuronal Organization & Head Circumference: Several autism brain studies have found evidence of increased neuronal cell replication, a lowered ratio of glia to neurons, and an increased number of glial cells (Bailey et al, 1996). Based on these and other neuropathological findings, autism can be characterized as "a disorder of neuronal organization, that is, the development of the dendritic tree, synaptogenesis, and the development of the complex connectivity within and between brain regions" (Minshew, 1996).

Mercury can interfere with neuronal migration and depress cell division in the developing brain. Post-mortem brain tissue studies of exposed Japanese and Iraqi infants revealed "abnormal neuronal cytoarchitecture characterized by ectopic cells and disorganization of cellular layers" (EPA, 1997, p.3-86; Clarkson, 1997). Developmental neurtoxicity of Hg may also be due to binding of mercury to sulfhydryl-rich tubulin, a component of microtubules (Pendergrass et al, 1997). Intact microtubules are necessary for proper cell migration and cell division (EPA, review, 1997, p.32-88).

Rat pups dosed postnatally with methylmercury had significant reductions in neural cell adhesion molecules (NCAMs), which are critical during neurodevelopment for proper synaptic structuring. Sensitivity of NCAMs to methylmercury decreased as the developmental age of the rats increased. "Toxic perturbation of the developmentally-regulated expression of NCAMs during brain formation may disturb the stereotypic formation of neuronal contacts and could contribute to the behavioral and morphological disturbances observed following methylmercury poisoning" (Deyab et al, 1999). Plioplys et al (1990) have found depressed expression of NCAM serum fragments in autism.

Abnormalities in neuronal growth during development are implicated in head size differences found in both autism and mercury poisoning. In autism, Fombonne and colleagues (1999) have found a subset of subjects with macrocephaly and a subset with microcephaly. The circumference abnormalities were progressive, so that, while micro- and macrocephaly were present in 6% and 9% respectively of children under 5 years, among those age 10-16 years, the rates had increased to 39% and 24% respectively. Another study, by Stevenson et al (1997), had found just one subject out of 18 with macrocephaly who had this abnormality present at birth. The macrocephaly in autism is generally believed to result from "increased neuronal growth or decreased neuronal pruning." The cause of microcephaly has not been investigated.

The most detailed study of head size in mercury poisoning, by Amin-Zaki et al (1979), involved 32 Iraqi children exposed prenatally and followed up to age 5 years. Eight (25%) had progressive microcephaly, i.e., the condition was not present at birth. None had developed macrocephaly, at least at the time of the study. The microcephaly has been ascribed to neuronal death or apoptosis from Hg intoxication.

Table XIII: CNS Lesions in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Primarily impacts CNS	Neurological impairments primary
Selectively targets brain areas - those unable to detoxify heavy metals or reduce Hg-induced oxidative stress	Specific areas of brain pathology; many functions spared
Damage to Purkinje and granular cells	Damage to Purkinje and granular cells
Accummulates in amygdala and hippocampus	Pathology in amygdala and hippocampus
Causes abnormal neuronal cytoarchitecture; interferes with neuronal migration and depresses cell division in developing brains; reduces NCAMs	Neuronal disorganization; increased neuronal cell replication, small glia to neuron ration, increased glial cells; depressed expression of NCAMs
Head size differences: progressive microcephaly	Head size differences: progressive microcephaly and macrocephaly
Brain stem defects in some cases	Brain stem defects in some cases

d. Neurons & Neurochemicals

The brains of autistic subjects show disturbances in many neurotransmitters, primarily serotonin, catecholamines, the amino acid neurotransmitters, and acetylcholine. Mercury poisoning causes disturbances in these same neurotransmitters: primarily serotonin, the catecholamines, glutamate, and acetlycholine.

Serotonin: Serotonin synthesis is decreased in the brains of autistic children and increased in autistic adults, relative to age-matched controls (Chugani et al, 1999), while whole blood serotonin in platelets is elevated regardless of age (Leboyer; Cook, 1990). Autistic patients frequently respond well to SSRIs as well as Risperidone (McDougal; 1997; Zimmerman et al, 1996). Likewise, a number of animal studies have found serotonin abnormalities from mercury exposure. For example, subcutaneous administration of methylmercury to rats during postnatal development increases tissue concentration of 5-HT and HIAA in cerebral cortex (O'Kusky et al, 1988).

Findings about serotonin abnormalities in mercury literature implicate interactions between mercury and intracellular calcium as well as mercury and sulfhydral groups:

> Many researchers have documented disruptions of intra- and extra-cellular calcium in neurons from mercury exposure (Atchison & Hare, 1994), including thimerosal (Elferink, 1999), and calcium metabolism abnormalities have been identified in autism (Plioplys, 1989; Coleman, 1989).
>
> Intracellular concentrations of Ca2+ are critical for controlling gene expression in neurons and mediating neurotransmitter release from presynaptic vesicles (Sutton, McRory et al, 1999). 5-HT re-uptake activity

and intrasynaptic concentration of 5-HT are regulated by Ca2+ in nerve terminals. Methylmercury causes a rapid, irreversible block of synaptic transmission by suppression of calcium entry into nerve terminal channels (Atchison et al, 1986). Thimerosal inhibits 5-HT transport activity in particular through interaction with intracellular sulfhydryl groups associated with Ca2+ pump ATPase (Nishio et al, 1996), for example, by modifying cysteine residues of the Ca(2+)-ATPase (Sayers et al, 1993; Thrower et al, 1996).

Dopamine: Studies have found indications both of abnormally high and low levels of dopamine in autistic subjects (Gillberg & Coleman, 1992, p288-9). For example, Ernst et al (1997) reported low prefrontal dopaminergic activity in ASD children, while Gillberg and Svennerholm (1987) reported high concentrations of homovanillic acid (HVA), a dopamine metabolite, in cerebro-spinal fluid of autistic children, suggesting greater dopamine synthesis. Pyridoxine (vitamin B6) has been found to improve function in some autistic patients by lowering dopamine levels through enhanced DBH function (Gillberg & Coleman, 1992, p289; Moreno et al, 1992; Rimland & Baker, 1996). Dopamine antagonists such as haloperidol improve some antipsychotic symptoms in ASD subjects, including motor stereotypies (Lewis, 1996).

Rats exposed to mercury during gestation show major alterations in synaptic dynamics of brain dopamine systems. The effects were not apparent immediately after birth but showed a delayed onset beginning at the time of weaning (Bartolome et al, 1984). A variety of mercuric compounds increase the release of [3H]dopamine, possibly by disrupting calcium homeostasis or calcium-dependent processes (McKay et al, 1986). Minnema et al (1989) found that methylmercury increases spontaneous release of [3H]dopamine from rat brain striatum mainly due to transmitter leakage caused by Hg-induced synaptosomal membrane permeability. SH groups may also be involved in the inhibition of dopamine binding in rat striatum (Bonnet et al, 1994). Pyridoxine deficiency in rats causes acrodynia, with features similar to human acrodynia (Gosselin et al, 1984).

Epinephrine and norepinephrine: Studies on autistic subjects have consistently found elevated norepinephrine and epinephrine in plasma, which suggests elevated levels of these transmitters in brain, as plasma and CSF norepinephrine are closely correlated (Gillberg and Coleman, 1992, p.121-122). Recently, Hollander et al (2000) have noted improvement in function in about half of their ASD subjects with administration of venlafaxine, a norepinephrine reuptake inhibitor. Mercury also disrupts norepinephrine levels by inhibiting sulfhydryl groups and thus blocking the function of O-methyltransferase, the enzyme that degrades epinephrine (Rajanna and Hobson, 1985). In acrodynia, blocking this enzyme resulted in high levels of epinephrine and norepinephrine in plasma (Cheek, Pink Disease Website). In rats, chronic exposure to low doses of methylmercury increased brain-stem norepinephrine concentration (Hrdina et al, 1976).

Glutamate: It has been observed that many autistics have irregularities related to glutamate (Carlsson ML, 1998). In autism, glutamate and aspartate have been found to be significantly elevated relative to controls (Moreno et al, 1992); and in a more recent

study of ASD subjects, plasma levels of glutamic acid and aspartic acid were elevated even as levels of glutamine and asparagine were low (Moreno-Fuenmayor et al, 1996).

Mercury inhibits the uptake of glutamate, with consequent elevation of glutamate levels in the extracellular space (O'Carroll et al, 1995). Prenatal exposure to methylmercury of rats induced permanent disturbances in learning and memory which could be partially related to a reduced functional activity of the glutamatergic system (Cagiano et al, 1990). Thimerosal enhances extracellular free arachidonate and reduces glutamate uptake (Volterra et al, 1992). Excessive glutamate is implicated in epileptiform activities (Scheyer, 1998; Chapman et al, 1996), frequently present in both ASD and mercurialism (see below).

Acetylcholine: Abnormalities in the cortical cholinergic neurotransmitter system have recently been reported in a post mortem brain study of adult autistic subjects (Perry et al, 2000). The problem was one of acetylcholine deficiency and reduced muscarinic receptor binding, which Perry suggests may reflect intrinsic neuronal loss in hippocampus due to temporal lobe epilepsy (see section below for discussions of epilepsy and ASD/Hg). Mercury alters enzyme activities (Koos and Longo, 1976, p.400), including choline acetyltransferase, which may lead to acetylcholine deficiency (Diner and Brenner, 1998), or Hg may inhibit acetylcholine release due to its effects on Ca2 homeostasis and ion channel function (EPA, 1997, p.3-79). In rats, chronic exposure to low doses of methylmercury decreased cortical acetylcholine levels (Hrdina et al, 1976). Methylmercury has also been found to increase spontaneous release of [3H]acetylcholine from rat brain hippocampus (Minnema et al, 1989) and to increase muscarinic cholinergic receptor density in both rat hippocampus and cerebellum, suggesting upregulation of these receptors in these selected brain regions (Coccini, 2000).

Demyelination: Evidence of demyelination has been observed in the majority of autistic brains (Singh, 1992). This is true of mercury poisoning as well. Mild demyelinating neuropathy was detected in two girls (Florentine and Sanfilippo, 1991), and an adult showed axonal degeneration with Hg-related demyelination (Chu et al, 1998). Methylmercury can alter the fatty acid composition of myelin cerebrosides in suckling rats (Grundt et al, 1980).

Table XIV: Abnormalities in Neurons & Neurochemicals from Mercury & in Autism

Mercury	Autism
Can increase tissue concentration of serotonin in newborn rats; causes calcium disruptions in neurons, preventing presynaptic serotonin release and inhibiting serotonin transport activities	Serotonin abnormalities: decreased serotonin synthesis in children; over-synthesis in adults; elevated serotonin in platelets; positive response to SSRIs; calcium metabolism abnormalities present
Alters dopamine systems; disrupts calcium and increases synaptosome membrane permeability, which affect dopamine activities; peroxidine deficiency in rats results in acrodynia	Indications of either high or low dopamine levels; positive response to peroxidine by lowering dopamine levels; positive response to dopamine antagonists
Increases epinephrine and norepinephrine levels by blocking the enzyme which degrades epinephrine	Elevated norepinephrine and epinephrine; positive response to norepinephrine reuptake inhibitors
Elevates glutamate; decreases glutamate uptake; reduces functional activity of glutamatergic system	Elevated glutamate and aspartate
Alters choline acetyltransferase, leading to acetylcholine deficiency; inhibits acetylcholine neurotransmitter release via impact on calcium homeostasis; causes cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus and cerebellum	Abnormalities in cholinergic neurotransmitter system: cortical acetylcholine deficiency and reduced muscarinic receptor binding in hippocampus
Causes demyelating neuropathy	Demyelation in brain

e. EEG Activity/Epilepsy

Abnormal EEGs are common in mercury poisoning as well as autism. In one study, half the autistic children expressed abnormal EEG activity during sleep (reviewed in LeWine, 1999). Gillberg and Coleman (1992) estimate that 35%-45% of autistics eventually develop epilepsy. A recent study by LeWine and colleagues (1999) using MEG found epileptiform activity in 82% of 50 regressive-autistic children. EEG abnormalities in autistic populations tend to be non-specific and consist of a variety of epileptiform discharge patterns (Nass, Gross, and Devinsky, 1998).

Unusual epileptiform activity has been found in a variety of mercury poisoning cases (Brenner & Snyder, 1980). These include (i) the Minamata outbreak - generalized convulsions and abnormal EEGs (Snyder, 1972); (ii) methylmercury ingestion through contaminated pork - all four affected children had epileptiform features and disturbances of background rhythms; two had seizures (Brenner & Snyder, 1980); (iii) mercury vapor poisoning - abnormal EEG in a 12 year old girl (Fagala and Wigg, 1992) and slower and attenuated EEGs in chloralkali workers with long term exposure (Piikivi & Tolonen, 1989); and (iv) exposure from thimerosal in ear drops and through IVIG - EEG with generalized slowing in an 18 month old girl with otitis media (Rohyans et al, 1984) and a

44 year old man (Lowell et al, 1996). More recently, Szasz and colleagues (1999), in a study of early Hg-exposure, described methylmercury's ability to enhance tendencies toward epileptiform activity and reported a reduced level of seizure-discharge amplitude, a finding which is at least consistent with the subtlety of seizures in many autism spectrum children (LeWine, 1999; Nass, Gross, and Devinsky, 1998).

Processes whereby neuronal damage is induced by epileptiform discharges are elucidated in a number of studies, many of which focus upon brain regions affected in autism. Importantly, neuronal damage in the amygdala can be an "ongoing delayed process," even after the cessation of seizures (Tuunanen et al, 1996, 1997, 1999). Alterations of cerebral metabolic function last long after seizures have occurred. In a model of seizure-induced hippocampal sclerosis, Astrid Nehlig's group describes hypometabolism having its regional boundaries "directly connected" to seizure-damaged locus (Bouilleret et al, 2000). That Hg increases extracellular glutamate would also contribute to epileptiform activity (Scheyer, 1998; Chapman et al, 1996).

These findings support a rationale:

> In susceptible individuals, mercury can potentiate or induce Hg-related epileptiform activity, which can have lower amplitude and be harder to identify. Furthermore, this low-level but persisting epileptiform activity would gradually induce cell death in the seizure foci and in brain nuclei neuroanatomically related to the seizure foci.

These studies have a more direct relevance to the possibility of Hg-induced cases of autism (i) because the amygdala are implicated in regard to core traits in autism, as described above, and (ii) because mercury finds its way into the amygdala (see above). Furthermore, these theoretical relationships are consistent with SPECT imaging studies by Mena, Goldberg, and Miller, who have demonstrated areas of regional hypoperfusion neuroanatomically associated with trait deficits in autism-spectrum children (Goldberg et al, 1999).

Table XV: EEG Activity & Epilepsy in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Causes abnormal EEGs and unusual epileptiform activity	Abnormal EEG activity; epileptiform activity
Causes seizures, convulsions	Seizures; epilepsy
Causes subtle, low amplitude seizure activity	Subtle, low amplitude seizure activities

III. MECHANISMS, SOURCES & EPIDEMIOLOGY OF EXPOSURE

a. Exposure Mechanism

Vaccine injections are a known source of mercury (Plotkin and Orenstein, 1999), and the typical amount of mercury given to infants and toddlers in this manner exceeds government safety limits, according to Neal Halsey of the American Academy of Pediatrics (1999) and William Egan of the Biologics Division of the FDA (1999).

Most vaccines given to children 2 years and under are stored in a solution containing thimerosal, which is 49.6% mercury by weight. Once inside humans, thimerosal (sodium ethylmercurithio–salicylate) is metabolized to ethylmercury and thiosalicylate (Gosselin et al, 1984). The vaccines mixed with this solution are DTaP, HIB, and Hepatitis B (Egan, 1999). Thimerosal is not an integral component of vaccines, but is a preservative added to prevent bacterial contamination. Many vaccine products are available without the thimerosal preservative; however, these alternatives have not been widely used (Egan, 1999). In addition, thimerosal is used during the manufacturing process for a number of vaccines, from which trace amounts are still present in the final injected product (FDA, personal communication; Smith-Kline press release on Hepatitis B, March 31, 2000).

Since at least 1977 clinicians have recognized thimerosal as being potentially dangerous, especially in situations of long term exposure (Haeney et al, 1979; Rohyans et al, 1984; Fagan et al, 1977; Matheson et al, 1980). For nearly twenty years the US government has also singled out thimerosal as a potential toxin (FDA, 1982). In response to the Food and Drug Administration (FDA) Modernization Act of 1997, which called for the FDA to review and assess the risk of all mercury containing food and drugs (*MMWR*, 1999, July 9), the FDA issued a final rule in 1998 stating that over-the-counter drug products containing thimerosal and other mercury forms "are not generally recognized as safe and effective" (FDA, 1998). In December 1998 and April 1999, the FDA requested US vaccine manufacturers to provide more information about the thimerosal content in vaccines (*MMWR*, 1999, July 9); and in July 1999, the CDC asked manufacturers to start removing thimerosal from vaccines and rescheduled the Hepatitus B vaccine so it is given at 9 months of age instead of at birth (CDC, July 1999). In November 1999, the CDC repeated its recommendation that vaccine manufacturers move to thimerosal-free products (CDC, November 1999).

Importantly, based on the CDC's own recommended childhood immunization schedule (and excluding any trace amounts), the amount of mercury a typically vaccinated two year old child born in the 1990s would receive is 237.5 micrograms; and a typical six month old might receive 187.5 micrograms (Egan, 1999). These amounts equate to 3.53 x 10^{17} molecules and 2.79 x 10^{17} molecules of mercury respectively (353,000,000,000,000,000 and 279,000,000,000,000,000 molecules). Since thimerosal is injected during vaccinations, the mercury is given intermittently in large, or 'bolus', doses: at birth and at 2, 4, 6, and approximately 15 months (Egan, 1999). The amount of mercury injected at birth is 12.5 micrograms, followed by 62.5 micrograms at 2 months, 50 micrograms at 4 months, another 62.5 micrograms during the infant's 6-month immunizations, and a final 50 micrograms at about 15 months (Halsey, 1999).

Although infancy is recognized as a time of rapid neurological development, to the best of our belief and knowledge, there are no published studies on the effect of injected ethylmercury in intermittent bolus doses in infants from birth to six months or to 2 years (Hepatitis Control Report, 1999; *Pediatrics*, 1999; EPA, 1997, p.6-56). In contrast, four government agencies have set safety thresholds for daily mercury exposure based on ingested fish or whale meat containing methylmercury. Two of these guidelines are based on adult values and two are for pregnant women/fetuses (Egan, 1999). Applying these guidelines to a bolus dose scenario (see Halsey, 1999 for bolus vs. daily dose discussion), the sum of Hg-doses given at 6 months of age or younger, correlated to infant weights, exceed all of the Hg-total guidelines for all infants. The 2 month dose is especially high relative to the typical infant body weight. Halsey (1999) has calculated the 2 month dose to be over 30 times the recommended daily maximum exposure, with babies of the smallest weight category receiving almost three months worth of daily exposures on a single day.

Halsey's observation is all the more important because even at doses which were not previously thought to be associated with adverse affects, mercury has resulted in some damage to humans (Grandjean et al, 1998). Given that ethylmercury is equally neurotoxic as methylmercury (Magos et al, 1985), and that injected mercury is more harmful than ingested mercury (EPA, 1997, p.3-55; Diner and Brenner, 1998), the amount of injected ethylmercury given to young children is cause for concern. The potential for Hg-induced harm is compounded by the special vulnerability of infants (Gosselin et al, 1984). Mercury, which primarily affects the central nervous system, is most toxic to the developing brain (Davis et al, 1994; Grandjean et al, 1999; Yeates and Mortensen, 1994), and neonates exposed to methyl (organic) mercury have been shown to accumulate significantly more Hg in the brain relative to other tissues than do adults (EPA, 1997, p.4-1). Mercury may also be more likely to enter the infant brain because the blood-brain barrier has not fully closed (Wild & Benzel, 1994). In addition, infants under 6 months are unable to excrete mercury, most likely due to their inability to produce bile, the main excretion route for organic mercury (Koos and Longo, 1976; Clarkson, 1993). Bakir et al (1973) have shown that those with the longest half-time of clearance are most likely to experience adverse sequelae, while Aschner and Aschner (1990) have demonstrated that the longer that organic mercury remains in neurons, the more it is converted to its inorganic irreversibly-bound form, which has greater neurotoxicity.

b. Population Susceptibility

Nearly all children in the United States are immunized, yet only a small proportion of children develop autism. The NIH (Bristol et al, 1996) estimates the current prevalence of autism to be 1 in 500. A pertinent characteristic of mercury is the great variability in its effects by individual. At the same exposure level of mercury, some will be affected severely, while others will be asymptomatic or only mildly impaired (Dale, 1972; Warkany and Hubbard, 1953; Clarkson, 1997). A ten-fold difference in sensitivity to the same exposure level has been reported (Koos and Longo, 1976; Davis et al, 1994; Pierce et al, 1972; Amin-Zaki, 1979). An example of variability in children is the mercury-induced disease called acrodynia. In the earlier half of this century, from one in 500 to one in 1000 children exposed to the same chronic, low-dose of mercury in teething

powders developed this disorder (Matheson et al, 1980; Clarkson, 1997), and the likelihood of developing the disease "appears to be dominated more by individual susceptibility and possibly age rather than the dose of the mercury" (Clarkson, 1992). Given the documented inter-individual variability of responses to Hg, and the young age at which exposure occurs, the doses of mercury given concurrently with vaccines are such that only a certain percentage of children will develop overt symptoms, even as other children might have trait irregularities sufficiently mild as to remain unrecognized as having been induced by mercury.

c. Sex Ratio

Autism is more prevalent among boys than girls, with the ratio generally recognized as approximately 4:1 (Gillberg & Coleman, 1992, p.90). Mercury studies have consistently shown a greater effect on males than females, except in instances of kidney damage (EPA, 1997). At the highest doses, both sexes are affected equally, but at lower doses only males are affected. This is true of mice as well as humans (Sager et al, 1984; Rossi et al, 1997; Clarkson, 1992; Grandjean et al, 1998; McKeown-Eyssen et al, 1983; see also review in EPA, 1997, p.6-50).

d. Exposure Levels & Autism Prevalence

Perhaps not coincidentally, autism's initial description and subsequent epidemiological increase mirror the introduction and use of thimerosal as a vaccine preservative. In the late 1930s, Leo Kanner, an experienced child psychologist and the "discoverer" of autism, first began to notice the type of child he would later label "autistic." In his initial paper, published in 1943, he remarked that this type of child had never been described previously: "Since 1938, there have come to our attention a number of children whose condition differs so markedly and uniquely from anything reported so far, that each case merits...a detailed consideration of its fascinating peculiarities." All these patients were born in the 1930s. Thimerosal was introduced as a component of vaccine solutions in the 1930s (Egan, 1999).

Not only does the effect of mercury vary by individual, as noted above, it also varies in a dose-dependent manner, so that the higher the exposure level, the more individuals that are affected. At higher dose levels, the most sensitive individuals will be more severely impaired, and the less sensitive individuals will be only moderately impaired, and the majority of individuals may still show no overt symptoms (Nielson and Hultman, 1999). The vaccination rate, and hence the rate of mercury exposure via thimerosal, has steadily increased since the 1930s. In 1999 it was the highest ever, at close to 90% or above, depending on the vaccine (CDC, 1999, press release). The rate of autism has increased dramatically since its discovery by Kanner: prior to 1970, studies showed an average prevalence of 1 in 2000; for studies after 1970, the average rate had doubled to 1 in 1000 (Gillberg and Wing, 1999). In 1996, the NIH estimated occurrence to be 1 in 500 (Bristol et al, 1996). A large increase in prevalence, yet to be confirmed by stricter epidemiological analysis, appears to be occurring since the mid-1990s, as evidenced by several state departments of education statistics reflecting substantial rises in enrolment of ASD children (California, Florida, Maryland, Illinois, summarized by Yazbak, 1999). These increases have paralleled the increased mercury intake induced by mandatory innoculations: in 1991, two vaccines, HIB and Hepatitis B, both of which generally

include thimerosal as a preservative, were added to the recommended vaccine schedule (Egan, 1999).

e. Genetic Factors

ASD is one of the most heritable of developmental and psychiatric disorders (Bailey et al, 1996). There is 90% concordance in monozygotic twins and a 3-5% risk of autism in siblings of affected probands (Rogers et al, 1999), a rate 50 to 100 times higher than would be expected in the general population (Smalley & Collins, 1996; Rutter, 1996). From 2 to 10 genes are believed to be involved (Bailey et al, 1996).

Individual differences in susceptibility to mercury are said to arise from genetic factors and these too may be multiple in nature (Pierce et al, 1972; Amin-Zaki, 1979). They include innate differences in (i) the ability to detoxify heavy metals, (ii) the ability to maintain balanced gut microflora, which can impair detoxification processes, and (iii) immune over-reactivity to mercury (Nielson and Hultman, 1999; Hultman and Nielson, 199; Johansson et al, 1998; Clarkson, 1992; EPA, review 1997, p.3-26). Many autistic children are described as having (i) difficulties with detoxification of heavy metals (Edelson & Cantor, 1998), possibly due to low glutathione levels (O'Reilly and Waring, 1993), (ii) intestinal microflora imbalances that can impede excretion (Shattock, 1997), and (iii) autoimmune dysfunction (Zimmerman et al, 1993). These characteristics might be reflective of the underlying "susceptibility genes" that predispose to mercury-induced sequelae and hence to autism.

As noted above, autism family studies show an exceptionally high concordance rate of 90% for identical twins. Most environmental factors, such as a postnatal viral infection, tend not to be present at exactly the same time or at the same level or rate for each twin. This would cause a difference in phenotype expression, and thus postnatal environmental influences in general reduce the concordance rate for identical twins. However, given the extremely high vaccination rate and the high likelihood of vaccination of one twin at the same time and with the same vaccines as the other twin, mercury-induced autism via vaccination injection, even though it is an environmental factor, would still lead to the high concordance rate seen in twins.

Furthermore, among identical twin pairs, the 90% concordance rate is for the milder phenotype: if one twin has pure classic autism, there is (i) a 60% chance that the other twin will have pure classic autism; (ii) a 30% chance that the other twin will exhibit some type of impairment falling on the autism spectrum, but with less severe symptoms; and (iii) a 10% chance the other twin will be unimpaired. The difference in symptom severity among the 40% of monozygotic pairs who do not exhibit classic autism may arise from either (i) a different vaccination history within pairs, or (ii) the tendency of thimerosal to "clump" or be unevenly distributed in solution, so that one twin might receive more or less mercury than the other. One study found a 62% difference in the mercury concentration of ampoules drawn from the same container of immunoglabulin batches containing thimerosal (Roberts and Roberts, 1979).

f. Course of Disease

Age of onset: Autism emerges during the same time period as infant and toddler thimerosal injections during vaccinations. As noted above, the recommended childhood vaccination schedule from 1991 to 1999 has called for injections of thimerosal starting at birth and continuing at 2, 4, 6, and approximately 15 months (Halsey, 1999); a similar schedule occurred prior to this time but for DTP alone. In the great majority of cases, the more noticeable symptoms of autism emerge between 6 and 20 months old – and mostly between 12 and 18 months (Gillberg & Coleman, 1992). Teitelbaum et al (1998), who have claimed the ability to detect subtle abnormalities at the youngest age so far, have observed these abnormalities at 4 months old at the earliest, the exception being a "Moebius mouth" seen at birth in a small number of subjects.

Symptoms of mercury poisoning do not usually appear immediately upon exposure, although in especially sensitive individuals or in cases of excessive exposure they can (Warkany and Hubbard, 1953; Amin-Zaki, 1978). Rather, there is generally a preclinical "silent stage," seen in both animals and humans, during which subtle neurological changes are occurring (Mattsson et al, 1981). The delayed reaction between exposure and overt signs can last from weeks to months to years (Adams et al, 1983; Clarkson, 1992; Fagala & Wigg, 1992; Davis et al, 1994; Kark et al, 1971). Consequently, mercury given in vaccines before age 6 months would not in most individuals lead to an observable or recognizable disorder, except for subtle signs, prior to age 6-12 months, and for some individuals, symptoms induced by early vaccinal Hg might not emerge until the infant had become a toddler (Joselow et al, 1972).

A few autism researchers have suggested a prenatal onset for autism (Rodier et al, 1997; Bauman & Kemper, 1994), which would preclude a vaccinal-mercury etiology. Others, however, have evidence that suggest post-natal timings (Bailey, 1998; Courchesne, 1999; Bristol Power, NICHD, Dateline Interview, 1999). The general consensus at this point is that the timing cannot be determined (Bailey et al, 1996; Bristol et al, 1996); and, further, that there is "little evidence" that prenatal or perinatal events "predict to later autism" (Bristol et al, 1996), even though clustering of adverse effects (suboptimality factors) are associated with autism (Prechtel, 1968; Bryson et al, 1988; Finegan and Quarrington, 1979). There is also a general agreement that, in the great majority of cases, autistic signs emerge among infants and toddlers who had looked "normal", developed normally, met major milestones, and had unremarkable pediatric evaluations (Gillberg & Coleman, 1992; Filipek et al, 1999; Bailey et al, 1996), so that autism presents as an obvious deterioration or regression, either before age two or before age three (Baranek, 1999; Bristol Power, NICHD, Dateline Interview, 1999; LeWine, 1999).

It is worthwhile to note that early and intensive educational and behavioral intervention can produce dramatic gains in function, and the gains made by these children "may be somewhat unique among the more severe developmental disabilities" (Rogers, 1996). This phenomenon further suggests that autism arises from an environmental overlay rather than being purely an organic disease. Additionally, at least one study has reported that "re-education and physical treatment" can improve outcomes in mercurialism (Amin-zaki, 1978).

Emergence of symptoms: The manner in which symptoms emerge in many cases of autism is consistent with a multiple low-dose vaccinal exposure model of mercury poisoning. From a parent's and pediatrician's perspective, such an individual is a "normal" looking child who regresses or fails to develop after thimerosal administration. Clinically relevant symptoms generally emerge gradually over many months, although there have been scattered parental reports of sudden onset (Filipek, et al, 1999). The initial signs, occurring shortly after the first injections, are subtle, suggesting disease emergence, and consist of abnormalities in motor behavior and in sensory systems, particularly touch sensitivity, vision, and numbness in the mouth (excessive mouthing of objects) (Teitelbaum et al, 1998; Baranek, 1999). These signs persist and are followed by parental reports of speech and hearing abnormalities appearing before the child's second birthday (Prizant, 1996; Gillberg & Coleman, 1992), that is, within several months of when additional and final injections are given. Finally, in year two, there is a full blossoming of ASD traits and a continuing regression or lack of development, so that the most severe expression of symptoms occurs at approximately 3-5 years of age. These symptoms then begin to ameliorate (Church & Coplan, 1995; Wing & Attwood, 1987; Paul, 1987). The exceptions are the subset of those with regression during adolescence or early adulthood, which may involve onset of seizures and associated neurodegeneration (Howlin, 2000; Paul, 1987; Tuunanen et al, 1996, 1997, 1999).

As in autism, onset of Hg toxicity symptoms is gradual in some cases, sudden in others (Amin-Zaki et al, 1979 & 1978; Joselow et al, 1972; Warkany and Hubbard, 1953). In the case of organic poisoning, the first signs to emerge are abnormal sensation and motor disturbances; as exposure levels increase, these signs are followed by speech and articulation problems and then hearing deficits (Clarkson, 1992), just like autism. Once the mercury source is removed symptoms tend to ameliorate (though not necessarily disappear) except in instances of severe poisoning, which may lead to a progressive course or death (Amin-Zaki et al, 1978). As in autism, epilepsy in Hg exposure also predicts a poorer outcome (Brenner & Snyder, 1980).

Long term prognosis: The long term outcomes of ASD and mercury poisoning show the same wide variation. Autism is viewed as a lifelong condition for most; historically, three-fourths of autistic individuals become either institutionalized as adults or are unable to live independently (Paul, 1987). There are, however, many instances of partial to full recovery, in which autistic traits persist in a much milder form or, in some individuals, disappear altogether once adulthood is reached (Rogers, 1996; Church & Coplan, 1994; Szatmari et al, 1989; Rimland 1994; Wing & Attwood, 1987).

Upon exposure, mercury entering the bloodstream tends to accumulate in tissues and organs, primarily the brain (Koos and Long, 1976; Lorscheider et al, 1995). Once inside tissues, and particularly the brain, mercury will linger for years, as shown on X rays of a poisoned man 22 years after exposure (Gosselin et al, 1984), as well as autopsies of humans with known mercury exposure (Pedersen et al, 1999; Joselow et al, 1972) and primate studies (Vahter et al, 1994). The continued presence of mercury in organs and the CNS in particualr would explain why autistic symptoms might persist, why researchers such as Zimmerman or Singh would detect an on-going immune reaction,

why epilepsy might not emerge until adolescence, or why sulfate transporters in the intestine or kidney might continue to be blocked.

Nevertheless, despite the continued presence of Hg in tissue, the degree of recovery from mercurialism varies greatly. Even in severe cases, there are reports of full or partial recovery (e.g., Adams et al, 1983; Vroom & Greer, 1972; Amin-Zaki et al, 1978). In less severe cases, especially those in which exposure occurs early in life, the more severe symptoms may ameliorate over time, but milder impairments remain, especially neurological ones (Feldman, 1982; Yeates & Mortensen, 1994; Amin-Zaki, 1974 & 1978; Mathiesin et al, 1999; Vroom and Greer, 1972; EPA 1997, pp.3-10, 3-14, and 3-75). The wide variation in outcome is believed to be due, again, to individual sensitivity to mercury, in this case, the ability of some victims to develop "immunity" or a "tolerance" to Hg even when the metal is still present in tissue (Warkany & Hubbard, 1953).

Course of Disease:
Typical Autism & Ingested Organic Mercury

Typical Autism Progression & Thimerosal Administration

Birth	2 mos	4 mos	6 mos	15 mos	2 yrs	3-5 yrs	6-18 yrs	Adults
Hg dose	Hg dose	Hg dose	Hg dose	Hg dose				
Delay (no signs).	Delay (no signs)	subtle signs – move-ment	subtle signs - sensory	definite signs - hearing & speech	full array of symptoms	Height of symptom severity	Sympto m amelioration	Occasion -al full or partial recovery

Temporal & Dose-Response Relationship for Effects of Ingested Methylmercury

Hg dose	Delay (no signs)	1st sign – sensory	2nd sign – move-ment	3rd sign – speech/ art-iculation	4th sign – hearing	full array of symp-toms	Sympto m amelioration (or death)	full or partial recovery

g. Thimerosal Interaction with Vaccines

As noted above, for most ASD children symptom onset is gradual, but for a significant minority it is sudden. Additionally, many parents believe there is a connection between their child's autism and his or her immunizations. The Cure Autism Now Foundation, for example, reports that half the parents who call its hotline mention such a connection (Portia Iversen, CAN president, personal communication). The association extends not only to the mercury-containing vaccines – DTP/DTaP, HIB, and Hepatitis B – but also to those without thimerosal, particularly the MMR (Bernard Rimland, president, Autism Research Institute, personal communication). Parents may describe a variety of post-vaccine scenarios: a fever followed by a short recovery period and then a more gradual symptom onset; onset of symptoms immediately and suddenly after inoculation with or without fever; or even a mildly impaired child whose condition worsened after vaccination (CAN Parent Advisory Board Internet list; St. John's Autism Internet list).

While it is possible that any temporal association between vaccination and emergence of autism is due to chance, Warkany and Hubbard, who successfully proved the connection

between acrodynia and mercury poisoning to the medical community 50 years ago, offer alternate explanations. In their 1953 article in *Pediatrics*, they made the following points:

(a) They noted that high fever accompanied by a rash after mercury administration can be signs of a "typical, acute, mercurial reaction," and "acrodynia may follow, immediately or after short intervals, acute idiosyncratic reactions to mercury." This reaction was independent of hypersensitivity to mercury, as detected from skin tests, as they reported that only 10% of acrodynia victims responded positively to Hg on patch tests.

Thus in ASD, the fevers and deteriorations seen by parents immediately after a thimerosal-containing vaccine injection may be a systemic reaction (and not a hypersensitivity response) to the mercury content, and this reaction may subsequently progress to the emergence of autism, just as topical mercury administration produced fever and then acrodynia over 50 years ago.

(b) Warkany and Hubbard provided some tentative observations that the administration of a vaccine, irrespective of whether or not it contains thimerosal, can set off a reaction to any mercuric compound that may also be given to a child, which in the case of acrodynia, would be topical mercury in powders or rinses. This inter-reactivity might explain the pronounced effects from the MMR among subsequently-diagnosed autistic children:

> "[One patient] underwent a fourteen day course of antirabies injections six weeks before outbreak of acrodynia. Ten days after completion of the therapy she was treated with ammoniated mercury ointment and subsequently acrodynia developed...[In another case] antirabies treatment preceded the disease by three months. In several children various immunization procedures preceded the onset of acrodynia in addition to [topical] mercurial exposure. This could be purely coincidental or the vaccination material may play a role as an accessory factor. It is noteworthy that many vaccines and sera contain small amounts of mercury as preservatives which are injected together with the biologic material. These small amounts of mercurial compounds could act as sensitizing substances. In several instances vaccination against smallpox preceded the development of acrodynic symptoms, and some patients were exposed to bismuth, arsenic, lead, and antimony in addition to mercury. Such observations deserve attention."

(c) Finally, these two researchers observed that some individuals would react to mercury and then, upon re-exposure, not show any effects, i.e., they had acquired an unexplained tolerance to it. In other cases, Hg sensitivity would be maintained. Rarely, though, would reactivity occur with the first dose: "more often the patient tolerates several" before the reaction occurs.

> "The organism can harbor appreciable amounts of mercury while remaining in perfect health, and then, for unknown reasons, these innocuous stores of mercury become toxic. It seems in such cases as if the barriers which held the mercury in check break down without provocation, or as if the mercury had been converted from a nontoxic to a toxic form..."

In ASD, this delayed sensitivity would explain why some might develop autism later, not after the first few vaccines, and it would also explain in part why the more vaccines that are given, the more likely it is that a given individual will develop a reaction since there are more "sensitizing" opportunities. Importantly, in susceptible individuals, the reactions described by Warkany and Hubbard are likely to occur if mercury's presence occurred via injected thimerosal.

IV. DETECTION OF MERCURY IN AUTISTIC CHILDREN

In the past, hair, urine, or blood tests from autistic subjects have mostly found lead rather than mercury (Wecker et al, 1985), but this is likely due (i) to lead's pervasiveness in our environment, coupled with autistic children's pica tendencies and general inability to detoxify *any* heavy metal (LaCamera and LaCamera, 1987; Edelson & Cantor, 1998); (ii) to the difficulty in detecting Hg, especially in older children exposed early in life, since remaining mercury is sequestered in tissue; and (iii) to the greater affinity of standard chelators used in challenge tests (e.g., DMSA) for lead over mercury, making lead more readily detectable in such exams (Frackelton and Christenson, 1998).

More recently, a number of parents of younger autistic children, in whom mercury is more likely to be detectable, have reported higher than expected levels of mercury in hair, blood, and urine samples. Cases studies are listed below, and more are in the process of documentation. Several parents have also noted improved function after chelation.

The Case Studies

We are providing data from several retrospective case studies of autistic children with associated tissue mercury burdens. In each case we have tried to identify potential sources of exposure, although we have not been able to identify the exact amounts in some cases due to inadequate documentation. This information does not purport to be a rigid scientific study, but rather an initial effort to demonstrate that there may be a problem with mercury toxicity in children with autism. Our primary objective is to show that considerable amounts of mercury are found in the bodies of some autistic children. The data we present were derived from many sources: hair, urine and blood. Some of the samples were baseline and others were obtained utilizing a provocative agent, either DMPS or DMSA. Typically a single dose of DMPS will provoke more mercury from the tissue than a single oral dose of DMSA. Excretion levels will also vary depending on the amount of DMPS or DMSA given. There are also variations among these factors in the case studies.

Identifier: 0001SM **Sex**: M **Age**: 5 **DOB**: 4-25-94

Prenatal and Postnatal History: Premature contractions, which required bedrest during the 2nd and 3rd trimesters. Scheduled C-section at term with good apgars. Birth weight 8 lbs. 3 oz. Vomiting milk based formula, which subsided with a switch to soy formula at 2 months.

Developmental Landmarks: Completely normal development, meeting all developmental milestones until 20 months of age. Speech present with two word phrases.

Regression and Symptoms: At 20 months an unexplained loss of speech and eye contact (lateral gaze). He began lining up trains, developed preservations, and showed a marked decrease in attention. Diagnosed autistic at 26 months of age. Formal psychological evaluation at 30 months found expressive speech at 14-16 months, cognitive at 12-18 months, fine motor at 18 months, and play skills at 12 months. He

was described as withdrawn with alternating inattention or repetitive manipulation of objects.

Exposure Sources: He received multiple vaccines with thimerosal preservatives his first year, including influenza vaccine. The documented exposure the first year was 136.5mcg mercury. Mother with 1 amalgam filling and minimal dietary exposure. Child with no dietary exposure the first year of life. Families estimated consumption of seafood 3 times monthly.

Mercury Levels: Hair mercury 2.6 mcg with a norm reference of less than 2mcg. DMPS provacation (3mg per kg. IV) 7-7-99 resulted in 87 mcg mercury per g urinary creatine. Intermittent treatment with oral DMSA continued for 2 months with normalization of hair mercury levels.

Response to Treatment: Parents claim significant improvement in speech and behavior, also documented on neuropsychological evaluation on 1-14 and 1-21-00. "His ability to use language for social purposes has clearly increased and he could maintain exchanges for several turns without excessive difficulty. He has improved in his ability to initiate interactions and invitation to other children to play. Academic function at or above grade level. Impressive and highly encouraging rate of progress."

Identifier: 0002CM **Sex**: M **Age**: 5 **DOB**: 12-1-94

Prenatal and Postnatal History: Unremarkable prenatal course. Birth weight 8lbs.8oz. Maintained above the 95th percentile for height and weight the first year of life.

Developmental Landmarks: All early developmental landmarks - crawling, walking, and talking - were obtained on schedule.

Regression and Symptoms: Child went from age appropriate to severe autistic regression between 18 to 20 months. He lost speech, eye contact and became inattentive and withdrawn. Symptoms at 3 years include extreme thirst, echolalia, toe walking, high pain threshold, sleep disturbances, hyperactivity and obsessive behaviors.

Exposure Sources: No maternal amalgam history and minimal dietary exposure. He received all recommended vaccines, although without manufacturer data we are unable to calculate total exposure at this time. Known exposure from hepatitis B vaccine, 37.5 mcg mercury.

Mercury Levels: Hair mercury was 2.21ppm at 3 years and 3 months of age with a lab reference of 0-1.5ppm. DMPS provocation utilizing 3 mg. DMPS/kg given IV revealed:

46 micrograms of mercury / g creatine on 12-18-98
86 micrograms of mercury / g creatine on 3-25-99
46 micrograms of mercury / g creatine on 7-27-99
36 micrograms of mercury / g creatine on 9-30-99
Normal reference for urinary mercury 0-3 micrograms / g creatine.

Between DMPS infusions the child received DMSA 100 mg. orally two days a week, with glutathione 75 mg. twice daily, glycine 900 mg. on day prior to DMSA and glycine 900 mg. on DMSA treatment days.

Response to treatment: On 3-22-00 the parents reported marked behavioral improvement, particularly over the past two months. He now responds to his name and follows instructions. He has developed original speech without echolalia, and obsessive behaviors have declined.

Identifier: 0003HC **Sex**: M **Age**: 3yr. 11mo. **DOB**: 4-11-96

Prenatal and Postnatal History: Prenatal history was unremarkable. Infant was thought to be 4 weeks premature, although birth weight was that of a term infant at 8lbs. 6oz. He developed jaundice shortly after birth and was treated with phototherapy. He was briefly given antibiotics for a suspected infection the first 3 days of life.

Developmental Landmarks: Parents report that his development was normal until 12 months. He was crawling but did not begin to walk until 18 months of age with the support of a walker.

Regression and Symptoms: Some concerns at 13 months, marked regression at 16 months. Six to seven spoken words in use at 12 months were entirely lost. Vacant stares predominated and he began biting his hands. Officially diagnosed autistic at 2 1/2 years of age.

Exposure Sources: Mother had 8 amalgams. He also received exposure via vaccine, but total dose is not available at this time.

Mercury Levels: Hair mercury at 2 years 7 months was below detection limits. DMSA provacative protocol with 10 mg per kg per dose three times daily for three days with 24 hr urine screen for heavy metals day 2 revealed:

3.2 micrograms of mercury / g creatine on 6-21-99
28 micrograms of mercury / g creatine on 9-13-99
13 micrograms of mercury / g creatine on 10-12-99
Normal lab reference 0-3 mcg Hg per g creatine.

Response to treatment: Parents feel certain that DMSA chelation has resulted in improvement in their son. They noticed almost immediate improvement during the three days of treatment along with dramatic improvement the past six months. He is "much more with it and curious about his world". Although he is still not talking, he is having frequent vocalizations. He just started running for the first time 6 weeks ago.

Identifier: 0004WR **Sex**: M **Age**: 6 **DOB**: 2-2-94

Prenatal and Postnatal History: Prenatal history unremarkable with the exception of breech presentation. C-section preformed and apgars were 9 and 10. Birth weight, 8lbs. 11oz. Normal postnatal course.

Developmental Landmarks: He easily met and exceeded all early developmental landmarks and was described as a pleasant, happy baby.

Regression and symptoms: Shortly after his first birthday he developed numerous infections and was hospitalized for a respiratory illness. He received antibiotics, steroids, and oxygen and was discharged on day three. By 15 months he had lost speech and interaction. At 18 months he developed a very limited diet with bouts of bloody, culture negative diarrhea. Officially diagnosed autistic at 5 yrs, although he had been receiving services for autism from the school system since age 3.

Exposure sources: This child received all early vaccines with thimerosal preservative. At 2 months of age he received 62.5 mcg of mercury which represented a 125 fold increase above EPA guidelines based on his weight. This occurred again at 4 months, 62.5 mcg mercury and 50 mcg mercury at 6 months, 11 months 12.5mcg mercury and at 18 months, 50 mcg mercury for a total of 237.5 mcg of mercury. Mother also reports 5 dental amalgams and minimal dietary exposure. Child has never eaten fish or seafood.

Mercury Levels: Hair analysis from 20 months revealed 4.8 ppm mercury with a reference range of 0-1ppm and aluminum 40.2 with a reference of 0-9ppm. Note this sample was not sent for analysis until the child was already 5 1/2 years at which time the mother became aware of his early mercury exposure from vaccines. A subsequent analysis at 5 ½ years revealed normal levels of mercury and elevated lead 1.14 ppm with a normal reference 0-0.5, aluminum 23.2, and antimony 0.017 with reference of 0-0.03 and bismuth 0.19 with reference of 0-0.11. Initial treatment with oral DMSA removed 17 mcg per g creatine lead with reference 0-15 mcg per g creatine. Oral cyclic chelation was continued for 5 cycles with lead again present at 15 mcg per g creatine down to normal levels at the 5th cycle.

Response to treatment: Parents report marked improvement with each round of chelation. The last two cycles were not as pronounced as the first 3 cycles of treatment. An increase in spontaneous language and a general overall increase in all areas of functioning were also noted.

Identifier: 0005ZH **Sex**: M **Age**: 10 **DOB**: 5-28-89

Prenatal and Postnatal History: Unremarkable pre- and postnatal course. Term vaginal delivery. Pitocin given for failure to progress. Birth weight 7 lbs. 14 oz., good apgars.

Developmental Landmarks: Mother reports he was a very alert and pleasant infant who easily obtained all his early developmental landmarks with the exception of crawling. He progressed directly to walking at 8 ½ months. He began to babble and had developed some speech the first year of life, which did not progress.

Regression and Symptoms: Parents were concerned about his speech delay but attributed it to other factors. He also developed a very picky diet with a preference for starches. He also would line up toys and repeat phrases but was not officially diagnosed autistic until 5 years of age.

Exposure Sources: Mother with multiple dental amalgams. DPT vaccine known to have mercury 25 mcg per dose at 2,4,and 6 months. Child did eat fish sticks as a toddler but parents switched to only farm raised fish.

Mercury Levels: A 24 hour heavy metal challenge at 9 years of age removed 67 mcg of mercury. Unfortunately, the parents were not able to financially afford further treatment at that time.

Identifier: 0006MA **Sex**: M **Age**: 4 ½ yrs. **DOB**: 8-24-95

Prenatal and Postnatal History: Uncomplicated pregnancy, term vaginal delivery, apgars 9 and 10, birth weight 7 lbs. 6 oz. Quickly learned to breast feed, unremarkable postnatal history.

Developmental Landmarks: Easily met all early developmental milestones. Described as being very social with good eye contact. He was saying Mama, bye-bye, and babbling at 14 months.

Regression and Symptoms: According to the parents, at 16 to 17 months he began to slide into his own world. He stopped responding to his name and making eye contact. He also lost language and social interactions. Parents also report muted emotions.

Exposure Sources: This infant was exposed to 100 mcg mercury the first six months of life via vaccines. No dietary exposure from seafood or fish to the child. Mother with 9 amalgam fillings and only occasional fish consumption during pregnancy.

Mercury Levels: Hair analysis without mercury detection. Heavy metals challenge urine 8.6 mcg / g / creatine with a norm reference of 0-2.5 mcg / g / creatine at 3 years 8 months of age. He is currently undergoing cyclic chelation therapy with oral DMSA.

Response To Treatment: Parents report that his level of awareness, eye contact, emotions, and receptive and expressive language have all improved since starting the chelation program.

Identifier: 0007EK **Sex**: M **Age**: 5 **DOB**:12-10-94

Prenatal and Postnatal History: Uncomplicated prenatal and postnatal history. Birth weight 8 lbs., apgars 9 and 9.

Developmental Landmarks: Easily met all early milestones. Parents report precocious language skills. At 10 months he was talking with phrases "oh, there it is."

Regression and Symptoms: At 12 months there was a major and obvious reversal in behavior. Speech, social interaction, and laughter began to fade away rapidly. He began toe walking, lost eye contact, grew inattentive, and developed repetitive behaviors.

Exposure Sources: Mother with 8 dental amalgams, no fish consumption. Infant received thimerosal in vaccines, but unable to calculate exposure at this time. At 3 years of age 8 amalgam fillings were placed with an initial improvement in behavior for 3 weeks. then a decline to a level much worse than before the dental work with progressive decline.

Mercury Levels: Prior to chelation non-detectable, 12-27-99. DMPS IM + oral DMSA/EDTA and DMSA/EDTA supp. (unspecified doses).
2-19-99 41 mcg / g creatine of urinary mercury.
DMSA supp. 250mg bid were used 3 x week, every other week subsequent to provocation testing. Oral DMSA provocation for urinary Hg pending.

Response to Treatment: Multiple dietary and secretin infusions are concurrent to the DMPS/DMSA chelation, but mother is firmly convinced that the latter are contributing to excellent behavioral and somatic gains. Improvement in eye contact within 2 days of DMSA is evident. Improvement in speech, sociability and playing with toys are seen consistently right after DMSA and are reported to be on a gradual upward trend. A full sentence was uttered on or about 3-1-00.

In addition to the above case studies, we have collected preliminary data on three autistic children who have not undergone chelation. These children also exhibit elevated levels of mercury.

Data on Non-Chelated ASD Children

Age	Sex	Mercury level and source of sample
2 ½ yrs.	Female	Heavy metal hair analysis 5.6ppm (ref.range 0-2)
4 ½ yrs.	Male	Hair analysis 1.2ug/g (ref. <0.4) PRBC 18.4 (ref <9)
5 yrs.	Male	Hair analysis 1.8 ppm PRBC 18.3 (ref.<9)

Discussion

Several observations from these case studies deserve mention. One is that all of the children experienced a regressive form of autism. Other findings are that (i) low levels of mercury in hair may be associated with large amounts of mercury excretion on provocation and (ii) initial levels of provoked mercury may not be as high as subsequent ones. Mercury in the hair will only reflect a current or recent exposure of approximately one year or the body's active detoxification of mercury. This was evident in a child with non-detectable levels of mercury in the hair and positive levels on provocation.

In the case studies there is also a trend of higher numbers for mercury in younger children (20 month hair sample of 4.8 ppm and 2 ½ year hair sample of 5.6 ppm). This may be related to the fact that the testing was performed closer to the time of exposure. Hair levels of mercury greater than 5.0 ppm are considered diagnostic for mercury poisoning (*Applied Toxicology*, 1992). Among the majority of these case studies much more modest elevations of mercury, if detected at all, were associated with high levels of provoked mercury.

There are no standards for provoked levels of mercury in children in the context of behavioral disorders. Therefore, we surveyed a large number of physicians treating adults with chronic health problems diagnosed as secondary to mercury. These clinicians advise that tolerable limits may vary according to the general health of the patient and associated health problems. All consulted agreed that in adults excretion of 50 mcg of

mercury per gm creatine after intravenous DMPS challenge is worrisome. We submit that the concern level for children should be even more stringent. High levels of mercury are demonstrated in some children without a history of fish consumption, amalgam burden, or known environmental exposure, suggesting the role of vaccines as a contribution to body burden.

The families who submitted these case histories wanted to tell their stories because their children are noticeably improved after treatment for mercury. Whether this improvement was sudden or gradual, the parents are convinced that lessening the mercury and heavy metal burden has helped their child. They ask us to request support for much needed research in this area.

DISCUSSION

How reasonable is it to claim that the most common form of autism, where there is normal development and then regression, could be caused by mercury poisoning? There are several reasons to believe that this process has indeed occurred.

Diagnostic Criteria Are Met

Medical literature demonstrates that mercury can induce autism-spectrum traits, and this association extends to mercury's localization within specific brain nuclei. In attempting to address "the totality of the syndrome" (Bailey et al, 1996), we have shown that every major characteristic of autism has been exhibited in at least several cases of documented mercury poisoning, and that every major area of biological and neurological impairment implicated in ASD has been observed with Hg exposure. Recently, government-directed studies have revealed that the amount of mercury given to infants receiving vaccinations exceeds safety levels. The timing of mercury administration via vaccines coincides with the onset of autistic symptoms. Case reports of autistic children with measurable mercury levels in hair, blood, and urine indicate a history of mercury exposure along with inadequate detoxification. Thus the standard criteria for a diagnosis of mercury poisoning in autism, as outlined at the beginning of this paper, are met. In other words, mercury toxicity is a significant contributing factor or primary etiological factor in many or most cases of autism.

Unique Form Would be Expected, Implicates Vaccinal Thimerosal

Symptoms manifested in mercury poisoning are diverse and vary by the interaction of variables such as type of mercury, age of patient, method of exposure, and so forth. Thus, although it could be argued that in all the thousands of cases of past Hg poisonings, no instance of autism could be found, such an argument fails to take into account the possibility of unique expression. It would be comparable to saying that, because in all the cases of Minamata disease no instance of acrodynia could be found, then acrodynia could not be caused by mercury poisoning. Since there are no case reports or systematic studies in the literature of the effects of intermittent bolus doses of injected ethylmercury on "susceptible" infants and toddlers, it would be reasonable to expect that symptoms arising from this form of mercury poisoning would present as a novel disease. In fact, given the high neurotoxicity of organic mercury, its known psychological effects, and the age at which it has been given in vaccines, it would almost be a given that the "novel disease" would present as a neurodevelopmental disorder like autism.

Conversely, the fact that autism meets the diagnostic criteria for mercury poisoning, yet has never been described as a mercury-induced disease, requires that the disorder must arise from a mode of mercury administration which has not been studied before. This would rule out other known sources of Hg like fish consumption or occupational mercury hazards, as these have been well characterized. It is possible that another under-investigated mercury route, such as maternal Hg exposures (e.g., from vaccinations, thimerosal-containing RhoGam injections during pregnancy, or dental fillings) or infant exposures to thimerosal-containing eardrops or eyedrops, might be a factor, and this cannot be ruled out.

Historical Precedent Exists

There is a precedent for large scale, undetected mercury poisoning of infants and toddlers in the syndrome that came to be known as acrodynia or pink disease. For over 50 years, tens of thousands of children suffered the bewildering, debilitating, and often life-long effects of this disease before its mercury etiology was established, as Ann Dally relates in *The Rise and Fall of Pink Disease* (1997, excerpts):

> "Acrodynia is a serious disease that was common, at least in children's clinics, during the first half of the present (20th) century. Reports abound of children too miserable to acknowledge their mothers, such as the child who kept repeating, "I am so sad." One unhappy mother was quoted as saying, "My child behaves like a mad dog." In most cases the condition improved spontaneously, but was often regarded as chronic. Mortality varied from 5.5% to 33.3% and was usually about 7%. Most physicians who speculated on the causes of pink disease believed in either the infective or the nutritional theory. No one seems to have suggested that it might be due to poisoning. It was a tradition to advise student doctors to treat cases of difficult teething with the mercury powders that were eventually to be revealed as the cause of the disease. The ill-effects of mercury on the mouth had been known at least since the time of Paraclesus, but it was not until 1922 that the pediatrician, John Zahorsky, commented on the similarity between pink disease and mercury poisoning. He dismissed rather than pursued his new idea of possible mercury poisoning and suggested a theory that was more in tune with current fashion. Most doctors, even those skilled in the use of calomel, associated mercury poisoning with adults (syphilis, industrial poisoning, hatters shakes) rather than with infants. By 1935 the disease was seen in every children's out-patient clinic.
>
> The mystery began to be solved in 1945 by Dr. Josef Warkany, of the Cincinnati Children's Hospital. He and his assistant found large amounts of mercury in the urine of a child with pink disease. They did not publish their findings until 1948, but it is noteworthy that the news seems not to have spread through the small and tightly knit pediatric world, where everyone knew everyone else. It was probably because the idea was unfashionable and contrary to the conventional wisdom. The theory that mercury poisoning caused pink disease was gradually accepted, but against resistance, particularly by older men and those in powerful positions. Mercury was withdrawn from most teething powders after 1954, initially through voluntary action by the manufacturers because of adverse publicity and probably in the hope of avoiding statutory prohibition. Pink disease almost disappeared. Later in the decade the theory was widely accepted and soon pink disease was no longer part of the usual pediatric out-patient clinic."

Thus, like acrodynia before it, autism may in fact be "just another" epidemic of mercury poisoning, this time caused by childhood vaccinal mercury rather than infant teething powders.

Barriers Preventing Earlier Discovery Are Removed

The priorities and methods of research experts in the autism and mercury fields have prevented the association between mercurialism and ASD to be recognized until recently.

The effects on humans of mercury-containing medicinals and home remedies used to be studied quite regularly by medical researchers (Warkany and Hubbard, 1953); but since, aside from vaccinal thimerosal, such products have declined dramatically in number since the 1950s and 1960s, most mercury researchers today focus on biochemical studies or environmental sources like fish and coal plants. Some mercury experts seem surprised to learn that Hg is present in infant vaccines (authors' personal experience), and as recently as 1997, when the EPA released its massive review of extant mercury research, vaccines were not even mentioned as a potential source. Thus it is not surprising that mercury experts have never investigated thimerosal as they have, say, contaminated whale meat consumption in the Faroes Islands or Hg exposure among Amazonian goldminers.

Likewise, it is not surprising that neither mercury experts nor autism professionals have ever investigated autism as a possible disease of mercury exposure. Since its discovery by Kanner, autism has been characterized in almost exclusively psychological terms. The descriptions have been such that the symptoms would be essentially unrecognizable as manifestations of poisoning to any mercury expert not looking closely. A perfect example is Kanner himself, who recorded feeding problems and vomiting in infants and concluded: "Our patients, anxious to keep the outside world away, indicated this by the refusal of food." Bruno Bettleheim, who dominated autism discourse in the 1950s and 1960s and blamed the entire disorder on "refrigerator mothers" who forced the withdrawal of the child, asserted, "the source of the anxiety is not an organic impairment but the child's evaluation of his life as being utterly destructive" (1967, reported in ARI Newsletter). In 1987, Robert Sternberg would propose a "unified theoretical perspective on autism" by defining the disorder in terms of a "triarchic theory of intelligence," and in the same publication Lorna Wing and Anthony Attwood would write:

> "Sometimes young autistic children will stand in a dejected posture, with tears streaming down their faces, as if they suddenly felt their helplessness in the face of a world they cannot understand."

Even as recently as 1995, a typical slate of articles in the dominant *Journal of Autism and Developmental Disorders* (April 1995) would consist of eight psychological pieces (example: "Generativity in the Play of Young People with Autism") and one biomedical one (on biopterin). Thus biomedical research in autism existed, but it was mostly relegated to the margins as psychology held center stage, and the symptomatic characteristics of autism continued to be presented in accord with psychological biases.

In the latter part of the 1990s, the situation on both sides changed. Congressional mandate led to the public quantification of the cumulative amount of mercury in vaccines, raising interest in understanding its effects. Parent organizations like CAN and NAAR, working with the NIH and other researchers, engineered an autism research agenda which is more heavily focused on underlying physiological mechanisms of the disease. With parents already suspecting a vaccine-autism link, the environment was right for investigations focused on the link between vaccinal mercury and autism.

MEDICAL & SOCIETAL IMPLICATIONS

Affected Population

The NIH (1999, web site) estimates that there are nearly half a million Americans who suffer from autism, a devastating, debilitating, and lifelong disorder. Given the role of thimerosal as a major contributing factor in ASD, basic and clinical research efforts should be focused on understanding how mercury leads to autism in susceptible individuals and on finding effective methods to address the resulting Hg damage. Such research might focus on the following areas, with others undoubtedly still to be identified:

(a) Chelation methods which will work across all body tissues and especially the brain. The current standard chelators – DMPS and DMSA - appear unable to cross the blood-brain barrier. Other promising but less studied chelators like alpha lipoic acid can cross the bbb (Fuchs et al, 1997) and should be studied in autism.

(b) Mechanisms to induce immunity to Hg and which might possibly reverse the Th2 shift or IFNg expression which mercury causes. The work of Hu and colleagues suggests that Hg can cause an immune reaction in any individual, but some are protected by a counteractive immunosuppressive response, and Warkany and Hubbard have pointed out that individuals who are Hg-sensitive can later become "immune". It may be possible to engineer these responses in autistic individuals through careful research.

(c) Mechanisms which might reverse Na-Si transporter blockage in the intestines and kidney, thereby normalizing sulfate absorption.

(d) Techniques to eliminate the Hg-induced epileptiform activities found in the majority of autistic children, as outlined by LeWine et al.

(e) Stem cell applications in autism to repair brain damage that occurred during development.

Other Disorders

As pointed out by David Hartman (1998), mercury's ability to cause a wide range of common psychiatric disturbances should be considered in their diagnosis, and it might also be productive in developing hypotheses about and designing research studies for these other disorders. The disorders might include depression, OCD, dementia, anxiety, ADHD/ADD, Tourette's, and schizophrenia. Mercury may play a role in the etiology of some cases of these conditions. Conversely, investigating mercury's wide ranging effects upon neurobiological processes may lead to a quicker understanding of the organic etiologies in these other diseases which are now seen with increasing frequency.

Vaccination Programs

Universal compliance with the recommended vaccine schedule is a governmental, medical, and societal goal, since "vaccines save lives" (CDC). Our goal is not to negatively impact childhood immunization rates. Instead, we have been careful to

distinguish between thimerosal and vaccines. Thimerosal is not a vaccine; it is a preservative. Except for trace amounts, vaccines without thimerosal are currently available for all routinely recommended immunizations for children under 6 years (Institute for Vaccine Safety, 1999). Furthermore, it is possible to remove mercury from existing products. Merck, for example, delivered and received FDA approval for a thimerosal-free Hepatitis B vaccine in a record-breaking two months from the time the FDA publicly encouraged manufacturers to develop thimerosal-free alternatives (Pless, 1999; Merck, 1999). Thus, any issues being raised here are related to how vaccine programs are run, not with vaccines themselves.

The issues, of course, are: (i) first, how thimerosal was allowed to remain a component of the immunization program, even after 1953 when Warkany and Hubbard specifically named vaccinal mercury as a possible factor in acrodynia, or 1982 when the FDA issued a notice singling out thimerosal as especially neurotoxic as well as ineffective as a preservative (Federal Register, 1982); and (ii) second, why thimerosal remains in over 30 vaccine products today (FDA, 1999), and why the FDA, as of March 2000, has only "encouraged" rather than required the vaccine manufacturers to remove the thimerosal (William Egan personal communication). Although the CDC has stated that no adverse effects from thimerosal have been found other than hypersensitivity reactions, the sad fact is there have been no direct studies on the long term effects of intermittent bolus doses of ethylmercury injected in infants and toddlers. As Altman and Bland have aptly demonstrated (1995), "absence of evidence is not evidence of absence."

These lapses in vaccine program oversight suggest that vaccine safety studies need to be bolstered. Current practice is to track adverse reactions only if they occur within one month of the vaccination. The experience with mercury clearly shows that an adverse event may not manifest for months if not years. Studies on adverse reactions must involve long term tracking of patients; they should investigate the impact of multiple injections as well as compare reactions to vaccines with and without various additives; and sample sizes need to be large enough to include especially sensitive groups. Finally, the FDA should require manufacturers to remove all remaining thimerosal from their vaccines immediately, so that another child is not lost to this terrible disease.

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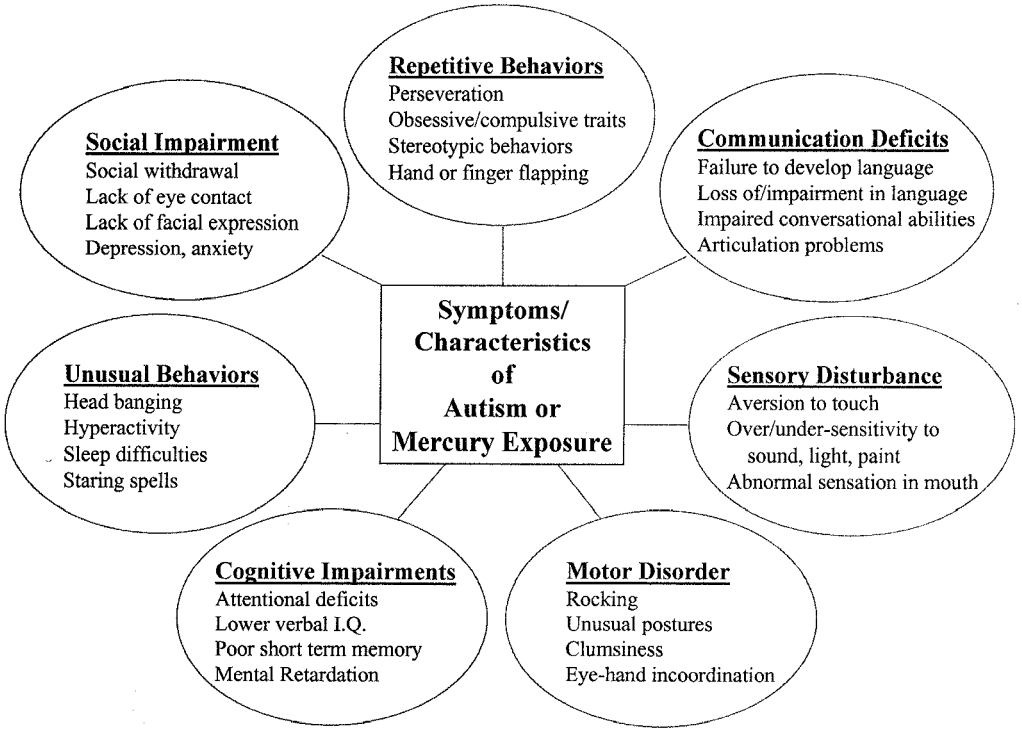
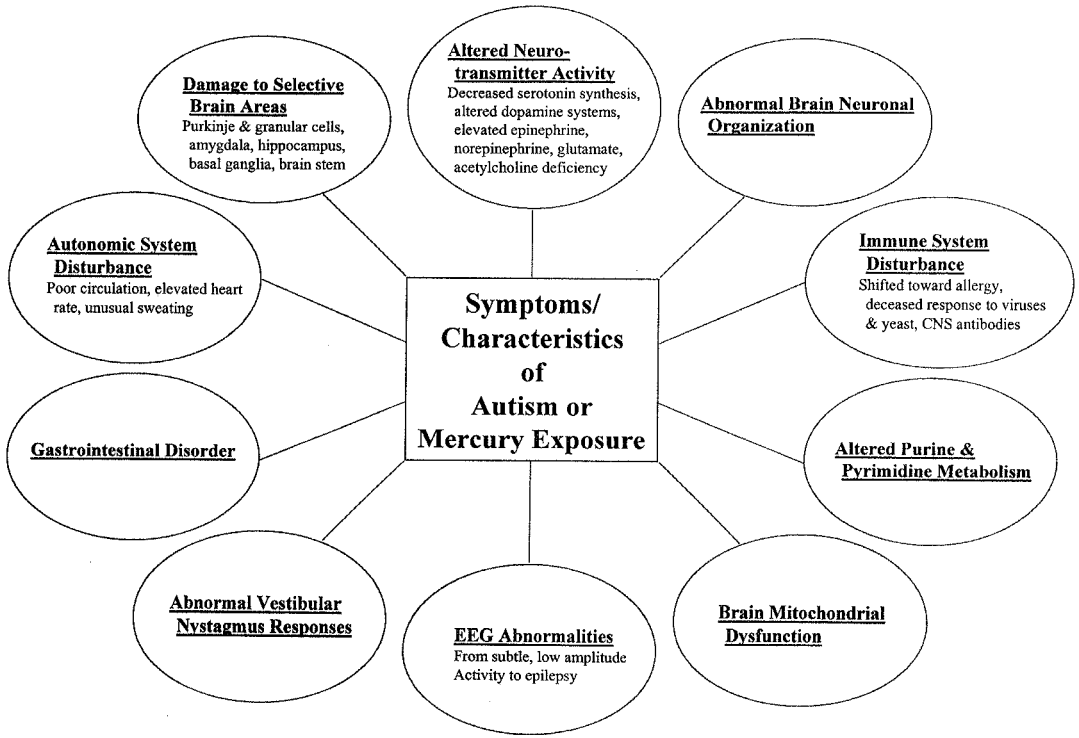
Autism & Mercury Poisoning Comparison

- Behavior -



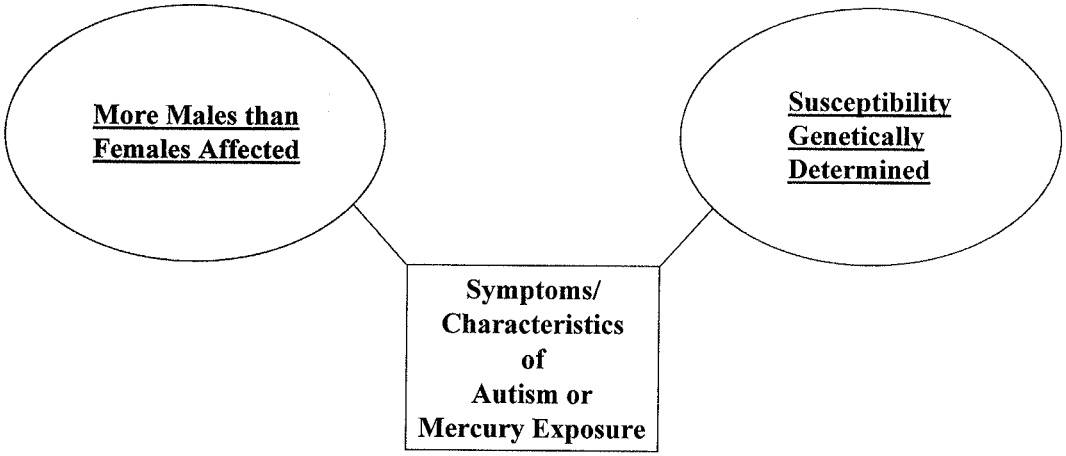
Autism & Mercury Poisoning Comparison

- Physiology -



Autism & Mercury Poisoning Comparison

- Population -

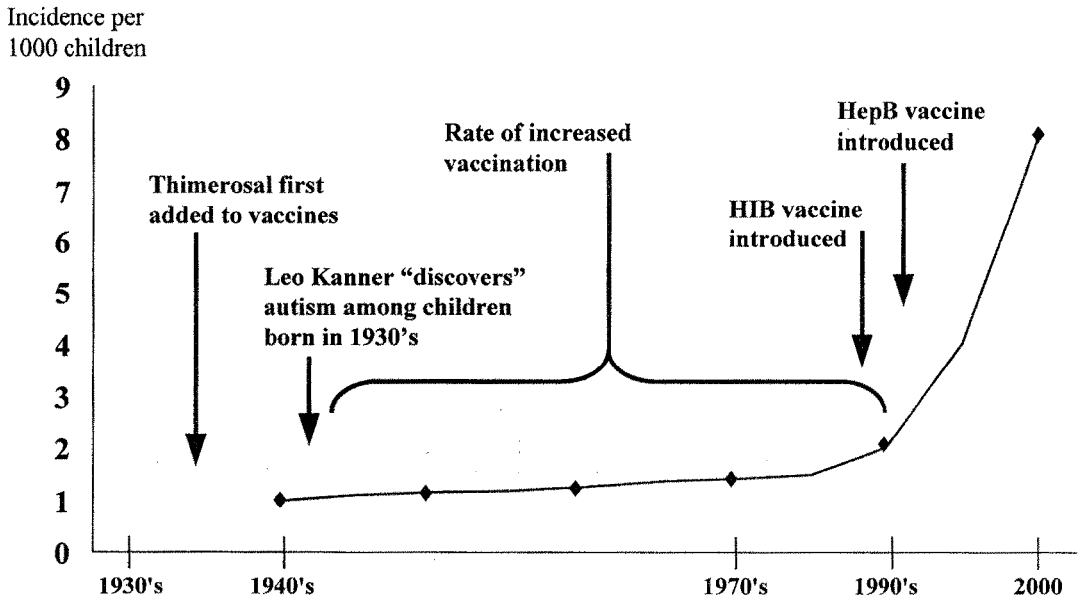


Studies implicate chemical toxins in neurodevelopmental disorders

- National Academy of Sciences (July 2000): report on methyl mercury
  - Suzuki et al (1973): toxicity of ethyl mercury similar to methyl mercury
- *Environmental Health Perspectives* (June 2000): association found between toxic chemicals and neurodevelopmental disorders such as autism
- Bristol-Powers (1996): autism caused by genetic and environmental factors

Thimerosal in vaccines implicated in autism

Autism Prevalence & Spread of Thimerosal Vaccines



Thimerosal in vaccines implicated in autism

- Autistic symptoms emerge after vaccination
- Vaccines contain toxic dose
- Davis et al (2000): association between thimerosal in vaccines and ADD, tics, speech delay, and neurodevelopmental disorders in general.

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Professional History

ARC Research 1986 – present

Founder and CEO of company, a full service market research and marketing consultant firm with offices in Cranford, New Jersey and Phoenix, Arizona. Conducts work for a variety of clients such as SBC Communications, Monster.com, United Van Lines, Budget Rent A Car, and Pace University.

TMP Worldwide 1979 – 1985

Responsible for various account management and marketing services responsibilities. TMP Worldwide is a marketing services and Internet company which owns Monster.com.

Education

Graduated with honors from Radcliffe College, Harvard University, in 1979.

Personal Data

Married, with three children.
Board Member, Cure Autism Now Foundation.
Executive Director, New Jersey Cure Autism Now.

U.S. Licensed Pediatric Vaccines

Product	Trade Name (first licensure)	Manufacturer	Dosage	Preservative and amount	Adjuvant	Other Additives	Mfg. Residuals
DTaP	ACEL-IMUNE (12/91)	Lederle Labs.	.5 ml	thimerosal 0.01%	AL(OH)$_3$/AlPO$_4$; Al 0.23mg	gelatin, tween	formaldehyde <0.02%
DTaP	Tripedia (8/92)	Aventis Pasteur Inc.	.5 ml	thimerosal 0.01%	Alum; Al 0.170mg	$NaPO_4$	formaldehyde <0.02%, tween
DTaP	Infanrix (1/97)	SKB	.5 ml	2-phenoxyethanol 2.5mg,	$Al(OH)_3$; Al ≤0.625mg		formaldehyde <0.02%, sodium chloride, tween
DTaP	Certiva (7/98)	North Amer Vaccine	.5 ml	thimerosal 0.01%	$Al(OH)_3$; Al 0.5mg		free formald. ≤10ppm, fetuin
Haemophilus b Conj. Vaccine (Meningococcal Protein Conj.)	PedvaxHIB (12/89)	Merck & Co., Inc.	.5 ml	liquid: None lyoph: thimerosal 0.02% *	$Al(OH)_3$; Al 225mcg	liquid: no lactose, sodium chloride 0.9% lyoph: lactose 2 mg	
Haemophilus b Conj. Vaccine (Tetanus Toxoid Conj.)	ActHIB, OmniHIB (3/93)	Aventis Pasteur, SA	.5 ml	single dose: none,	None	sucrose 8.5%	
Haemophilus b Conj. Vaccine (Diphtheria CRM197 Protein Conj.)	HibTITER (6/94)	Lederle Labs.	.5 ml	single dose: none, multi dose: thimerosal 0.01%		sodium chloride 0.9%	
Haemophilus b Conj. Vaccine (Meningococcal Protein Conj.) and Hepatitis B	Comvax (10/96)	Merck & Co., Inc.	.5 ml	none	$Al(OH)_3$; Al 225mcg	sodium chloride 0.9%, sodium borate	yeast protein, formald.
Hepatitis B Vaccine (Recombinant)	RECOMBIVAX HB (7/86)	Merck & Co., Inc.	.5 ml	Two formulations: (1) thimerosal 50 mcg (2) thimerosal-none	$Al(OH)_3$; Al 0.25mg	sodium chloride 0.9%,	yeast protein, formald.
Hepatitis B Vaccine (Recombinant)	Engerix-B (8/89)	SKB	.5 ml	none	$Al(OH)_3$; Al 0.25mg	sodium chloride & phosphate buffers	thimer.< 0.5 mcg mercury
M, M, and R Virus Vaccine Live	M-M-R II (4/71)	Merck & Co., Inc.	.5 ml	None	None	sorbitol, 14.5mg, neomycin 25mcg, gelatin (sucrose 1.9mg, culture medium, phosphate, glutamate)human albumin 0.3mg sodium chloride	FCS <1ppm
Pneumococcal Vaccine 7-valent Conj. Vaccine (CRM197 Protein)	Prevnar (2/00)	Lederle	.5 ml	None	$AlPO_4$, 0.125mg Al		
Poliovirus Vaccine Inactivated	IPOL	Aventis Pasteur, SA	.5 ml	2-phenoxyethanol 0.5%, formald 0.02%	None		neomycin <5ng, streptomycin

	(12/90)						200ng, polymyxin B, 25ng, calf serum protein <1ppm
Tetanus & Diphtheria Toxoids ads.	No trade name (7/70)	Lederle	5ml	thimerosal 0.01%	$AlPO_4$; Al 0.3mg	sodium bicarbonate, physiological saline	formaldehyde <0.02%
Tetanus & Diphtheria Toxoids ads.	No trade name (1/78)	Aventis Pasteur, SA	5ml	thimerosal 0.01%	$ALPO_4$; Al 0.26mg	sodium chloride, sodium phosphate	formaldehyde
Tetanus & Diphtheria Toxoids ads.	No trade name (7/70)	MPHBL	5ml	thimerosal 0.01%	$AlPO_4$ 2.0mg	sodium chloride, sodium hydroxide, aluminum chloride	formaldehyde < 0.02%
Tetanus & Diphtheria Toxoids ads.	No trade name (9/70)	Wyeth	5ml	thimerosal 0.01%	$ALPO_4$; Al 0.85mg	sodium chloride, HCL, sodium hydroxideto adjust pH	free formaldehyde 0.02%
Varicella Virus Vaccine Live	Varivax (3/95)	Merck & Co., Inc.	.5 ml	None	None	sucrose 2.5mg, glutamate 0.5mg, gelatin 12.5mg, potassium chloride 0.08mg, sodium chloride 3.2mg, sodium phosphate dibasic 0.45mg, glutamate 0.5mg potassium phosphate monobasic 0.08mg	neomycin, EDTA, FBS sodium phosphate monobasic cellular DNA/protein

* No longer manufactured

Kids at Risk

Chemicals in the environment come under scrutiny as the number of childhood learning problems soars

BY SHEILA KAPLAN AND JIM MORRIS

For more than 40 years, the family shared the big house and two trailers a mile from the Monsanto chemical plant, on the west side of Anniston, Ala. In time, the 18 of them learned to put up with the rotten-cabbage odor that wafted through town. The plant, after all, is what stood between many residents and poverty. Besides, there were family troubles: Jeanette Champion, 44, is nearly blind and has what she calls a "thinking problem." Her 45-year-old brother, David Russell, can't read or write. Her 18-year-old daughter, Misty Pate, has suffered seizures and bouts of rage. Misty's 15-year-old cousin, Shane Russell, reads at a second-grade level.

The Monsanto plant has made industrial and pharmaceutical chemicals since the 1930s. But for decades it also saturated west Anniston with polychlorinated biphenyls. PCBs have long been linked to cancer. More recently, however, researchers have discovered evidence tying the compounds to lack of coordination, diminished IQ, and poor memory among children. So when the extent of the PCB contamination in Anniston finally became clear a few years ago, a hazy picture came into focus. Perhaps the multigenerational problems of some families were not the result of poverty or bad genes. Perhaps they were caused by the chemicals in the ground.

More than 20 years ago, when Champion was still threading looms in the cotton mill, toxicologist Deborah Rice was conducting studies on young monkeys for Health Canada. The studies strongly suggested that substances like PCBs and mercury didn't just cause cancer or birth defects—the only problems for which they were tested in the United States. They also suggested that even at extremely low levels, these substances could affect the developing human brain. When given doses comparable to what a child would receive, the monkeys became impulsive and distracted and couldn't learn.

Many scientists were slow to see the significance of such research. Why worry about the loss of a few IQ points, they argued, when the real threat of chemical exposure was life-threatening disease? Today, however, a dramatic increase in learning disabilities has forced Environmental Protection Agency officials to acknowledge that they have ignored a much broader problem. One of every six children in America suffers from problems such as autism, aggression, dyslexia, and attention deficit hyperactivity disorder. In California, reported cases of autism rose 210 percent, from 3,864 to 11,995, between 1987 and 1998. In New York, the number of children with learning



Left: Will Redwood, 6, plays at home in suburban Atlanta. EPA workers clean up after taking soil and water samples in Oxford, Ala.

● *"Like driving 90 miles per hour in the rain."*

PHOTOGRAPHY BY KENNETH JARECKE—CONTACT FOR *USN&WR*

disabilities jumped 55 percent, from 132,000 to 204,000, between 1983 and 1996. It was in the midst of reports like these that the EPA last week essentially banned the popular pesticide Dursban as an unacceptable risk to children.

Experts have advanced a variety of theories for the increase in disorders, including better diagnostic methods. But a growing body of evidence suggests that compounds called neurotoxicants may be contributing significantly to the problem. Neurotoxicants are found in substances as common as tuna, lawn sprays, vaccines, and head-lice shampoo. Fetuses and infants exposed to these chemicals during critical windows of development, researchers now believe, may be at far higher risk for childhood learning problems than once thought. A new study from the National Academy of Sciences suggests that a combination of neurotoxicants and genes may account for nearly 25 percent of developmental problems. Chemicals alone may account for only 3 percent of cases, the study shows, but they can trigger many more. "Think of the genes as the country road," says John Harris of the California Birth Defects Monitoring Program. "And the neurotoxicants as driving 90 miles per hour in the rain."





The lead factor. Although inconclusive, the studies on neurotoxicants are intriguing. Researchers at the State University of New York–Oswego, in a federally funded study, showed that babies who had significant amounts of PCBs in their umbilical cords performed more poorly than unexposed babies in tests assessing visual recognition of faces, ability to shut out distractions, and overall intelligence. Herbert Needleman, of the University of Pittsburgh, examined 216 youths convicted in the juvenile court of Allegheny County, Pa., and 201 nondelinquent youths. In a study released last month, Needleman found that the delinquents had significantly higher bone-lead levels. In March, Frederica Perera, of Columbia University's Joseph L. Mailman School of Public Health, reported that air-sampling "backpacks" worn by 72 pregnant women in New York City picked up high concentrations of three neurotoxic pesticides that could cause disorders in their fetuses.

Chemical manufacturers—as well as some researchers and regulators—are not convinced by such findings. "There is no reason to believe we have an epidemic [of chemical-related illness] on our hands," says Robert MacPhail, chief of the EPA's Neurobehavioral Toxicology Branch. "There are still a jillion tests that have to be carried out." Robert Kaley, director of environmental affairs for Solutia, a 1997 spinoff of Monsanto's chemical operations, says that "everybody's jumping to conclusions. These kinds of links are premature at best and speculative at worst."

But the new findings, coming on the heels of more than two dozen earlier studies, have prompted the U.S. Department of Health and Human Services to dig deeper into the issue. The agency is expected to ask Congress for $1 billion to track up to 100,000 children from the womb through high school to assess the effects of chemical exposure on childhood development. U.S. Surgeon General David Satcher, who grew up in Anniston, finds the existing evidence compelling enough.







Jeanette Champion (far left); the McFarlane children (above), bounded by the Monsanto plant; Chadrick Anderson, 6, on trampoline near Monsanto dump

● *"These kids are different. Their wiring's not right."*

"How long do you wait," he asks, "before you take the necessary action to protect children?"

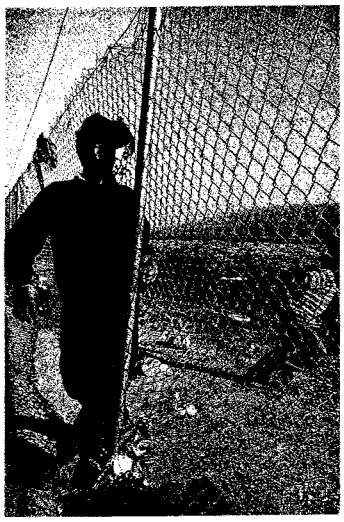
The answer, in the case of the EPA, appears to be a long time. More than a dozen high-ranking current and former EPA officials say the agency has failed to exert its authority to obtain data on chemical exposure from manufacturers and to restrict the use of neurotoxicants that may be harmful to kids. The EPA's enforcement record with the chemical industry is hardly an activist one. Between 1989 and 1998, it managed to get neurotoxicity data on only nine pesticides and three industrial chemicals.

The chemical industry, meanwhile, has effectively rebuffed the few efforts the EPA has made to address the issue. In 1998, the agency tried to force makers of some of the most common chemicals to test their products for hazards to children. But the EPA backed down under election-year pressure from both political parties and decided on a voluntary system. The agency and industry are still arguing about what tests will be required. Chemical companies are among the best-connected businesses in Washington. Since January 1999, chemical manufacturers have given nearly $4.2 million to presidential candidates, congressional campaigns, and national political parties. The revolving door is nothing new in the nation's capital, but it seems to spin to particularly good effect for the Chemical Manufacturers Association. This year, the CMA retained a former top White House environmental aide who helped Al Gore develop a plan to address what the vice president called "the special impact industrial chemicals may have on children." Today, the aide, Beth Viola, is working to make

the plan more industry friendly, thus contributing to delays.

Potentially hazardous chemicals should be judged "guilty until proven innocent," says EPA adviser and Yale University Prof. John Wargo. But the EPA doesn't work that way. The agency requires chemical manufacturers to prove that their products do not cause cancer or birth defects, but it does not require them to provide data on neurological effects—even though the technology for such testing now exists. The EPA is caught in a bind: It can't require a company to submit data without proof that a product is harmful. But it can't prove harm without the data. "We're in the dark," says Ward Penberthy, an EPA deputy director.

Children are particularly vulnerable to toxic chemicals. Normal brain development begins in the uterus and continues through adolescence. It requires a series of complex processes to occur in a carefully timed sequence: Cells proliferate and move to the correct spot, synapses form, neural circuits are refined, and neurotransmitters and their receptors grow. Neurotoxicants may slow, accelerate, or otherwise modify any of these processes. Says Philip Landrigan of New York's Mt. Sinai School of Medicine: "You end up with gaps in the wiring."



The idea that substances in the environment can harm the human brain is not new. In ancient Rome, miners were felled by what the medical literature of the time called "lead colic." The Mad Hatter in Lewis Carroll's *Alice's Adventures in Wonderland* comes from the 19th-century expression "mad as a hatter," a reference to mercury's effects on felt-hat makers. Over the past 70 years, adults and children around the world have been poisoned—and, in some cases, killed—by mercury in fish, PCBs in rice oil, a fungicide in seed grain, and a rat-killing agent in tortillas. After hearings in 1985, the House Committee on Science and Technology reported that there were 850 known neurotoxicants, any of which "may result in devastating neurological or psychiatric disorders that impair the quality of life, cripple and potentially reduce the highest intellect to a vegetative state." The report prompted virtually no action.

Today, however, the federal government is under increasing pressure from pediatricians, academics, and its own scientists, all clamoring for more testing of neurotoxicants. Agency officials are focusing on the following areas:

Pesticides. Organophosphate pesticides are domesticated versions of wartime nerve agents. The best known, Dursban and Diazinon, have been on the market since 1965 and 1956, respectively. The active ingredient of Dursban, chlorpyrifos, is found in some popular Raid sprays and Black Flag roach and ant killer. After reexamining the toxicity of chlorpyrifos, however, the EPA announced last week that it will ban nearly all household uses of it and restrict its use on tomatoes, apples, and grapes. The EPA found that Dursban could damage the brain. It also determined that children could receive up to 100 times the safe dose in some cases.

Diazinon, one of 37 other organophosphates under review, could be next. A preliminary EPA analysis recently found that a child could inhale up to 250 times the safe amount after a basic "crack and crevice" treatment by an exterminator. Linda Meyer, a toxicologist with Novartis, which makes Diazinon, says that the EPA extrapolated from a worst-case Novartis study—in which rats were placed in a chamber pumped full









Clockwise from left: Children of agricultural workers in Gonzales, Calif., near farmland sprayed with chemicals; crop-duster at work; workers having lunch

● *"Exposure to these . . . pesticides can cause neurological effects."*

of the pesticide in aerosol form. As a result, Meyer says, "the risk for children is grossly overestimated." Novartis also notes that the EPA, in its draft analysis, states that animal studies of Diazinon have revealed "no evidence of abnormalities in the development of the nervous system."

The chemical industry prefers to police itself, when given a choice. But this approach seldom works, as evidenced by the EPA's failed attempt to restrict a pesticide known as chromated copper arsenic, or CCA. The compound is applied to pressure-treated wood and commonly found on decks and playground equipment. Since the late 1970s, EPA researchers have reported that CCA poses a special threat to pregnant women and children because it combines three neurotoxic compounds. People can be exposed to CCA by breathing fumes from unfinished wood during home repair or construction. As a structure ages, the compound may leach out into the dirt. In lower doses, according to numerous studies, CCA can impair intelligence and memory.

The EPA tried to restrict CCA in 1984, but homebuilders' and wood preservers' groups lobbied Congress so hard that the EPA retreated, asking only that retailers distribute advisories that the compound could endanger children. A decade later, the effort had gone nowhere. "We checked retailers," said John McCauley of the Kentucky Department of Agriculture, "and they had no clue what a consumer information sheet was." The EPA promised to decide on new restrictions by 1998, but officials now say the agency won't act until at least next year.

Mercury. When toxicologist David Brown helped prepare a mercury study for eight Northeastern states and three Canadian provinces in 1997, he knew that fish in the region's lakes would contain mercury; he just didn't know how much. As it turns out, the numbers were considerably higher than he expected. "The most pristine lakes," he says, "had the highest levels." Brown, formerly with the Agency for Toxic Substances and Disease Registry, did the math and concluded that a pregnant woman who ate a single fish from one of these lakes could, in theory, consume enough mercury to harm her unborn child.

But the Food and Drug Administration has no enforceable limit for mercury in fish—only a guideline of 1 part per million, which the National Academy of Sciences deems "inadequate to protect the developing fetus." Mike Bolger, chief of the FDA's Division of Risk Assessment, says the agency hasn't set a limit primarily because "the science has to be sorted out."

That shouldn't be surprising. For years, operators of the coal-fired power plants and trash incinerators responsible for most mercury pollution have been working to quash attempts to further regulate mercury. When the EPA concluded in 1996, for example, that more than 1.6 million Americans were at risk of mer-



cury poisoning, industry lobbyists persuaded the agency not to make the report public for more than a year. It was released only after a group of senators complained. Lawmakers in states with substantial fishing and utility interests responded to the report by calling for yet another study, this time by the NAS. The new report, to be released next month, is expected to agree that current mercury levels are unsafe. But advocates for tighter regulations aren't expecting any quick changes in policy. "The reason," says Democratic Sen. Patrick Leahy of Vermont, "is that mercury has a constituency in Washington."

Jonathan and Jenna DeCosta suffer from attention problems and bouts of anger.

● *"There is no reason to believe we have an epidemic . . . on our hands."*

There is also evidence that mercury found in some childhood vaccines can hamper development. Will Redwood, for instance, a 6-year-old from suburban Atlanta, seemed perfectly normal at birth. Within two years, he had stopped interacting with his family. By age 5, he was diagnosed with a mild form of autism. His mother, Lyn, a nurse practitioner, read that some childhood vaccines contain the mercury-based preservative thimerosal, cumulative doses of which could be harmful. She had a lock of Will's hair analyzed, and it was found to be loaded with mercury. In his first round of vaccinations alone, given when he was 2 months old, Will received 62.5 micrograms of mercury, or 125 times the EPA's daily limit. No one can say whether the vaccines—which contained the maximum amount of thi-

FISH, FRUIT, FLEAS

How to protect your kids

It will be years before federal regulators and industry agree on which substances should be tested for developmental neurotoxicity and how tests should be done. But new and expectant parents needn't wait to take precautions. Lynn Goldman, a pediatrician who teaches at Johns Hopkins University School of Hygiene and Public Health, headed the EPA's pesticide and toxic chemicals office from 1993 to 1998. She offers the following tips:

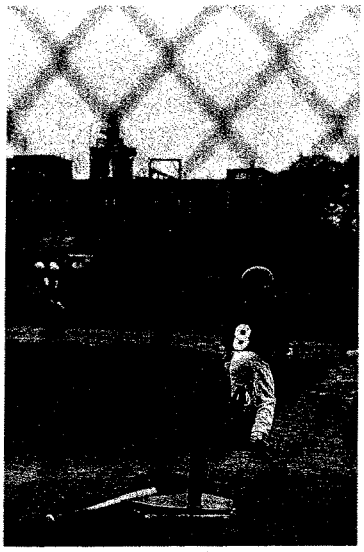
● **Home repairs:** To avoid the danger of lead poisoning, do painting and remodeling well before you move in, or postpone the work until the child is much older. If you live in an older neighborhood, have your water tested; there may be lead coming in from the pipes.

● **Fish:** Eat from lower down the food chain. Predator fish, such as tuna, shark, and swordfish, are more likely to have mercury or PCB build-up from the compounded effects of eating smaller fish. Avoid the fatty part of the fish, which is where toxins gather. Several states have advised pregnant women not to eat more than one 7-ounce can of tuna each week. The EPA's Web site, *www.epa.gov*, lists all state fishing warnings.

h. ...sal—caused Will's autism. And experts say that parents should not withhold inoculations. In a statement last year, a group of manufacturers said that vaccines containing thimerosal "have been administered to billions of children and adults worldwide, with no scientific or medical data to suggest that it poses a public health risk." Still, the American Academy of Pediatrics raised enough questions last year that vaccine manufacturers have agreed to phase out thimerosal as soon as possible.

PCBs. The EPA banned the manufacture of polychlorinated biphenyls in 1977, but the compounds continue to haunt children. PCBs are a well-known cancer risk, but recent studies show that they can also impair learning and memory. EPA adviser Joseph Jacobson and Sandra Jacobson of Wayne State University reported in 1996 that children in Michigan with significant prenatal exposures were three times as likely as un-e... ...ed children to have low IQ ... and twice as likely to lag be-hi... in reading comprehension.

Jeanette Champion says that her family's mental difficulties now make sense. She and roughly 5,000 others are suing St. Louis-based Solutia, which made PCBs in Anniston under the Monsanto name from 1935 to 1971, seeking compensation for what they claim are pollution-related maladies and property devaluation. One of the plaintiffs is Karen McFarlane, who lives near the plant with her husband and five children. McFarlane, 31, attended special school and has failed four times to get her GED. Six-year-old Derrick Hubbard has speech, vision, and memory problems. "If we go over his ABCs, he forgets them right away," says his mother, Dessa. Gadsden, Ala., psychiatrist Judy Cook is astounded at how many local children have IQs in the "borderline retarded" range and exhibit a penchant for violence. "These kids are different," she says. "Their wiring's not right."



Little Leaguers in Wallingford, Conn., play regularly beside a toxic-chemical factory.
● *"... we still don't have a smoking gun ... but there are bullets all over the floor."*

In February, the Agency for Toxic Substances and Disease Registry reported that "PCBs in soil in parts of Anniston present a public health hazard" and that some adults and children had elevated amounts of the chemicals in their blood. Exposures, the agency speculated, "may still be occurring at high levels." The EPA has identified 22 other sites in Anniston that may contain dangerous amounts of PCBs, metals, and solvents. Solutia's Kaley concedes there may have been "historical exposure." But, he says, "We do not believe that people are currently being exposed." Nevertheless, the company has spent more than $30 million to clean up its Anniston site and surrounding land, bought out about 100 properties, and made a tentative settlement offer of $44 million to landowners along downstream waterways.

That prospect aside, there are still many unanswered questions about neurotoxicants and their effects on children. The dearth of data will continue to stymie parents like Terry DeCosta, who believes that pollution from the Tosco oil refinery in Clyde, Calif., contributed to the anger and attention problems in both her children. According to the EPA, Tosco discharged more than 1 million pounds of pollutants into the air in 1998, many of them neurotoxicants. When the DeCostas sued the refinery, however, their case was dismissed for lack of causation. Richard Jackson, of the Centers for Disease Control and Prevention, says that the easy work is done. "We've been able to find the things that are so toxic that they make people dizzy and fall down," he says. Now comes the harder work of identifying and regulating compounds that insidiously misarrange the brain. "I've heard people say we still don't have a smoking gun," says Chris De Rosa of the Agency for Toxic Substances and Disease Registry. "And then I've heard others say, 'Yes, but there are bullets all over the floor.'" ●

● **Pesticides and related products:** Use chemicals only to control a problem, not to prevent one. Use bait stations instead of sprays. If infestation does occur, hire a professional exterminator, who i... ...pecially trained in app... chemicals. If you mus... the spraying yourself, wear the proper mask and gloves. A dust mask is not effective against chemical vapors.

● **Fruits and vegetables:** Organic is your best bet; otherwise, scrub the produce with water before eating or cooking. Soap or new pesticide removal products are not necessarily more effective.

● **Pets:** To control fleas, ask your veterinarian for the new oral or topical treatments. They are more expensive than collars and powders, but they are safer because your child won't be as exposed. They are also more effective.

● **Dry cleaning:** Avoid chemicals such as perchlorethylene, which is found in dry-cleaning products. If you dry clean frequently, use a cleaner who uses the new nonsolvent processes. Air out clothes before you put them away.

For additional information: The American Academy of Pediatrics, (202) 347-8600 or *www.aap.org*; Greater Boston Physicians for Social Responsibility, (617) 497-7440; Natural Resources Defense Council, 1200 New York Avenue, N.W., #400, Washington, DC 20005, (202) 289-6868, *www.nrdc.org*. —S.K.

Mr. BURTON. Thank you.

Mr. Enayati.

Mr. ENAYATI. Good afternoon. My name is Albert Enayati. I am president of the Cure Autism Now! Foundation, New Jersey chapter. Our foundation headquarters are located in Congressman Waxman's district. My wife Sima and I are scientists who have worked for pharmaceutical companies. We have a child with autism.

Mr. Chairman, in 1971, when my wife and I were growing up in Iran, a tragic event was taking place in our neighboring country Iraq. In October of that year, Iraq imported more than 90,000 tons of grain treated with methyl mercury. Much of the grain was used as daily baked bread. The reports from Iraq were shocking. The extensive mercury poisoning caused thousands of Iraq farmers and their families to become neurologically damaged. Hundreds died. The Iraqi episode is not unique. Similar misfortunes include mercury epidemics in Minamata, Japan, Guatemala and Russia. In the first half of the century, poisoning of infants and toddlers by mercury in teething powders led to acrodynia, or Pink Disease.

Today, another mercury tragedy is unfolding, this time among our children. As a scientist and a parent, I sadly declare that ethyl mercury in vaccines has been causing autism, attention deficit disorder and other neurodevelopmental diseases in children who, as susceptible infants and toddlers, were injected with thimerosal, a vaccine preservative which is 49.6 percent ethyl mercury by weight.

In 1982, 18 years ago, an FDA panel concluded that thimerosal is toxic, causes cell damage, can cause allergic reactions, and is not effective in killing bacteria or halting their replication. A recent hepatitis control report details how FDA, via its own Committee on Biologics, had failed, for 17 years, since the 1982 report, to follow their own organizational directives which specify ensuring product safety. Fortunately, because of the FDA Modernization Act of 1997, the CBER was forced to evaluate thimerosal in vaccines.

By 1998, the CBER's thimerosal study had run into difficulty. It is against Federal statutes to add toxic material to childhood vaccines, and thimerosal appeared to be contrary to this important law. CBER staff then searched for safety data and guidelines but found none. In fact, the CBER learned that there is very limited literature available on ethyl mercury.

The CBER team then compared ethyl mercury intake with Federal guidelines for safe mercury intake, but again the CBER ran into difficulty. Thimerosal is injected in bolus doses and metabolized in humans to ethyl mercury but all theoretical guidelines for safe mercury intake were based upon ingested methyl mercury. Left with no choice, the CBER team assumed that the toxicity of thimerosal injected in bolus doses was equivalent to that of methyl mercury ingested gradually.

Armed with this assumption, they compared the vaccinal ethyl mercury intake in children 6 months old to the suggested safe limits by EPA. It was then that they made a remarkable discovery: Even without considering infants and toddlers' susceptibility to neurotoxic effects, the mercury intake from vaccinations in the first 6 months of life far exceeded the limit set by EPA.

I believe that the FDA record justifies concluding that the U.S. immunization program has been in violation of Federal statutes.

Presumptions about safety have superseded safety guidelines and appropriate testing. Dangerous substances in vaccines remain untested. This negligence is inexcusable. Thousands of children and their families have been neurologically impaired by physician-injected ethyl mercury and while this has happened, the responsible supervisory agency, the FDA, was asleep at the wheel.

Mr. Chairman, despite the FDA warning in 1982 and the known toxicity of thimerosal, the FDA allowed the continued injection of cell damaging neurotoxic product into our children. Furthermore, since 1990, the FDA and CDC increased the likelihood of neurological damage by allowing thimerosal to be injected into day-old and 2-month-old infants. I am here because of my son Payam. For more than a year, he passed his developmental milestones, but after his DPT and MMR shots, Payam began not responding to his name, no longer ran to greet me when I returned from work. His spoken language disappeared and he no longer responded to his parent's words. Within a few months he had begun biting himself, hitting his head against the wall, flapping hands, toe walking and running aimlessly around the house. Even sleep patterns had deteriorated. All these traits appear in medical literature about mercury poisoning. Mr. Chairman, every symptom of my son's autism parallels traits known in mercury poisoning.

Many experts would have us believe that my son's regression was coincident with his vaccination. However, as a trained scientist, my reading of mercury literature indicates that every trait that defines autism can be induced by organic mercury. Not surprisingly, the FDA and CDC have asked vaccine producers to initiate a gradual discontinuance of using vaccines containing thimerosal. However, no family needs a neurologically impaired child. Injecting ethyl mercury in infants and toddlers ought to be discontinued immediately and clinical research to be initiated regarding mechanisms of treatment.

Thank you, Mr. Chairman.

Mr. BURTON. Thank you. Ms. Birt.

Ms. BIRT. Thank you. My name is Liz Birt. I live in Wilmette, IL with my husband and children, Sarah age 8, Matthew age 6 and Andrew age 4. I would like to thank you for holding this hearing today and allowing me to testify.

I have sat in this room before as a member of the audience. On April 6 of this year I listened as the chairman's opening statement detailed in part the story of my son Matthew. Matthew is classified as autistic, a diagnosis made entirely on behavioral observations. However, he has physical problems, including antibodies to myelin basic protein, abnormal EEG, inflammatory bowel disease and live measles virus in his terminal ileum. Matthew's immunologist at a teaching hospital believes that the thimerosal contained in the vaccines contributed to the development of these medical conditions and they have led to his contraction of the live measles virus by priming this immune symptom for an adverse reaction.

I am also here testifying as an advocate for not only the immediate recall of thimerosal containing vaccines but for fundamental change. This is unfortunately a failure to assign responsibility for vaccines which are mandatory for all children. The manufacturers, the FDA and the CDC, NIH and the AAP all share responsibility

for allowing this neurotoxin to remain in vaccines. This is the mandate of the FDA. The American public relies on this agency with its scientific experts to protect us. Yet for some unknown reason this issue was ignored. Why are American children today being exposed to vaccines which on a conservative basis subject them to 30 times the allowable amount of mercury for an adult? Why weren't the most basic calculations done to ensure that these products are safe? It is the children like my son who were injured in the name of the greater good who, just like the soldiers returning from the Vietnam War, are now being ignored.

I am here today to let the members of the committee know that these children have voices, and the voices of their parents and the grandparents, some of which are in this room today, will be heard however unpleasant the message. We want these products off the market immediately. Not one more child should be vaccinated with these vaccines.

Members of the committee may ask how does a member of the public speak with such conviction. Everything that is an official governmental publication paints a picture of complete safety. However, it does not take a genius to be able to discern the truth from the spin, deliberate material misrepresentations and even fraud contained in some of these publications.

The CDC's fact sheet on thimerosal states "thimerosal is a mercury containing preservative that has been used since the 1930's. It is used to ensure the medical products stay potent and sterile. It has been used in medicines as well as medical products such as throat sprays and contact lens solutions." This I submit would leave the average American parent to conclude that thimerosal is not a toxic substance.

What is missing is since 1977 clinicians have recognized thimerosal as being potentially dangerous. For nearly 20 years the U.S. Government has singled out thimerosal as a potential toxin. My question to the committee members and to the FDA is: Why is thimerosal even in these vaccines if it was determined in 1982 by the FDA that it was not even safe or effective as a bacteriostatic agent: Why has this product not been recalled?

This fact sheet states mercury exposures from vaccines containing thimerosal are within the safety margins included in exposure guidelines established by Federal agencies. The reality is there are no established safety margins published by any Federal agency for thimerosal exposure in infants and toddlers, and American children today are receiving many multiples of the EPA daily exposure guidelines for mercury for adults.

Why aren't the parents being told the truth by the CDC? If these statements were held to the same standards that we have for SEC rules, all of these people would be subject to prosecution. The CDC's own Vaccine Safety and Development Officer is on record as stating that

> Part of our problem is, unlike efficacy doses where there was a real effort on the part of the World Health Organization case definition ahead of time, similar efforts were not done for safety.
>
> The CDC is currently working with several large HMOs and a large link data base to study adverse events. The data base will study single validation, new vaccines and new schedules. Future topics could include examining communication of vaccine risk and defining the biological basis of groups at risk for adverse events.

Finally, of all of the positive things that were done by the Vaccine Compensation Act of 1986, one thing that they more or less neglected was research. They found a mechanism to fund an injury compensation program after the injury has already happened, but there is no way at this point to fund the research to try to prevent such injuries.

Why wasn't a safety definition developed? Why isn't it important to identify those at risk for adverse vaccine events? Why isn't research funded?

We must have accountability today. Conflicts of interest on vaccine committees at the FDA and CDC must be eliminated. The stakes are too high. We as parents need information on which to base informed consent. When my son was vaccinated at 2 days of life, I was only told after the vaccine was given. How can this type of process allow parents to receive the type of information that they need to make their decisions regarding the care of their children? We are the caregivers of our children, not these agencies.

Members of the committee, I urge you to support a petition to be filed this week by the Coalition for Safe Minds. This petition calls for the immediate recall of all vaccines containing thimerosal. These vaccines should never be used. Our country is experiencing an epidemic of neurodevelopmental disorders. These conditions cause not only heartbreak to the affected families, but the financial ramifications are immense to our entire country.

Thank you.

[The prepared statement of Ms. Birt follows:]

Testimony of Elizabeth Birt, Before the Committee on Government Reform U.S. House of Representatives Oversight Hearing Entitled "Mercury in Medicine - Are We Taking Unnecessary Risks?" July 18, 2000

Mr. Chairman and members, my name is Liz Birt. I reside in Wilmette, Illinois a suburb north of the City of Chicago with my husband and three children, Sarah age 8, Matthew age 6 and Andrew age 4. I would like to thank you for both holding this hearing and allowing me to testify before you today.

I have sat in this room before as a member of the audience; on April 6th of this year I listened to Congressman Burton's opening statement in which he detailed in part the story of my little boy, Matthew. Matthew was born in January 1994. He developed normally until age 15 months when he received his MMR and HiB vaccinations. After these vaccinations he ran a fever and developed a terrible ulcerated rash on his diaper area. The rash and fever resolved itself but the diarrhea persists even today, five years later. Very gradually, from April of 1995 through November of 1995 we noticed changes in Matthew's behavior. He stopped talking and began engaging in self stimulating behaviors like jumping and hand flapping. He did not respond to his name and avoided eye contact.

In early 1996 we started our search for an answer as to what happened to our previously outgoing, bright eyed, verbal, affectionate toddler. Matthew was initially diagnosed with "otitis media" an inflammatory condition of the ear which can cause a hearing impairment. We thought to ourselves this is easy- a simple operation and our little boy will come back to us. Little did we realize the horrible road we were now on. Matthew's condition did not improve- in fact it worsened. In November of 1996 we took Matthew for a developmental assessment. We were told that Matthew was delayed and he was categorized by the psychologist as having "pervasive developmental delay" a/k/a "PDD". The developmental specialist told us not to worry and that he believed that Matthew would catch up with his peers with appropriate intervention.

However, Matthew's condition only proceeded to deteriorate. By early 1997 Matthew began not sleeping at night. He would awaken almost every night and start jumping in his bed, screaming and crying. This frequently would go on for hours. Either my husband or myself would stay awake trying to comfort him. We consulted numerous medical specialists but no one was able to help us. After a particularly frustrating visit with a pediatric immunologist in November of 1998 when Matthew developed a horrible case of shingles,(a condition only individuals with depressed immune systems or the elderly develop), I made the determination that I could no longer rely on the medical community to address Matthew's physical deterioration. It would have to be my responsibility. So I set out alone armed with my greatest resources, my unending love for my child and a "maternal" instinct telling me that my little boy had been injured and there had to be a way to help him recover.

I began by reading every book and article available on autism, corresponding with parents and researchers on the internet and cultivating friendships and relationships with cutting edge physicians and researchers. As an attorney I had been trained in law school and professional practice to research methodically, closely examine all evidence and to be able to fully argue

both points of an issue. Since late 1998 I have been able to find the following medical facts about Matthew's physical condition: 1) he has tested positive for antibodies to myelin basic protein; 2) he has had abnormal EEGs; 3) he has inflammatory bowel disease; and 4) he has live measles virus in his terminal ileum. The diagnosis of these medical conditions have allowed me to work with physicians to design specific treatments to help Matthew. He now sleeps through the night, is no longer in pain from horrible constipation and reflux, has a more normal EEG, is starting to be toilet trained and is beginning to speak and also use sign language to structure phrases to communicate with his family and peers in his school environment. In short, Matthew's body is starting to heal. I believe, and so does Matthew's immunologist that the thimerosol contained in the vaccines Matthew was given contributed to these medical conditions. I have prepared Chart I which illustrates some of Matthew's physical conditions compared to those of mercury poisoning; they are remarkably similar. In addition, I have prepared Chart II illustrating the amount of mercury which Matthew received at each physician visit.

I am here testifying also as an attorney and advocate for not only the immediate removal and recall of thimerosal containing vaccines by the FDA but for fundamental change within the FDA and CDC.

Before I describe the petition which will be filed today with the Department of Health and Human Services I would like to frame the legal and regulatory environment in which I believe this has occurred. It is unfortunately about a failure in the process to assign responsibility for products which are mandatory for all children to enter school in this country. The manufacturers, the FDA, the CDC, the NIH, the medical associations such as the AAP and AMA all must share responsibility for allowing a product like thimerosol to remain on the market which has been determined in published federal regulations since 1982 to be unsafe and ineffective. This is the mandate of the FDA; the American public relies on this agency with its scientific experts to protect us from dangerous, untested products. Yet for some unknown reason, the FDA has chosen to ignore this issue. Why are American children being exposed to thimerosol containing vaccines which when injected into them cause them to receive 30 times the allowable amount of mercury for an adult on a daily basis? Before we as a society mandated universal vaccination for the "greater good" why weren't the most basic calculations done to ensure that these products are safe? I am afraid that the sad truth in all of this is that in the rush to pass the Vaccine Compensation Act in 1986 no one fully recognized the danger of shifting the risk from the manufacturer to the recipient of the vaccine. It is the children like Matthew who were injured in the name of public health who just like the soldiers returning from the Vietnam War are now being ignored. However, I am here today to let the members of the committee know that these children have voices and those voices of their parents and grandparents, some of which are in this room today, will be heard, however unpleasant the message is. We want these products off the market immediately NOT ONE MORE CHILD should be vaccinated with a thimerosol containing vaccine.

Members of the committee may ask "How does a member of the public speak with such conviction?" Everything that is officially published from the Vaccine Information Statements which must be given when a child is vaccinated under the terms of 42 U.S.C. 300aa-26 to the information posted on the CDC's National Vaccine Program Office web page paints a picture of complete safety and integrity with these products.

However, it does not take a genius to be able to discern the truth from the "spin", deliberate material misrepresentations and even fraud contained in these publications.

One glaring example of the distortion of facts is the CDC's own National Vaccine Program Office Fact Sheet on vaccines and thimerosol. This Vaccine Fact Sheet makes some rather benign statements regarding thimerosol. For example, "Thimerosol is a mercury containing preservative that has been used since the 1930s. It is used to ensure the medical products stay potent and sterile. It has been used in medicines as well as medical products such as throat sprays and contact lens solutions." This I submit would lead the average American parent to conclude that thimerosol is not a toxic substance.

What is missing from this Vaccine Fact Sheet is the fact that since 1977 clinicians have recognized thimerosol as being potentially dangerous. For nearly 20 years the US government has singled out thimerosol as a potential toxin. In response to the Food and Drug Administration (FDA) Modernization Act of 1997, the FDA issued a final rule in 1998 (the first proposed rule was issued in 1982) stating that over-the-counter drug products containing thimerosol "as not generally recognized as safe and effective" 63 FR 19799. In December of 1998 and April 1999 the FDA requested US vaccine manufacturers to provide more information about the thimerosol content in vaccines (MMWR, 1999, July 9). In July of 1999 the FDA issued a letter requesting information from US vaccine manufacturers for removing or reducing thimerosol in vaccines. Finally in May of 2000 the FDA issued another letter to US vaccine manufacturers requesting an update on progress made to remove thimersol from vaccines. My question to the committee and to the FDA why is thimerosol even in these vaccines if it was determined in 1982 by the FDA that it was not safe or even effective as a bacteriostatic agent?

Additionally, this Vaccine Fact Sheet goes on to state "Mercury exposure from vaccines containing thimerosol is within the safety margins included in exposure guidelines established by Federal agencies". "Some children, depending on which vaccines they receive and when they receive them, may be exposed to more thimerosol than other children. However, these levels are still within the safety margins included in exposure guidelines established by Federal agencies".

The reality is:1) there are no established safety margins published by any federal agency for thimerosol exposure in infants and toddlers; and 2) American children today are receiving many multiples of the EPA daily exposure guidelines for mercury for ADULTS. I have attached to my testimony Table II which illustrates the amount of mercury my son Matthew was exposed to from his vaccinations. It ranged from 69 times to 9.6 times the daily limit. Also, it should be noted by the committee members that I was concerned about the number of vaccines my children received at one time so I insisted that my pediatrician give no more than two vaccinations at one visit. Many children receive far more vaccines at one office visit than this. If material misrepresentations such as these were made in financial documents which corporations are required to file under the Securities and Exchange Committee rules, those individuals would be subject to criminal prosecution for fraud.

Among other misstatements contained the CDC's Vaccine Fact Sheets are those regarding the ability of the CDC and FDA to track vaccine adverse events. The Vaccine Safety Fact Sheet states: "The National Vaccine Program Office supports continued vigilance, so that any risk from a vaccine is quickly recognized and so that measures can be taken to make sure that vaccines are even safer. The CDC National Immunization Program and the Food and Drug Administration have systems in place for monitoring reports of reactions. Among those is the Vaccine Adverse Event Reporting System (VAERS)."

This I submit to members of the committee would lead the average American parent to conclude that the FDA and CDC have systems in place to monitor adverse vaccine reactions and take action when problems are immediately identified.

The reality is that as recently as 1996 weaknesses in the VAERS system were reported at a Vaccines & Related Biologicals Advisory Committee meeting to include 1) the passivity of the surveillance system; 2) underreporting; 3) lack of a control population; 4) inability to determine causal relationships; 5) imprecise definition of "serious" events; and 6) a lack of a mechanism to detect late adverse events". See, FDA Pink Sheet, April 15, 1996, attached as Exhibit A. In other words, ten years after passage of the Vaccine Compensation Act of 1986 the system in place for detecting adverse events associated with vaccines was determined to be ill-conceived and unworkable.

To further illustrate the problems with the entire system I refer the committee members to the FDA Pink Sheet attached as Exhibit B. It is entitled "Vaccine Standardized Safety Definition Needed for Future Trials". In this FDA Pink Sheet, CDC Vaccine Safety & Development Officer, Robert Chen, M.D. is quoted as making the following statements at a National Institute of Allergy & Infectious Diseases conference: 1) "Part of our problem is that unlike the efficacy dose where there was a real effort on the part of the WHO case definition ahead of time, similar efforts were not done for safety"; 2) "The CDC is currently working with several large HMOs in a large linked database to study adverse events... The database will study signal validation, new vaccines and new schedules... Future topics could include examining communication of vaccine risks and defining the biological basis of groups at risk for vaccine adverse events"; and 3) "Of all of the positive things that were done by the Vaccine Compensation Act of 1986, one thing that they more or less neglected was research. They found a mechanism to fund an injury compensation program after the injury has already happened, but there's really no way at this point to fund the research to try to prevent such injuries." See, FDA Pink Sheet, June 17, 1996.

As a parent and advocate I am deeply concerned about the safety and integrity of the vaccine program in general. Why wasn't a safety definition developed? Why isn't it important to identify the biological basis of groups at risk for adverse vaccine events? Why isn't research funded to prevent vaccine injuries? We must have responsibility and accountability put back into the system. Conflicts of interest on vaccine committees at the FDA and CDC must be eliminated. The stakes are too high. In addition, the parents need full disclosure of both benefits and risks for the vaccines which they are mandated by their state governments to give. The first time that Matthew was vaccinated in the hospital I never even gave consent. I was only informed after the vaccine was administered. How can this type of process allow parents to

receive the information they need in order to make decisions regarding the health care of their children? I submit that in reality there is no informed consent when it comes to vaccines.

Members of the committee I urge you to support this petition by the Coaltion for SAFE MINDS (Safe Alternatives For Elimination of Mercury Induced Neurological Disorders). This petition calls for the immediate recall of all vaccines containing thimerosol under the Federal Drug and Cosmetic Act. Our country is experiencing an epidemic of neurodevelopmental disorders including Autism, ADHD and ADD. These conditions cause not only heartbreak to the affected families, the financial ramifications of inaction are immense not just to the families who often must pay for medication and therapy out of pocket since it is not typically covered by insurance, but the school districts flooded with children with learning disabilities and eventually long term care including institutionalization for children whose needs are the greatest.

TABLE I

MATTHEW

PHYSICAL & SOCIAL CHARACTERISTICS

	MERCURY POISONING		**AUTISM**
1.	Social Deficits	1.	Social Deficits
2.	OCD Traits	2.	OCD Traits (Enjoys twirling fabric)
3	Loss of Speech	3.	Loss of Speech-Said "Mama", "Dada","Doggie", "Hi", Bye", Set-Go; Counted to Ten; "Sarah"
4.	Ready- Sound Sensitivity	4.	Frequently covers ears when loud noise occurs eg. dogs barking
5.	Abnormal touch sensation; touch aversions	5.	Has difficulty at times being held
6.	Involuntary jerking movements arm flapping, rocking	6.	Arm flapping, rocking especially when excited
7.	Rashes, Dermatitis	7.	Eczema & Dermatitis
8	Myelin Basic Protein autoantibodies	8.	Myelin Basic Protein autoantibodies
9.	Low Serum Serotonin	9.	Low Serum Serotonin
10	Abnormal EEG	10.	Abnormal EEG
11.	Gastrointestinal disturbances	11.	Diarrhea/Constipation

TABLE II

MATTHEW

AGE	VACCINE	MERCURY EXPOSURE NO. OF MICROGRAMS	MULTIPLE OF EPA DAILY LIMIT FOR ADULT
2 days	Hep. B	12.5	34.7
1 mo.	Hep. B	12.5	34.7
2 mo.	DTaP	25.0	69.4
3 mo.	HiB	25.0	38.4
4 mo.	DTaP	25.0	34.4
5 mo.	HiB	25.0	30.3
7 mo.	DTaP	25.0	27.7
10 mo.	HiB	25.0	22.7
15 mo.	HiB	25.0	20.8
17 mo.	Hep. B	12.5	9.6
19 mo.	DTaP	25.0	19.2

Vaccine Fact Sheets

About NVPO
Bulletins
Calendar
Citation Information
Immunization Glossary
Main Menu
Immunization Concepts
Immunization Laws
If We Stop Vaccinating
Vaccine Safety
Q&A
Diseases that Vaccines Prevent
Some of the People Who Stand Behind Vaccinations
10 Tips on Evaluating Immunization Information on the Internet
Vaccine Fact Sheets
National Vaccine Plan
NVAC
NVAC Resolutions
Pandemic Influenza Info
Publications
Customer Satisfaction Survey
Welcome Center

In easy-to-understand languege
*Note: The terms "**immunization**," "**vaccination**," and "**inoculation**" are used to mean essentially the same thing throughout this site.*

VACCINES AND THIMEROSAL

Thimerosal: A Brief Overview

- Thimerosal is a mercury-containing preservative that has been used since the 1930s. It is used to ensure that medical products stay potent and sterile. It has been used in medicines as well as medical products such as throat sprays and contact lens solutions.
- Thimerosal contains a mercury compound called ethyl mercury. In recent years, Federal agencies have developed specific guidelines to help prevent anyone from taking in too much mercury.
- Mercury is a chemical element found in the environment, foods (particularly seafood), and some household products. Everyone is exposed to mercury during their lifetime.

Thimerosal and Vaccines

- Thimerosal is added in tiny amounts to some vaccines to prevent them from spoiling and to keep germs from growing in the vaccine. It is currently used in more than 30 licensed vaccines and other medicines marketed in the U. S.
- There is no evidence that children have been harmed by the amount of mercury found in vaccines that contain thimerosal.
- Mercury exposure from vaccines containing thimerosal is within the safety margins included in exposure guidelines established by Federal agencies.
- Some children, depending on which vaccines they receive and when they receive them, may be exposed to more thimerosal than other children. However, these levels are still within the safety margins established by Federal agencies.
- Vaccines that contain thimerosal sometimes cause redness and soreness at the site of injection.
- Parents should consult their child's health care provider before vaccination if they believe the child may be allergic or sensitive to products that contain thimerosal.

Making Safe Vaccines Even Safer

- The Federal government is requiring vaccine manufacturers to work towards eliminating or reducing mercury in any products currently available on the market.
- The Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and other Federal agencies routinely monitor and conduct research to examine any new evidence that would suggest possible problems with the safety of vaccines.

CDC, National Immunization Program: http://www.cdc.gov/nip

Last Updated: 2/2000

CDC Centers for Disease Control and Prevention

National Vaccine Program Office

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Vaccine Safety

Travelers' Health

Search NVPO

Search

About NVPO
Bulletins
Calendar
Citation Information
Immunization Glossary
Main Menu
Immunization Concepts
Immunization Laws
If We Stop Vaccinating
Vaccine Safety
Q&A
Diseases that Vaccines Prevent
Some of the People Who Stand Behind Vaccinations
10 Tips on Evaluating Immunization Information on the Internet
Vaccine Fact Sheets
National Vaccine Plan
NVAC
NVAC Resolutions
Pandemic Influenza Info
Publications
Customer Satisfaction Survey
Welcome Center

Table of Contents

- The safety record on vaccines
- Vaccine risks
- How vaccine safety is tested
- How vaccine safety is monitored
- Parents have a role in vaccine safety, too
- In the rare event that something goes wrong: The National Vaccine Injury Compensation Program (VICP)

The safety record on vaccines

Vaccines are very safe. Today, the United States has the safest, most effective vaccine supply in history. Vaccines have provided Americans with tremendous health benefits, with a minimum of risk. In 1996, almost 81.6 million immunizations were given in the U.S. alone, and many billions more have been given safely around the world.

The prosperity of any nation is directly linked to the health of its population. The widespread availability and acceptance of immunization in America has prevented a huge burden of disease, complications, and deaths from polio, measles, pertussis (whooping cough), tetanus (lockjaw), diphtheria, mumps, and rubella ("German" measles). As recently as 1990, *Haemophilus influenza* type b was a common, devastating illness and the leading cause of bacterial meningitis in U.S. children. Now most pediatricians (doctors who specialize in diseases of childhood) just finishing their training have never seen a case, thanks to immunizations.

Table of contents

Vaccine risks

As with any medical procedure or medication, immunizations are associated with a risk of an adverse reaction. Typical reactions may include warmth, redness, and tenderness at the site of the injection, and irritability. Potential serious reactions vary according to the type of immunization, and include the potential for seizures, damage to the brain or central nervous system, and death. However, most reactions are minor and treatable. There are so few deaths that could plausibly be connected to vaccine, and the risk is so small, that it is hard to assess statistically.(1)

The National Vaccine Program Office supports continuous vigilance, so that any increase in risk from a vaccine is quickly recognized and so that measures can be taken to make vaccines even safer. The CDC National Immunization Program and the Food and Drug Administration (FDA) have systems in place for monitoring reports of reactions. Among these is the Vaccine Adverse Event Reporting System (VAERS) , which is described more fully below in the section titled "How Vaccine Safety Is Monitored."

Vaccines have been so successful in preventing disease in the U.S. that in recent years, the annual number of reports to VAERS have exceeded the total number of reports of routine childhood vaccine-preventable disease. This may lead some people to believe that the vaccines are dangerous. *However, based on the very large numbers of data collected nationwide through the various data systems, the risk of a serious adverse reaction to an immunization is extremely small. The risk of the disease itself is substantially more serious than the risk of the immunization.* The risks of specific vaccines are posted on the CDC National Immunization Program home page, which you can access by clicking here.

LEVEL 1 - 16 OF 48 ARTICLES

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The Pink Sheet

58(16): T&G-18-T&G-17

April 15, 1996

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VACCINE PHASE IV ADVERSE EVENT-FOCUSED STUDIES UNDER FDA CONSIDERATION by Vaccine Adverse Event Reporting System administrators at the agency and at the Centers for Disease Control & Prevention. FDA Division of Biostatistics & Epidemiology Director Susan Ellenberg, PhD, listed the Phase IV studies based on VAERS data as one of several improvements of the system under consideration while speaking at the Vaccines & Related Biological Products Advisory Committee April 11.

The VAERS program, which began in 1990, was assessed by an outside expert review panel of physicians last August. They presented their report to VAERS administrators six weeks ago and summarized their findings at the advisory committee meeting.

The review team suggested that more directed Phase IV trials be performed by manufacturers. "Pre-licensure safety trials and more directions from the FDA to pharmacies and manufacturers regarding the post-marketing surveillance" are needed "so that there could be more direction" and earlier post-licensure safety information "that may not have been identified pre-licensure could rapidly be identified," said review team chair and advisory committee member Mary Glode, MD, Children's Hospital of Denver, in her feedback on the physician report.

Ongoing VAERS improvement initiatives include better automatic reporting and methods of monitoring vaccine lots, developing expanded follow-up procedures, assessing overall quality assurance and increasing communication with providers and the public, Ellenberg said.

Initiatives under consideration include assessment of reporting efficiency, using nested case control studies, making the VAERS form more specific and user-friendly, and more specifically requesting information from physicians. Several factors motivated the VAERS review: the fact that the program is conducted by two agencies and is relatively new; the growing public concern over vaccine safety; and the complexity of monitoring and assessing the data, Ellenberg said.

In the review team presentation, Glode made recommendations and detailed assessments of the system's strengths and weaknesses. VAERS' strong points include its ability to generate hypotheses regarding specific adverse events, the timeliness of its data, wide geographic representation, assessment of

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vaccine lot-to-lot variability, detection of new adverse events and the diverse input for reporting, Glode said.

Weaknesses the team observed with VAERS included the passivity of the surveillance system, under-reporting, uncertainty of the denominator of vaccines used, lack of a control population, inability to determine causal relationships, imprecise definition of "serious" events, and lack of a mechanism to detect late adverse events.

Identifying new reactions and contraindications and monitoring the safety of vaccine lots are goals the VAERS administration articulated. While the team said the goals were appropriate, they also added that without case control studies, VAERS is unlikely to identify new vaccine contraindications. They suggested that a system be devised to send out additional surveillance forms when serious or rare side effects are reported.

The team suggested re-defining 'serious' events "in the face of changing indications for hospitalizations." More follow-up should be done on new or unusual adverse events, Glode added. Of an approximate 10,000 total adverse event reports to VAERS per year, 1,000 are classified as 'serious.'

The committee recommended that VAERS be compared to the Large-Linked Data Base in regard to efficiency of reporting and types of adverse events reported. It also suggested continuing the development of computer-driven protocols and increasing public and health care provider education. Ellenberg told the review team that three factors needed to be considered in implementing its recommendations: funding for some of the initiatives, the ability to develop needed collaborations, and legal and bureaucratic issues. "For example, changing the definition of serious....It may be difficult to formally change this definition at a national level."

The VAERS and LLDB projects were compared at the National Vaccine Advisory Committee earlier this year: "LLDB is capable of providing denominators and is therefore the most useful hypothesis testing system and is understandably complex. [However], it does not have the same stability of funding as the VAERS program," NVAC Chair Ed Marcuse, MD, University of Washington, said. In 1994, VAERS was awarded a five-year contract totaling $ 4.3 mil. for operations ("The Pink Sheet" Jan. 29, T&G-2).

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responders, 56% responded after three months of therapy, 10% responded after six months and 24% responded after 10-13 months.

Using Kaplan-Meier estimates, the median duration of response to Remisar was seven months, P&U said. Twenty four of 105 Remisar patients eventually underwent cystectomy; 19 had CIS reported in their pathologic findings.

Three Phase II safety trials evaluated 134 patients, most of whom "had a history of cigarette smoking," P&U investigator Dennis Schneck, MD/PhD, said. "Cigarette smoking is the number one cause" of bladder cancer, P&U reported. A pre-treatment history of cardiovascular disease was reported in 43% (57/134) of patients. Cardiovascular adverse events were experienced by 29.8% (40/134) of patients.

Serious medical events that were "possibly or probably drug-related" (vomiting, dyspepsia, palpitations, myocardial infarction, thrombocytopenia, rash, seizure, neuropathy, myalgia and pain) were experienced by 9% of patients (12/134), the company said. Four patients (3%) died within 30 days of taking Remisar, with the deaths attributed to MI, cerebral infarction, hepatic metastases and suicide, the company said. One of the deaths was considered 'potentially drug-related' by P&U.

American Cancer Society 1996 statistics report approximately 52,900 new cases of bladder carcinoma in situ are diagnosed each year and 11,700 deaths/year are due to the disease. Bladder cancer is the fifth most common cancer in the U.S. and the fourth most common for American males, P&U said.

Males are diagnosed with bladder cancer three times more often than females, with both usually being in their fifth to seventh decades at diagnosis. On average, patients with bladder CIS "have a five-year survival rate of 80%," the committee's Raghavan said.

LEVEL 1 - 15 OF 48 ARTICLES

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The Pink Sheet

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VACCINE STANDARDIZED SAFETY DEFINITION SAFETY NEEDED FOR FUTURE TRIALS. CDC Vaccine Safety & Development Activity Chief Robert Chen, MD, said at a National

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Institute of Allergy & Infectious Diseases conference on pertussis vaccines June 5. Noting that the safety trials for acellular pertussis vaccines differed in design, schedule and methods, Chen called the results useful for comparing "relative, but not absolute, magnitude."

"Part of our problem is that unlike the efficacy dose, where there was a real effort to agree on the WHO [World Health Organization] case definition ahead of time, similar efforts were not done for safety," Chen said.

The Centers for Disease Control & Prevention is working with several HMOs in a large-linked database to study vaccine adverse events, Chen said. There are currently 500,000 children under age seven in the database, and CDC is planning to expand it to adolescents and adults ("The Pink Sheet" Jan. 29, T&D-2). The database will study signal validation, new vaccines and new schedules, Chen said. Future topics could include examining communication of vaccine risks and defining the biological basis of groups at risk for vaccine adverse reactions.

Chen suggested that the compensation program for vaccine adverse events could be used to fund vaccine investigations. "Of all the positive things that were done by the National Childhood Injury Compensation Act of 1986, one thing that they more or less neglected was" research, he said. "They found a mechanism to fund an injury compensation program after the injury has already happened, but there's really no way at this point to fund the research to try to prevent such injuries," Chen maintained.

Postmarketing studies should "differentiate early reactions from late reactions because I think they are quite different," urged Stanley Plotkin, MD, Pasteur Merieux Connaught. Vaccine adverse effects that occur quickly tend to be allergic reactions, while those that occur later are hypotonic-hyporesponsive episodes, he said.

"To really study this you would need to do very large studies," Plotkin said. "I calculated a study of 47,000 in order to show an increase of relative risk of two-fold" in hypotonic-hyporesponsive episodes.

Kathryn Edwards, MD, Vanderbilt University, said postmarketing studies should examine vaccine delivery. "The reality is that several vaccines will need to be administered at one visit," she said. "It's not a question of whether to combine, but there is an issue of whether they're in the same limb, in different limbs or the same syringe."

Speakers also suggested that safer acellular pertussis vaccines could expand immunization into adults. "Philosophically, the reasons to do it are both to reduce the morbidity and to reduce the transmission of the disease," Colin Marchant, MD, Massachusetts Public Health Biologic Labs, said. "We should give it a try if we can persuade [doctors] that they have enough morbidity . . . that they should get immunized for themselves as well" as reducing transmission to children.

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Mr. BURTON. Thank you.

Dr. Cave.

Dr. CAVE. My name is Stephanie Cave. I am in family practice in Baton Rouge, LA. I want to express my deep appreciation to you and to the members of the committee for allowing me to testify. I am presently treating over 300 autistic children, with an additional 150 waiting to get in. Dr. Amy Holmes, the physician-parent of an autistic child, joined in February to help with the overwhelming numbers of children with this problem. We are treating children from all over the United States and getting calls from many places around the globe. This is truly an epidemic. If you have any idea that it is not, I invite you to sit in my office for 2 hours.

Mercury can exist as a pure element or in various forms of organic and inorganic mercury and it affects the immune system and neurological systems at a very basic level. The timing of infant vaccines with mercury corresponds to critical periods of neuronal development. The blood brain barrier is not fully developed in the infant or toddler. The fetus is at risk of exposure to toxins during gestation, including methyl mercury from seafood eaten by the mother or other sources, Rhogam, which we have already mentioned, given at 28 weeks gestation, and the influenza vaccine given during pregnancy. These metals can be passed not only transplacentally, but also through breast milk to the infant at a time when the liver detoxification process is not perfected to the point of removing the metals.

We have measured this detoxification process, and we have found it to be woefully inadequate in the developmentally delayed children. The organic ethylmercury injected in bolus through vaccines enters the brain and converts to inorganic mercury, which cannot cross back over the blood brain barrier. This form is more likely to cause autoimmune antibodies to brain tissue, and this is what we are seeing in these children.

I believe that the introduction of the hepatitis B vaccine in 1991 has sparked this recent epidemic because of thimerosal. When added to the mercury imparted through the DPT and HIB, the exposure to mercury exceeds EPA safe limits for the metal if you consider a bolus dose on a single day. The EPA limits are usually related to ingested mercury, which is partially cleared by the liver. Injecting boluses of ethyl mercury presents an entirely different, another scenario. The 2-month dose of mercury is at least 30 times higher than the recommended daily maximum exposure set by the EPA.

During the 1990's, infants received 12.5 micrograms of mercury at birth, followed by 12.5 micrograms at 1 month, 62.5 micrograms at 2 months, 50 micrograms at 4 months, 50 micrograms at 6 months, 50 micrograms at 15 to 18 months; a total of 237.5 micrograms for a child who at best weighs 10 kilograms. This far exceeds the safety limits if you consider bolus dosing. Safety limits would be more like 1 to 1.5 micrograms.

In establishing normal safety limits, if there is such a thing for a metal as toxic as mercury, bolus injections were not considered. Consider a nurse giving an injection who is not shaking the vial according to directions before drawing out the vaccine dose. This

would give a chance that child receiving the last dose could get as much as 10 times the usual amount in one dose.

There was an article in the Journal of Pediatrics in May 2000 that showed mercury in the blood of infants at birth prior to the hepatitis B injection. After the vaccine, the levels rose in the blood of the infants tested. In some preterm infants, there were levels that measured 10 times that seen in term infants. The bile production is minimal in infancy, making it more difficult for metals to be cleared from the body. When added to a vaccine, the metals are even more dangerous because the vaccines trigger immune reactions that increase the permeability of the GI tract and the blood/brain barrier.

The injection of mercury appears to affect only certain children but I fear that we've underestimated the devastation by concentrating only on the autistic children. We're measuring elevated levels of mercury in other children with milder difficulties like learning disabilities, ADHD, Asperger's Syndrome and many others. We do not have any idea what the scope of this problem is at this point. And there are no safety standards for infants getting bolus doses of ethylmercury. We cannot compare the effects of a bolus dose in an infant to a daily dose in an adult. There are no parameters for comparison.

We have simplified the problem in our practice. We test all developmentally delayed children for the presence of heavy metals. Hair is screened, followed by a determination in urine after a challenge of an oral chelator, DMSA, and it is rare that we find any child with a developmental problem who does not have increased levels of mercury in the urine after a chelator challenge. An interesting phenomenon is that we are finding many more lead-intoxicated children than blood screens would indicate. And lead amplifies the toxicity of ethylmercury in the brain.

We performed a number of tests on blood, urine, hair, and stool in the autistic children. The abnormal findings that we see in autism involving the immune system, GI tract, and central nervous system are also seen in mercury poisoning. These include but are not limited to changes in T lymphocytes, low levels of glutathione, low sulfate levels, IgA deficiency, and the presence of myelin basic protein antibodies in the brain. The children are responding well to the use of oral chelators and supplements which take out heavy metals. We are measuring levels in the urine as we treat. The changes in the children are remarkable with each dose of a chelator. This treatment may take months to complete but the chance for recovery is evident on a daily basis.

Because mercury has such far-reaching effects in the destruction of function in many systems of the body, our treatment also involves nutritional repletion of cellular chemistry, normalization of gastrointestinal bacteria, dietary programs and restoration of liver detoxification systems.

Our medical training did not adequately prepare us for this challenge. We have learned little about testing heavy metals and even less about treating. The word "chelation" is not in the vocabulary of most physicians. A few physicians who are treating these children are inundated with them in their practices now. The good news is that they're responding well to the therapy. The changes

in neurological functioning are remarkable with each day of treatment.

It is imperative that we stop giving heavy metals to children through vaccines when their bodies can least handle such an insult. We're seeing the link on a daily basis. The children are recovering steadily but the treatment is expensive and tedious. It would make more sense for us to eliminate the cause of the problem by deleting thimerosal from the vaccines now and by withdrawing current lots containing thimerosal from pediatric offices and health units. We also need to channel funds for research into the clinical trials needed to explore the link between mercury and developmental problems in children.

I brought some slides of just a couple of the children before and after treatment. It's kind of hard to see. The child on the left has a blank stare, he has no speech. On the right he's smiling. He is now speaking. He's speaking in sentences. And this is following the nutritional treatment and the removal of metals.

Second slide. This is a child before treatment on the left: bleary-eyed, no speech at all, irritable, self-injurious, hands flapping. And on the right, I think you can see the change. And this child had a lot of metal. He had lead, he had mercury, he had aluminum. We're finding a lot of aluminum in these children. I think aluminum is going to end up being as big a problem as mercury if we keep putting it into the vaccines.

On the left, again no speech, blank eyes, blank stare, little frowning look; and on the right, I think you can see the mother's smile as well as you can see the child's smile. This was a twin, by the way. And she now has two speaking twins.

One more? OK. I think we're back to the start. Thank you.

[The prepared statement of Ms. Cave follows:]

My name is Stephanie Cave. I am in family practice in Baton Rouge, Louisiana. I want to express my deep appreciation to you, Mr. Burton, and to the members of your committee for allowing me to testify today.

I am presently treating over 300 autistic children with an additional 150 waiting to get in as soon as we can accommodate them. Dr. Amy Holmes, the physician-parent of an autistic child, joined me in February to help with the overwhelming numbers of children with this problem. We are treating children from all over the United States and getting calls from many places around the globe. This is truly an epidemic.

Autism was first described in 1943 by Kanner. Thimerosal, a mercury containing preservative, was first used in the vaccines in the early 1930s. Prior to 1970 the prevalence of autism was 1 in 2000. In 1970 it was 1 in 1000 and in 1996 the NIH estimated it to be 1 in 500. In the year 2000 reports from the education sector revealed the incidence to be 1 in 150.

Mercury can exist as a pure element or in various forms of inorganic and organic mercury. It affects the immune system and neurological systems at a very basic level. The timing of infant and toddler vaccines, with mercury, corresponds to critical periods of neuronal development. The blood brain barrier is not fully developed in the infant or toddler. The fetus is at risk of exposure to toxins during gestation including methyl mercury from seafood eaten by the mother. Other sources of heavy metals are amalgam fillings in the mother, Rhogam which is usually given to Rh negative mothers around 28 weeks gestation, and the influenza vaccine given during pregnancy.

These metals can be passed not only transplacentally, but also through breast milk to the infant at a time when the liver detoxification process is not perfected to the point of removing the metals. We have measured this detoxification process and have found it to be woefully inadequate in the developmentally delayed children. The organic ethyl mercury, injected in bolus through vaccines, enters the brain and converts to inorganic mercury, which cannot cross back over the blood brain barrier. This form is more likely to cause autoimmune antibodies to brain tissue. Similar antibodies appear in autism.

I believe that the introduction of the Hepatitis B vaccine in 1991 has sparked this recent epidemic because of the thimerosal. When added to the mercury imparted through the DTP and HIB the exposure to mercury exceeds the EPA safe limits for the metal considering a bolus dose on a single day. The EPA limits are usually related to ingested mercury, which is partially cleared by the liver. Injecting boluses of ethyl mercury presents another scenario. The two- month dose of mercury is at least 30 times higher than the recommended daily maximum exposure as set by the EPA.

During the 1990's infants received 12.5 mcg of mercury at birth followed by 12.5 mcg at one month, 50 mcg at 2 months, 50 mcg at 4 months, 62.5 mcg at 6 months, 50 mcg at 15 to 18 months. The total of 237.5 mcg for a child, who at best weighs 10 kg, far exceeds the safety limits if you consider bolus doses. In establishing normal safety levels, if there is indeed such a thing for a metal as toxic as mercury, bolus injections were not

considered. If the nurse giving the injection did not shake the vial according to directions before drawing out the vaccine dose, there is a chance that the child receiving the last dose could get as much as 10 times the usual amount in one dose.

Stajeck and Lopez (Journal of Pediatrics, May, 2000) have shown mercury in the blood of infants at birth prior to the hepatitis B injection. After the vaccine, the levels rose in the blood of the infants tested. In some preterm infants there were levels that measured ten times that seen in term infants. The bile production is minimal in infants, making it more difficult for metals to be cleared from the body. When added to a vaccine, the metals are even more dangerous because the vaccines trigger immune reactions that can increase the permeability of the gastrointestinal tract and blood brain barrier.

Mercury affects precisely those parts of the brain affected in autism—the cerebellum, amygdala, and frontal cortex accounting for the myriad of symptoms in mercury poisoning and autism. When displayed, these symptoms superimpose on each other. The following are prevalent in both: social withdrawal, depression, lack of eye contact, delayed speech, increased sound and touch sensitivity, tremors, seizures, poor concentration, poor memory, repetitive behaviors, sleeping problems, self-injurious behaviors, rashes, anorexia, accelerated cell death in the central nervous system, and prevalence of autoimmune disorders.

The injection of mercury appears to affect only certain children, but I fear that we have underestimated the devastation by concentrating on the autistic children. We are measuring elevated levels of mercury in other children with milder difficulties like learning disabilities, ADHD, and Asperger's Syndrome. We do not have any idea what the scope of this problem is at this point. There are no safety standards for infants getting bolus doses of ethyl mercury. We cannot compare the effects of a bolus dose in an infant to a daily dose in an adult. There are no parameters for comparison.

We have simplified the problem in our practice. We test all developmentally delayed children for the presence of heavy metals. Hair is screened followed by a determination in urine after a challenge of an oral chelator, DMSA (2,3 Dimercaptosuccinic acid). It is rare that we find any child with a developmental problem who does not have increased levels of mercury in the urine after a chelator challenge. An interesting phenomenon is that we are finding many more lead intoxicated children than blood screens would indicate. Lead amplifies the toxicity of ethyl mercury in the brain.

We perform a number of tests on blood, urine, hair and stool in the autistic children. The abnormal findings that we see in autism involving the immune system, GI tract, and central nervous system are also seen in mercury poisoning. These include, but are not limited to changes in T lymphocytes, low levels of glutathione, low sulfate levels, IgA deficiency, and the presence of myelin basic protein antibodies in brain. The children are responding well to the use of oral chelators and supplements, which take out heavy metals. We are measuring levels in urine as we treat. The changes in the children are remarkable with each dose of a chelator. This treatment may take months to complete, but the chance for recovery is evident on a daily basis. Because mercury has such far-

reaching effects in the destruction of function in many systems of the body, our treatment also involves nutritional repletion of cellular chemistry, normalization of gastrointestinal bacterial balance, dietary programs, and restoration of liver detoxification systems.

Our medical training did not adequately prepare us for this challenge. We learned little about testing for heavy metals and even less about treating. The word chelation is not in the vocabulary of most physicians. The few physicians who are treating these children are inundated with them in their practices. The good news is that they are responding well to the chelation treatment. The changes in neurological functioning are remarkable with each day of treatment.

It is imperative that we stop giving heavy metals to children through vaccines when their bodies can least handle such an insult. We are seeing the link on a daily basis. The children are recovering steadily, but the treatment is expensive and tedious.

It would make more sense for us to eliminate the cause of the problem by deleting thimerosal from the vaccines now and by withdrawing current lots containing thimerosal from the pediatric offices and health units. We also need to channel funds for research into the clinical trials need to explore the link between mercury and developmental problems in children.

[illegible]

REFERENCES

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Thimerosal Content in Some U.S. Licensed Vaccines

Vaccine	Brand Name	Manufacturer	Thimerosal Concentration[1]	Mercury mcg|0.5ml
DTaP	Acel-Imune	Lederle Laboratories	.01%	25
	Tripedia	Pasteur Merieux Connaught	.01%	25
	Certiva	North American Vaccine	.01%	25
	Infanrix	SmithKline Beecham	0	0
DTwP	All Products		.01%	25
DT	All Products		.01%	25
Td	All Products		.01%	25
TT	All Products		.01%	25
DTwP-Hib	Tetramune	Lederle Laboratories	.01%	25
Hib	ActHIB	Pasteur Merieux Connaught	0	0
	TriHIBit	Pasteur Merieux Connaught	.01%	25
	HibTITER (multi dose) Single dose	Lederle Laboratories	.01% 0	25 0
	Omni HIB	SmithKline Beecham	0	0
	Pedvax-HIB liquid[2]	Merck	0	0
	COMVAX[3]	Merck	0	0
	Prol-HIB[4]	Pasteur Merieux Connaught	.01%	25
Hepatitis B Virus	Engerix-B	SmithKline Beecham	.005%	12.5
	Recombivax HB	Merck	.005%	12.5

Hepatitis A	Havrix	SmithKline Beecham	0	0
	Vaqta	Merck	0	0
IPV	IPOL	Pasteur Merieux Connaught	0	0
OPV	Orimune	Lederle Laboratories	0	0
MMR	MMR-II	Merck	0	0
Varicella	Varivax	Merck	0	0
Rotavirus	Rotashield	Wyeth-Ayerst	0	0
Lyme	LYMErix	SmithKline Beecham	0	0
Influenza	All		.01%	25
Meningo-Coccal	Menomune A, C, AC and A/C/Y/W-135	CLI	.01%	25
Pneumo-coccal	Pnu-Imune 23	Lederle Laboratories	.01%	25
	Pneumovax 23	Merck	0	0
Rabies	Rabies Vaccine Adsorbed	Bioport Corporation	.01%	25
	IMOVAX	Pasteur Merieux Connaught	0	0
	Rabavert	Chiron	0	0
Typhoid Fever	Typhim Vi	Pasteur Merieux Connaught	0	0
	Typhoid Ty21a	Vivotef Berna	0	0
	Typhoid vaccine	Wyeth-Ayerst	0	0
Yellow Fever	YF-Vax	Pasteur Merieux Connaught	0	0
Anthrax	Anthrax vaccine	BioPort Corporation	0	0

Table footnotes

1. A concentration of 1:10,000 is equivalent to a 0.01% concentration. Thimerosal is approximately 50% Hg by weight. A 1:10,000 concentration contains 25 micrograms of Hg per 0.5 mL.
2. A previously marketed lyophilized preparation contained .005% thimerosal.
3. COMVAX is not approved for use under 6 weeks of age because of decreased response to the Hib component.

HAIR MULTIELEMENT ANALYSIS REPORT

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LAB. NO.: 98339-0025 ACCT.: 17719
PATIENT: Hunter
DOCTOR: Stephanie F. Cave, MD
OFFICE:
AGE: 2 SEX: M

Elements Regarded As Toxic

TOXIC ELEMENTS	PATIENT LEVEL (parts per million)	ONE STANDARD DEVIATION ABOVE MEAN	TWO STANDARD DEVIATIONS ABOVE MEAN → HIGH	MORE THAN TWO STANDARD DEVIATIONS ABOVE MEAN
luminum	6	**********	8	
ntimony	0.157	**********	.15*	
rsenic	0.122	**********	.15	
eryllium	0.027	**********	.03	
ismuth	0.026	**	.3	
admium	0.066	****	.25	
ead	1.2	********	2.0	
ercury	<dl .240		1.5	
ickel	0.11	***	0.7	
latinum	0.003	***	.02	
ilver	0.06	***	0.4	
hallium	<dl .001		.05	
horium	<dl .001		..01	
in	0.1	**	0.3	
ranium	0.009	*	.2	

TOTAL TOXIC REPRESENTATION **********

SAMPLE SIZE: 0.20 g
SAMPLE TYPE: head hair
DATE SAMPLED: 11/30/98
DATE IN: 12/05/98
DATE OUT: 12/07/98
OFFICE CODE: 2-1
ICP-MS analyzed
RACE: caucasian
HAIR COLOR:
HAIR PREPS:
SHAMPOO:

Ratios

	PATIENT RATIO	EXPECTED RANGE
CA/MG	3.6	4- 15
CA/P	1.1	2.6- 6.1
MG/K	1.2	2.0- 4.5
NA/K	2.2	1.8- 4.5
ZN/CU	16.2	4- 12
ZN/CD	>999	>800

Elements Regarded As Nutrients

	PATIENT LEVEL (parts per million)	LOW ◆ REFERENCE RANGE ● HIGH	NUMERICAL VALUE OF REFERENCE ◆ RANGE ●
alcium	296	**********	125- 350
agnesium	81	**********	12- 28
odium	149	**********	18- 85
otassium	68	**********	12- 40
opper	7	**********	8- 15
inc	116	***	95- 135
ron	7	**********	10- 20
anganese	0.45	*******	0.30- 0.52
hromium	0.29	**********	0.35- 0.80
obalt	0.028	*******	0.020- 0.045
anadium	0.025	*********	0.009- 0.080
olybdenum	0.068	*********	0.030- 0.080
oron	5.25	**********	0.80- 2.80
odine	0.4	**********	0.3- 1.2
ithium	0.043	**********	0.010- 0.040
hosphorus	265	**********	132- 192
elenium	1.574	**********	0.950- 1.700
trontium	1.67	**********	0.18- 0.85
ulfur	52822	**********	44000- 54500

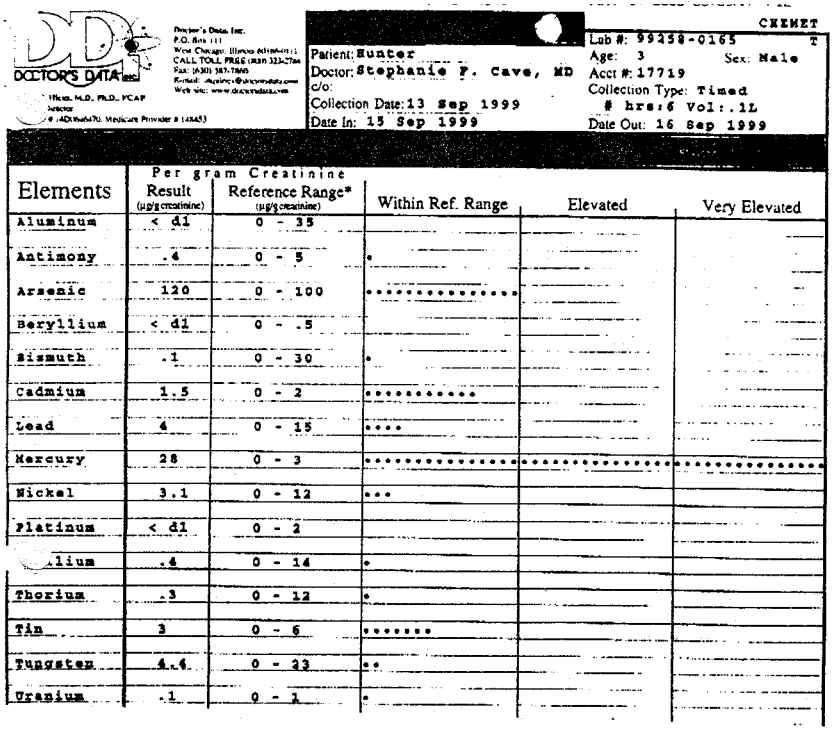
Other Elements

ELEMENT	PATIENT LEVELS	EXPECTED RANGE	ONE STANDARD DEVIATION HIGH → TWO STANDARD DEVIATIONS HIGH →
arium	2.20	0.40- 2.50	**********
ermanium	0.042	0.003- 0.028	**********
[illegible]	0.074	0.020- 0.150	
[illegible]	0.655	0.100- 0.700	**********
irconium	0.135	0.020- 0.500	

COMMENTS:

LABORATORY DIRECTOR: James T. Hicks, MD, Ph.D., FCAP • CLIA ID NO. 14D0846470 • MEDICARE PROVIDER NO. 149453 • TAX ID NO. (FEIN) 93-0941825

dl=detection limit, r/a=currently not available, qns=quantity not sufficient



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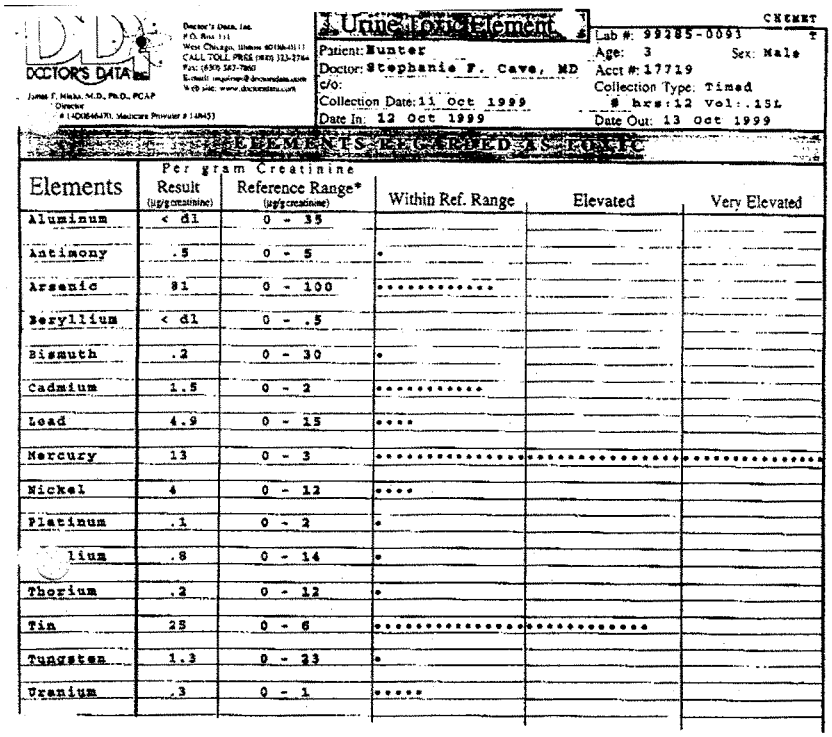
Director
14D0646470; Medicare Provider # 148453

CHEMET

Patient: Hunter
Doctor: Stephanie F. Cave, MD
c/o:
Collection Date: 13 Sep 1999
Date In: 15 Sep 1999

Lab #: 99258-0165 T
Age: 3 Sex: Male
Acct #: 17719
Collection Type: Timed
hrs:6 Vol:.1L
Date Out: 16 Sep 1999

Elements	Per gram Creatinine Result (µg/g creatinine)	Reference Range* (µg/g creatinine)	Within Ref. Range	Elevated	Very Elevated
Aluminum	< dl	0 - 35			
Antimony	.4	0 - 5	•		
Arsenic	120	0 - 100	••••••••••••••		
Beryllium	< dl	0 - .5			
Bismuth	.1	0 - 30	•		
Cadmium	1.5	0 - 2	••••••••••		
Lead	4	0 - 15	••••		
Mercury	28	0 - 3	••••••••••••••••	••••••••••••••••	••••••••••••••••
Nickel	3.1	0 - 12	•••		
Platinum	< dl	0 - 2			
[illegible]lium	.4	0 - 14	•		
Thorium	.3	0 - 12	•		
Tin	3	0 - 6	•••••••		
Tungsten	4.4	0 - 23	••		
Uranium	.1	0 - 1	•		



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James F. Mitchell, M.D., Ph.D., FCAP
Director
1426464670, Medicare Provider # 14845

Urine Toxic Element

CNEMET

Patient: Hunter
Doctor: Stephanie F. Cave, MD
c/o:
Collection Date: 11 Oct 1999
Date In: 12 Oct 1999

Lab #: 99285-0093
Age: 3 Sex: Male
Acct #: 17719
Collection Type: Timed
hrs: 12 Vol:.15L
Date Out: 13 Oct 1999

ELEMENTS FLAGGED AS TOXIC

Elements	Per gram Creatinine Result (µg/g creatinine)	Reference Range* (µg/g creatinine)	Within Ref. Range	Elevated	Very Elevated
Aluminum	< dl	0 - 35			
Antimony	.5	0 - 5	•		
Arsenic	81	0 - 100	••••••••••••		
Beryllium	< dl	0 - .5			
Bismuth	.2	0 - 30	•		
Cadmium	1.5	0 - 2	••••••••••		
Lead	4.9	0 - 15	••••		
Mercury	13	0 - 3	•••••••••••

FAX NO. : 225 757 4541 Jul. 17 2000 08:10AM P14

HAIR MULTIELEMENT ANALYSIS REPORT

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FEDEX: 3755 Illinois Avenue, St. Charles, IL 60174-2420

LAB. NO: 98352-0070 ACCT: 17719
PATIENT: Joseph AGE: 3 SEX: M
DOCTOR: Stephanie F. Cave, MD
OFFICE:

SAMPLE SIZE: 0.19 g
SAMPLE TYPE: head hair
DATE SAMPLED:
DATE IN: 12/18/98
DATE OUT: 12/22/98
OFFICE CODE: 2-1
ICP-MS analyzed
RACE: caucasian
HAIR COLOR:
HAIR PREP:
SHAMPOO:

Elements Regarded As Toxic

TOXIC ELEMENTS	PATIENT LEVEL (parts per million)	ONE STANDARD DEVIATION ABOVE MEAN	TWO STANDARD DEVIATIONS ABOVE MEAN →	MORE THAN TWO STANDARD DEVIATIONS ABOVE MEAN → HIGH
Aluminum	26	**********	3**********	**********
Antimony	2.004	**********	.13**********	**********
Arsenic	0.781	**********	.15**********	
Beryllium	<cl .002		.07	
Bismuth	0.213	**********	.3	
Cadmium	0.595	**********	.23******	
Lead	15.3	**********	2.0**********	**********
Mercury	<cl .240		1.5	
Nickel	0.64	*****	0.7	
Platinum	<cl .001		.02	
Silver	0.35	**********	0.4	
Thallium	<cl .001		.09	
Thorium	<cl .001		.01	
Tin	0.5	*********	0.8	
Uranium	0.012	*	.2	
TOTAL TOXIC REPRESENTATION		**********	**********	**********

Ratios

	PATIENT RATIO	EXPECTED RANGE
CA/MG	18.0	4- 15
CA/P	1.0	2.6- 6.1
MG/K	0.2	2.0- 4.5
NA/K	0.4	1.8- 4.5
ZN/CU	6.0	4- 12
ZN/CD	119	>800

Elements Regarded As Nutrients

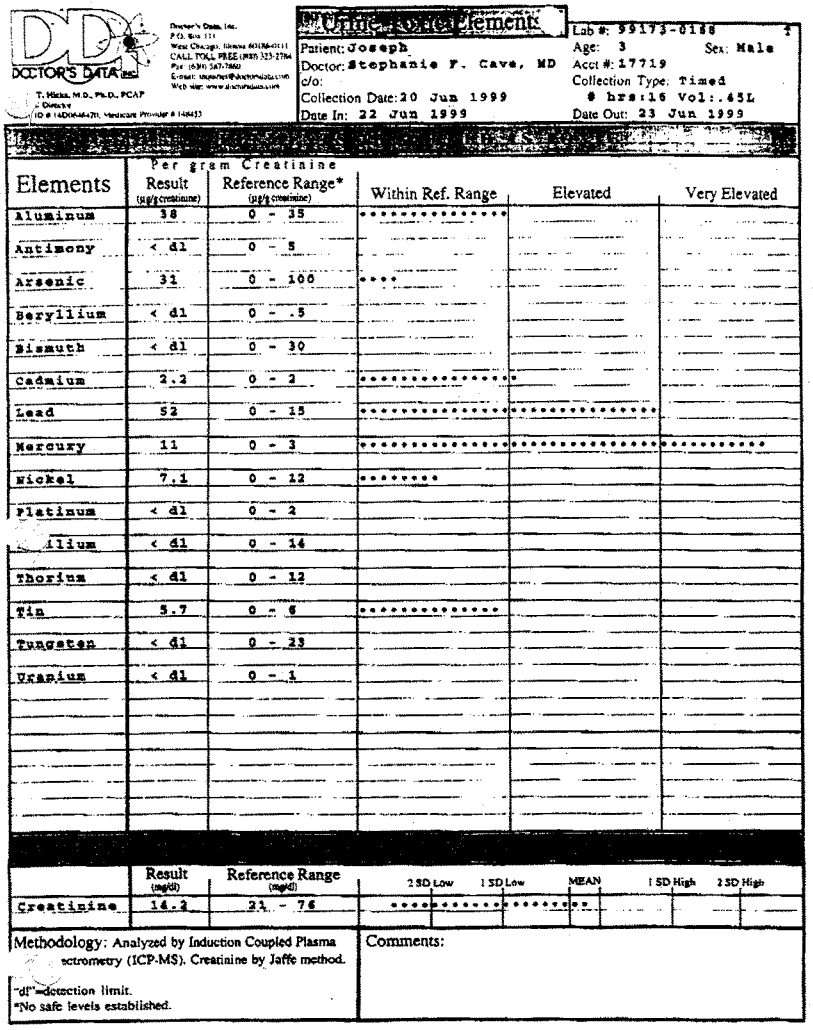
NUTRIENT	PATIENT LEVEL (parts per million)	LOW ◆ REFERENCE RANGE ● HIGH	NUMERICAL VALUE OF REFERENCE ◆ RANGE ●
Calcium	217	*****	125- 350
Magnesium	12	**********	12- 28
Sodium	19	**********	18- 85
Potassium	49	**********	12- 40
Copper	12	****	8- 15
Iron	71	**********	95- 135
Zinc	13	*******	10- 20
Manganese	0.98	**********	0.30- 0.52
Chromium	0.42	*****	0.35- 0.80
Cobalt	0.017	**********	0.020- 0.045
Vanadium	0.127	**********	0.009- 0.050
Molybdenum	0.143	**********	0.030- 0.080
Boron	2.45	**********	0.80- 2.60
Iodine	1.4	**********	0.3- 1.2
Lithium	<cl .007	**********	0.010- 0.040
Phosphorus	211	**********	132- 192
Selenium	1.822	**********	0.950- 1.700
Strontium	0.62	******	0.18- 0.85
Sulfur	51362	*******	44000- 54500

Other Elements

ELEMENT	PATIENT LEVELS	EXPECTED RANGE	ONE STANDARD DEVIATION HIGH →	TWO STANDARD DEVIATIONS HIGH →
Barium	1.226	0.40- 2.50		
Germanium	0.008	0.003- 0.028		
Rubidium	0.067	0.020- 0.150		
Tellurium	1.027	0.100- 0.700	**********	
Zirconium	1.365	0.020- 0.800	**********	**********

COMMENTS:
st checked

cl=detection limits n/a=currently not available, insufficient for calculation



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Director
ID # 14D0646470, Medicare Provider # 148453

Urine Toxic Elements

Lab #: 99173-0188 T
Patient: Joseph
Age: 3 Sex: Male
Doctor: Stephanie F. Cave, MD
Acct #: 17719
c/o:
Collection Type: Timed
Collection Date: 20 Jun 1999
hrs:16 Vol:.45L
Date In: 22 Jun 1999
Date Out: 23 Jun 1999

Elements	Per gram Creatinine Result (µg/g creatinine)	Reference Range* (µg/g creatinine)	Within Ref. Range	Elevated	Very Elevated
Aluminum	38	0 - 35	•••••••••••••••		
Antimony	< dl	0 - 5			
Arsenic	31	0 - 100	••••		
Beryllium	< dl	0 - .5			
Bismuth	< dl	0 - 30			
Cadmium	2.2	0 - 2	•••••••••••••••		
Lead	52	0 - 15	•••••••••••••••	•••••••••••••••	
Mercury	11	0 - 3	•••••••••••••••	•••••••••••••••	•••••••••••
Nickel	7.1	0 - 12	••••••••		
Platinum	< dl	0 - 2			
[illegible]ilium	< dl	0 - 14			
Thorium	< dl	0 - 12			
Tin	5.7	0 - 6	•••••••••••••••		
Tungsten	< dl	0 - 23			
Uranium	< dl	0 - 1			

	Result (mg/dl)	Reference Range (mg/dl)	2 SD Low	1 SD Low	MEAN	1 SD High	2 SD High
Creatinine	14.2	21 - 76	••••	••••••••	••••••••		

Methodology: Analyzed by Induction Coupled Plasma [illegible]ectrometry (ICP-MS). Creatinine by Jaffe method.

"dl"=detection limit.
*No safe levels established.

Comments:

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Nicholas, M.D., Ph.D., FCAP
Director
CLIA #14D0644793, Medicare Provider # 18433

CHEMET

Lab #: 99279-0080 †

Patient: Joseph Age: 4 Sex: Male
Doctor: Stephanie F. Cave, MD Acct #: 17719
c/o: Collection Type: 24 hour
Collection Date: 3 Oct 1999 24 hour volume: .25 L
Date In: 6 Oct 1999 Date Out: 7 Oct 1999

Elements	Per gram Creatinine Result (µg/g creatinine)	Per gram Creatinine Reference Range* (µg/g creatinine)	Per 24-Hour Result (µg/24-hour)	Per 24-Hour Reference Range* (µg/24-hour)		Elevated	Very Elevated
Aluminum	< dl	0 - 35	< dl	0 - 37			
Antimony	.3	0 - 5	< dl	0 - 7			
Arsenic	28	0 - 100	3.9	0 - 140	•		
Beryllium	< dl	0 - .5	< dl	0 - .6			
Bismuth	< dl	0 - 30	< dl	0 - 30			
Cadmium	.9	0 - 2	.1	0 - 3	•		
Lead	47	0 - 15	6.7	0 - 20	••		
Mercury	.8	0 - 3	< dl	0 - 5			
Nickel	1.7	0 - 12	.2	0 - 20	•		
Platinum	< dl	0 - 2	< dl	0 - 2			
Thallium	.3	0 - 14	0	0 - 14	•		
Thorium	.1	0 - 12	< dl	0 - 13			
Tin	5.8	0 - 6	.8	0 - 11	•		
Tungsten	.7	0 - 23	.1	0 - 23	•		
Uranium	.1	0 - 1	< dl	0 - 2			

	Result (µg/24-hours)	Reference Range (µg/24-hours)	2 SD Low	1 SD Low	MEAN	1 SD High	2 SD High
Creatinine	.142	.31 - .8					

Methodology: Analyzed by Induction Coupled Plasma ectrometry (ICP-MS). Creatinine by Jaffe method.

"dl"=detection limit.
*No safe levels established.

Comments:
(Post provocative challenge.) See fax copy

Copy mailed to pt. 10-12-99

Chelation of Mercury for the Treatment of Autism

Amy S. Holmes, M.D.

July 15, 2000

DRAFT

I. Autism - Etiology

Autism and disorders resembling autism can be caused by a number of disorders, including Fragile X Syndrome, tuberous sclerosis, and phenylketonuria, and by at least one notable chromosomal abnormality, an inverted duplication of a portion of chromosome 15. But for the vast majority of cases of autism today, there is no strictly genetic explanation. As with many chronic disorders, most cases of autism appear to be caused by some genetic predisposition coupled with some early environmental insult.

Several recently-released reports point to the occurrence of an autism "epidemic" with the latest incidence figures quoted to be on the order of 1 out of every 250 children. The *Report on Autism to the California Legislature* released in 1999 documents a large increase in full-blown DSM IV autism alone, with other disorders increasing at the same rate as population growth. F. E. Yazbak, M.D. found similar rates of increasing incidence in other states reported in his *Autism 99 : A National Emergency*. The Center for Disease Control's own investigation of Brick township, New Jersey found a very high incidence of autism as well. Some noted sources attribute the apparent increase in autism incidence to better diagnoses on the part of pediatricians and the various pediatric specialties. Most, however, are unable to fully accept this simplistic explanation because the diagnosis is strictly a behavioral one, and it is highly doubtful that the highly skilled diagnosticians of earlier years could have overlooked such obvious behavioral anomalies occurring in such a large proportion of children. Furthermore, since it is impossible to have a "genetic epidemic", one must examine possible early environmental insults for clues to explain the increase in autism cases.

Bernard, et al, have written an excellent article comparing autism with mercury poisoning. All aspects of both disorders are examined, including symptoms, signs and findings on common laboratory tests. The parallels between the two disorders is disturbingly obvious, even to the most casual reader. This, coupled with many case reports of clinical improvement among autistic children upon removal of at least a small part of their whole-body load of mercury, seems to indicate that most cases of autism today are, in fact, cases of mercury poisoning. The early environmental insult, in these cases, is mercury exposure that overwhelmed the body's attempts at detoxification.

How does mercury gain access to a fetus or an infant? First of all, mercury is ubiquitous. It is in our water supply. In this setting, it exists mainly in cationic (1+ or 2+) form. This form is largely unabsorbed. Fish and shellfish are a known source of organic mercury (methyl mercury). Organic mercury is absorbed reasonably well by the gastrointestinal tract. Exposure via these two routes is common, but it is far exceeded by exposure via dental amalgams and thimerosal-containing vaccines. Mercury vapor is known to be released from dental amalgams, and it is known to cross

the placenta with ease. It is not too far-fetched to assume that some mercury vapor (Hg - 0) is released from the dental amalgams of the mother, she inhales the vapor, it enters her bloodstream, some crosses the placenta and enters the developing fetus. Once metallic mercury (vapor, Hg - 0) enters the cell, it can be easily converted to its cationic form, and in this form, readily binds to sulfhydryl groups on enzymes and other proteins. Once tightly bound via this mechanism, it is in the body for a long time. Thimerosal-containing vaccines are now given with abandon. Upon its arrival into our world, the newborn is greeted with a Hepatitis B vaccine. He then receives several more doses of this vaccine along with 3 DPT vaccines, and at least one HIB vaccine. All three of these vaccines contain relatively large amounts of thimerosal, which is 49.6% ethyl-mercury by weight. It was not long ago that the only vaccine containing thimerosal was the DPT vaccine. But, the Hepatitis B vaccine was made "mandatory" in 1991 and the HIB vaccine a few years earlier. Is it a coincidence that the incidence rate of autism has soared in the 1990's? Is it better diagnosis or is it more mercury early in life? Add onto these noted exposures the thimerosal-containing RhoGam injection. A reasonable conclusion of greatly increased mercury exposure to developing fetuses, newborns and young infants being responsible for the obvious autism "epidemic" is almost inescapable.

Why isn't every child equally affected ? Why are some children so affected while most seem totally unaffected by what seems to be an almost equal mercury exposure? The answer is unknown but has been suggested by Steven Edelson's publication in Toxicology and Industrial Health 1998. In this landmark work, he measured four of the Phase II liver detox pathways in the liver - glucuronidation, sulfation, glycine conjugation, and glutathione conjugation. All autistic subjects tested were found to have impairments in at least one of these four pathways. Problems with glucuronidation were found in all subjects. Granted, the sulfate wasting problem in autism is probably an effect of mercury toxicity rather than a cause, but Edelson's work suggests a possible mechanism whereby only a small proportion of children are affected. Perhaps the affected children were, at least at the time of exposure, unable to quickly and efficiently get rid of the mercury to which they were exposed.

II. Testing for Mercury Toxicity

Poisoning with most heavy metals is detected easily with blood tests. For example, if a person has detectable lead in his body, he will have some detectable lead in his blood. In fact, the gold standard for the detection of poisoning for most heavy metals is a test of intracellular content using red blood cells. Hair and urine levels of heavy metals are a general reflection of blood levels. Also, getting rid of most heavy metals such as lead with chelating agents is not difficult, and the dosing schedule does not impact the outcome of treatment. This is because most heavy metals in the body exist in a reasonably equal equilibrium between their preferred storage sites and the bloodstream.

This is not the case with mercury. After an exposure, detectable levels are present in the blood for only a short time, on the order of weeks to a few months. This is because mercury, unless eliminated, quickly becomes tightly bound to sulfhydryl-containing enzymes and other proteins in

the liver, kidney, lining of the gastrointestinal tract, and brain. So, if any reasonable time has elapsed after a significant mercury exposure, little if any mercury will be detected in the blood, urine or hair.

The only way of directly detecting the amount of mercury present in the liver, kidney, GI tract, and brain is via biopsy of these organs. This is NOT a recommended procedure. Besides, the real issue is not how much mercury is present, but how mercury-toxic the patient really is. Mercury has well-documented effects on different laboratory tests, so this is the preferred way of measuring mercury toxicity. The list below is only a partial list of helpful lab tests, and does not reflect at all the effect of mercury on the brain itself.

Lab Tests Useful for Evaluating Mercury Toxicity

1. CBC with differential
   - high MCV
   - high monocytes
   - high eosinophils
2. Serum electrolytes
   - low CO2
3. Liver function tests
   - elevated liver enzymes
4. RBC intracellular trace minerals
   - classic picture is normal calcium, potassium, and copper with low to borderline-low values of magnesium, molybdenum, selenium, vanadium, chromium, and zinc.
5. Hair Elements (Doctor's Data Lab)
   - A. Elevated levels of other heavy metals (not mercury)
   - B. "Scattered" pattern of hair essential elements
   - C. High hair calcium
6. Plasma Amino Acids
   - low in at least half of essential amino acids
   - low in taurine
7. Urine Organic Acid Test (MetaMetrix is best for our purposes)
   - A. Uncoupling of Oxidative Phosphorylation
     1. Elevated fatty acid metabolites
     2. Elevated lactate
     3. Elevated hydroxymethylglutarate
   - B. Partial blocks of several Krebs cycle enzymes
   - C. Elevated homovanillate (reflects elevated dopamine)
   - D. Impaired Detoxification (usually several abnormalities)
     1. Glutathione depletion (elevated pyroglutamate)
     2. Very high sulfate/creatinine ratio (sulfate wasting in urine)
8. Urine D-glucaric acid (Doctor's Data Lab)
   - elevated
9. Fractionated Urine Porphyrins (hard to do correctly, especially if not potty-trained)
   - elevated coproporphyrin
   - elevated precoproporphyrin (not available commercially yet)

10. Immune System Tests ($$$$)
    A. Elevated CD4 cells, low CD8 cells, elevated CD4/CD8 ratio (opposite of AIDS)
    B. Low NK cells
    C. Elevated serum IgE

Note : No one, even the most toxic person, has all these lab abnormalities present.. Even the most mercury-toxic will have some normal results. But, with half or more results abnormal, one can be reasonably sure that the patient is heavy metal-toxic.

Some signs of mercury toxicity affecting the brain and immune system can be found on physical exam. Below is a very partial list:

Abnormalities on Physical Exam Found in Mercury Toxicity
1. Dilated pupils
2. Sweaty hands and feet
3. Pathologic reflexes - Babinski most common
4. Very brisk knee jerks
5. Slight esotropia
6. Rashes, eczema
7. Elevated heart rate

And there are MANY others.

Because of the known kinetics of mercury in the body, there are some abnormalities that will not be found unless the mercury exposure was recent. These are:

1. Elevated hair mercury
2. Elevated blood mercury
3. Elevated intracellular (RBC) mercury
4. Elevated urine mercury

A "challenge" test with any chelating drug is of no medical use, unless it is necessary to convince an insurance company to pay for treatment. Some companies will not pay for treatment even with a "positive" test. Everyone will excrete some mercury on a challenge test, and the amount excreted, unless it is VERY large, does nothing to prove toxicity. Furthermore, even those who excrete very little mercury in response to a "challenge" may be very mercury-toxic. Their mercury may be so tightly bound in various organs that little will actually be chelated during the short time period of a challenge test. It is far better to rely on signs found on physical examination and the above laboratory abnormalities to correctly diagnose or exclude mercury toxicity.

III. Treatment of Mercury Toxicity

In order to be a good chelator of mercury, a molecule must have two opposed (in 3-D structure) sulfhydryl groups or other groups that bind well to mercury. The effect of having these two opposed groups is to bind divalent cationic mercury (Hg 2+) in sort of a "pincer grasp", making it very difficult for mercury to leave the chelator to bind to another molecule. Some compounds that meet this requirement are :

1. DMPS (2,3 dimercaptopropane sulfonate)
2. DMSA (*meso*-2,3 dimercaptosuccinic acid)
3. Lipoic acid
4. BAL - Dimercaprol - NOT RECOMMENDED

Those compounds which have only 1 sulfhydryl or other mercury-binding group are poor chelators simply because they do not bind mercury tightly enough to keep it from binding to other molecules. Among these compounds are MSM and cysteine. Their net effect may be simply moving mercury around to other sites in the body. One substance that may have some good chelating properties is cilantro. The problem with this substance is that it is unknown at the present time exactly what the ingredient present in cilantro might be that may give it good chelating properties. Without knowing the identity of the actual chelating substance, it is impossible to know how much and how often it should be given. Also it is impossible to determine if all cilantro has the same amount of the unknown substance. It is probably a good idea NOT to use cilantro for chelating mercury until more is known about the substances involved.

Because of the known kinetics of mercury in the body, it is necessary to maintain a reasonably steady blood level of the chosen chelator over an extended period of time. The half-lives of DMPS, DMSA, and lipoic acid dictate the dosing frequency of each necessary to maintain steady blood levels :

1. DMPS (oral) - dose every 8 hours
2. DMSA - dose every 4 hours
3. Lipoic acid - dose every 3 to 4 hours

DMPS can be used , but must be used orally every 8 hours to maintain steady blood levels. This drug is not recommended for several reasons :

1. DMPS is not approved for use in children. It has NEVER been tested for safety and efficacy in children.
2. It is much more expensive than the others.
3. The oral form must be obtained from a compounding pharmacist.
4. It is very unlikely to be covered by insurance.

DMSA is an excellent chelator of most heavy metals including mercury. When used appropriately, it is safe and effective. When used inappropriately, it can create disasters such as seizures. DMSA has survived the testing necessary for FDA approval for use in children. This means it has been tested **in children** and was found to be both safe and effective. Despite the FDA's poor record in testing and approving vaccines, the procedures for testing and approval of drugs are quite rigorous. The only approved use for DMSA is for the treatment of lead poisoning in children. Fortunately, DMSA is not very selective about which heavy metal it chelates, and binds to mercury

quite readily. Despite claims of DMSA's ability to cross the blood-brain barrier (BBB), it is doubtful that it really does so. The study cited most often as proving DMSA's ability to cross the BBB was done in rats. Rats are known to **not** have a good BBB. DMSA is water-soluble and not very lipid-soluble. This characteristic alone raises some doubts about its true ability to cross the BBB.

Lipoic acid fits the molecular criteria of a good chelator. It has two diametrically-opposed sulfhydryl groups capable of tightly binding mercury in a "pincer grasp". It also has the advantage of being lipid-soluble which implies an innate ability to cross cell and mitochondrial membranes and the BBB more easily than DMSA.

An ideal course of chelation therapy for mercury poisoning should include the following:
1. First, getting rid of the loosely-bound body mercury.
2. Then chelating the more tightly-bound mercury including that in the brain.
3. Appropriate nutritional support designed to counteract mercury's known effects and to make the patient more comfortable while mercury is being moved around.
4. Appropriate monitoring tests (especially important in non-verbal children) to check on blood counts, kidney and liver function, and mineral levels, and to gauge how much mercury is being excreted.

One such ideal course might be :
1. DMSA alone - low-dose based on lean body mass, given every 4 hours on a week-on, week-off schedule, until urine mercury levels off at a low value (usually 2 to 6 months).
2. DMSA plus lipoic acid - also low doses at frequent time-intervals, on an on and off schedule, until no more mercury comes out in the urine.
3. Appropriate nutritional support might include essential fatty acids, fat and water-soluble vitamins, and minerals.
4. Routine monitoring tests probably should include :
    A. CBC with differential count
    B. Serum electrolytes
    C. Liver function tests
    D. Urinalysis
    E. RBC intracellular minerals (may or may not be necessary)

It is very desirable to monitor urine mercury levels on DMSA and DMSA/lipoic acid. Granted most mercury is normally excreted through the feces, but DMSA greatly increases urinary excretion of mercury, and the measurement of fecal mercury is somewhat unreliable because there is no way of standardizing the amount measured. Fecal mercury results are reported in mcg/g fecal dry weight. Anything that changes the dry weight of feces, such as the fiber content of the diet, will change the results. Consequently, there is no way of reliably comparing the results of one test to another in the same patient. Urine mercury is standardized in two ways - mcg/g creatinine and mcg/24 hours. A 24-hour urine collection is impossible for most children. Mcg/g creatinine is preferred since creatinine is excreted relatively constantly over time in the same person. This fact allows easy and reliable comparison of test results over time in a particular patient.

When undertaking a course of chelation for mercury, one important point is to do it in cycles consisting of "on" and "off" periods. Give the patient as much time off chelation as on chelation. If any abnormal results show up in the routine monitoring tests, it is best to stop chelation for a while, retest, and resume chelation when the results have normalized.

It is extremely advisable to chelate safely under the supervision of a physician. Several reasons for this are obvious. First of all, DMSA is available by prescription only (although Thorne Research makes a product called Captomer that appears to be DMSA - be careful with this mainly because the amounts stated on the labels of nutritional supplements are not always accurate). Also, it is advisable to have some medical professional ordering and interpreting the results of all the lab tests. This is of utmost importance in those children without good verbal skills. Finding a good physician who will help your child can be difficult but is well worth the effort involved.

IV. Prognosis

This area is the most difficult to assess at the present time. Will the complete removal of mercury from the body, especially the brain, actually cure autism? Or, are the neurons and supporting cells so permanently damaged that complete reversal cannot be expected? Unfortunately, there is not enough data available to make any true conclusions at this time.

But, there are some suggestions that a cure of autism might be possible with removal of all mercury. The first suggestion of this possibility is the complete reversal of neurologic disorders in adults upon mercury removal. But adults have fully-developed brains present before they were poisoned. It is possible that similar improvements might not be observed in children because the mercury was introduced prior to brain maturation. On the other hand, children have far superior healing abilities and greater brain "plasticity" than adults, so their capacity for compete normalization might be greater than that for adults.

The data currently available, although very limited, suggests that cures of autism upon complete removal of toxins are very possible, and the prognosis is dependent on the age of the child at the time of complete removal of toxins. Three age groups have been identified :
1. Up to adrenarche (generally around 7) - complete recovery possible
2. Past adrenarche, prior to puberty - probably not complete recovery, but language and social gains are possible along with elimination of problem behaviors (aggression, self-injurious behaviors, etc.)
3. After puberty - probably no language or social gains, but possible elimination of problem behaviors (aggression, self-injurious behaviors, etc.)

As more data becomes available, the prognosis for all age groups will be better defined.

V. Unanswered Questions

There are many more unanswered questions than can be listed, but here is a partial list:

1. Is mercury the only heavy metal involved or are most cases of autism attributable to a mixed-metal toxicity with mercury heading the list?
2. Are non-metal toxins involved at all in the etiology of autism?
3. Are there any other treatments currently available that work as well or better than DMSA followed by DMSA plus lipoic acid? What about new treatments on the horizon?
4. What is the actual underlying factor(s) that makes some fetuses, newborns, and infants particularly sensitive to the effects of mercury exposure?
5. Are non-drug, non-supplement treatments (sauna, massage, etc.) of any benefit in detoxification?

VI. Conclusion

It appears likely that most cases of autism are the result of mercury poisoning at a very early age. Effective treatments for safely removing mercury from the liver, kidney, GI tract, and brain are available today. Patient prognosis is probably dependent on age at the time of complete mercury removal, but more data is needed before definite conclusions can be made.

Mr. BURTON. Thank you, Dr. Cave. Sounds like you're doing real good work down there. We'll check all the references that you used as well as your statement.

Doctor.

Mr. APOSHIAN. May I have the first slide, please?

Mr. Chairman, members of the committee, I have been asked to review mercury toxicity with you for a short period of 5 minutes. And with your permission, I'll dispense with the usual introductory remarks and get to the point.

May I have the next slide, please? The next slide, please.

The next slide will tell you about the different forms of mercury. We have elemental mercury, we have organic mercury, and we have mercuric mercury that we usually call inorganic. The elemental mercury you're probably familiar with as far as the silvery liquid that most children play with at some time in their lives. It is dangerous because it emits mercury vapor at room temperature or when it's in our mouth, as we will talk about in a moment. It's a very dangerous poison.

The organic mercury, methylmercury, comes from fish—the fish that you eat, certain kinds of fish. And thimerosal comes from the vaccines and other medical preparations. A recent FDA list pointed out there are 217 medical preparations listed with the FDA that contain organic mercurials; 217.

And finally, the slide mentions mercuric mercury that we'll speak about in a moment. As far as the sources and forms of brain mercury, this is shown in the next slide. You may not be able to see that, but on the left is a tooth, underneath is thimerosal, and over to the right hand side is a fish. The greatest exposure to mercury of the American population comes from the amalgams in their mouths. This has been clearly established. The mercury amalgams in your mouth, the so-called silver fillings, contain 48 to 50 percent of elemental mercury. These fillings continuously emit mercury vapor which will go to the brain and is converted to mercuric mercury, as is pointed out there.

On the far right-hand side, you'll see a picture of a fish. Certain fish contain methylmercury; again, very rapidly taken up from the GI tract, transported quickly to the brain, and converted very slowly to mercuric mercury. And then on the bottom left-hand side, you'll see thimerosal, which again will be taken up by the brain and quickly converted to mercuric mercury.

Now, one of the findings of the recent National Academy of Sciences report is that you really cannot consider any form of mercury alone. Let me just read you the one statement from the prepublication form of this report. It says: Prospective data on all sources of mercury exposure such as vaccines and dental amalgams and dietary intakes of methylmercury are essential to understanding the effects of environmental mercury exposure on any outcomes.

May I have the next slide, please? This will show you the target organs of various forms of mercury: mercury vapor of the brain, methylmercury of the brain, thimerosal of the brain, and mercuric mercury if it's taken up from outside of the body, the kidney. What's important to find out is all three of the first three forms are

neurotoxic, neurotoxic in particular in the brain. By neurotoxic, we mean it will damage nerves and it will damage brain tissues.

The next slide, please. Neurotoxicity of mercury. I think the first statement is that the mercury stays in the brain. I can't quite see the slide myself from here. The mercury remains in the brain. My colleague, Mary Aposhian, has looked for the last 10 years for compounds that would bring mercury out of the brain. There is no such therapeutic agent that we know of. Most of the research in this country, as far as getting mercury out of the brain, is supported by the family of a former Vice President of the United States. It is believed that that Vice President died of mercury toxicity. That family has done more for studying basic mercury toxicity than probably any other foundation or government in our country.

The most sensitive organs: brain of fetus, brain of children, brain of adults. Again, the brain of the fetus is uniquely susceptible to mercury toxicity, as are the brains of children and the brains of adults. We're mature. What I would like you to remember is a child is not a small adult. The metabolism, the biology of the child, is quite different. The child has developing organs. The fetus has developing organs. And we know that mercury will stunt certain metabolic reactions involved in development.

The next slide, please. The final slide points out that which damages the brain. Again, the recent National Academy of Science report really introduced something quite novel as far as the thinking of the scientific community. And that is, as you look at all this—these slides, the central compound, the central form of mercury here is mercuric mercury. Mercuric mercury vapor converts into mercuric mercury, thimerosal converts to mercuric mercury, as does methylmercury. So this is probably the culprit, mercuric mercury. The report points out that we must consider methylmercury and mercuric mercury as well as thimerosal in order to understand the neurotoxicity of mercury.

Let me just say as a final statement that there is no need to have thimerosal in a vaccine. There are other agents that can be used that are known to be safe.

Thank you for your attention.

Mr. BURTON. Thank you, Doctor.

[The prepared statement of Mr. Aposhian follows:]

201

Mercury Toxicity

Presentation

To

COMMITTEE ON GOVERNMENT REFORM

House of Representatives

Congress of the United States

Washington, DC

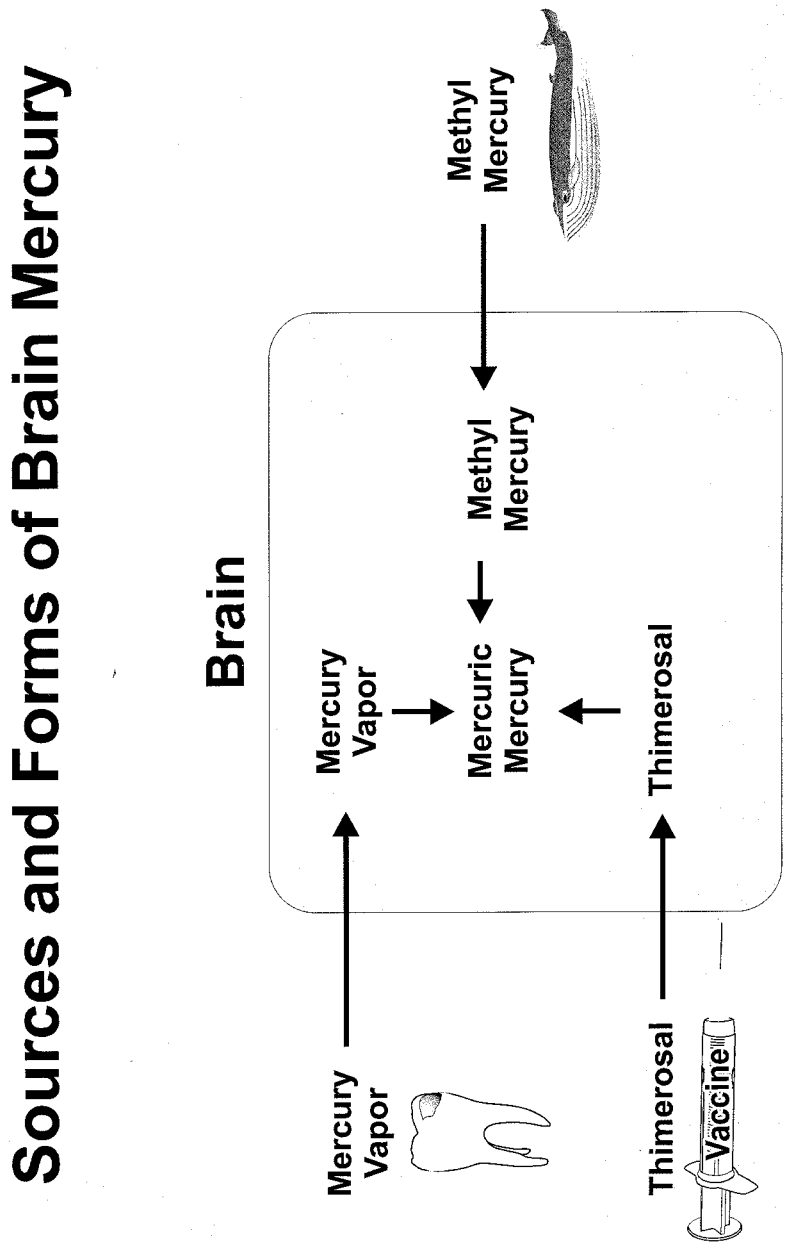
JULY 18, 2000

COPIES OF SLIDES

H. Vasken Aposhian, Ph.D.
Professor of Molecular and Cellular Biology
Professor of Pharmacology
The University Of Arizona
Tucson, Arizona

Forms of Mercury

1. Elemental mercury
   - "Liquid silver"
   - Mercury vapor
2. Organic mercury
   - Methylmercury
   - Thimerosal
3. Mercuric mercury


Sources and Forms of Brain Mercury
Brain
Mercury Vapor
Mercuric Mercury
Thimerosal
Methyl Mercury
Methyl Mercury
Mercury Vapor
Thimerosal
Vaccine

Target Organs

1. Mercury vapor → brain
2. Methylmercury → brain
3. Thimerosol → brain
4. Mercuric mercury → kidney

Neurotoxicity of Mercury

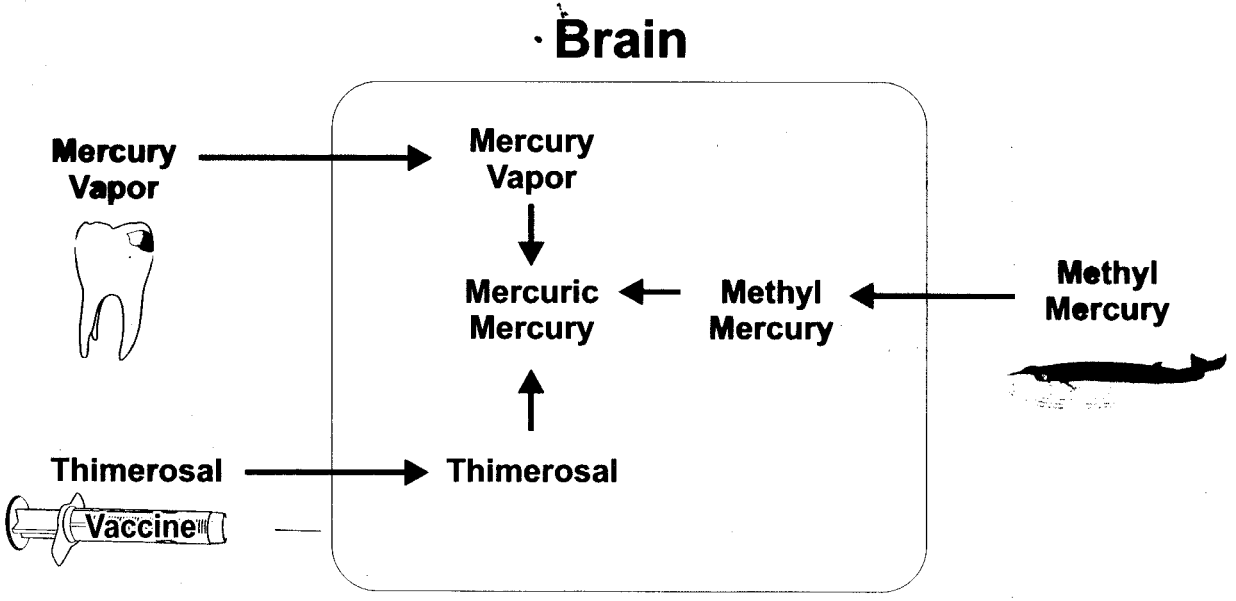
1. The mercury remains in the brain

2. Most sensitive organ:
   - Brain of fetus
   - Brain of children
   - Brain of adults

3. A child is not a small adult! Organs are developing!

Sources and Forms of Brain Mercury

Which damages the brain?



Mr. BURTON. Dr. Humiston.

Dr. HUMISTON. Mr. Chairman and members of the committee, I applaud your efforts to bring parents, scientists, and policymakers together around the issue of autism. I am grateful for the opportunity to share my perspective as a parent, pediatrician, and public health researcher.

Last week, my baby Quinn demonstrated developmental skills that thrilled my husband and me. He pulled his father's hand toward a pile of rocks, used his other hand to point toward a puddle, and said, "dad ock bla-bla," which meant, "Daddy, throw this rock in the water." Unfortunately, Quinny is 7½ years old.

The worst day of my life was not the day the developmental pediatrician told me, almost apologetically, that my son was autistic. The worst day came later when the specialists told me that Quinn's progress was minimal after a year and a half of intense therapy, and that this made his prognosis grave. My family's response was very typical. We reached out and embraced a succession of therapies, each touted as a lifesaver. We heard that gluten allergy was the cause, and we changed Quinn's diet. Later we tried, for example, a phenol-free diet, megavitamins, anti-yeast medications, and cranio-sacral massage. Each therapy was supposed to get at the cause of Quinn's autism. Each therapy was expensive, and each for my son was a failure.

You may wonder what would make a reasonable person pursue such an array of untested and unproven approaches. Well, I am a desperate mother. I am desperate to help my son quickly during his early years when we'd expect rapid brain development. I am desperate because the science lags so far behind my son's needs. My family has been blown by every wind, every theory, to explain this pervasive developmental disorder, and we are tired. We are physically tired, financially tired, emotionally tired. So I am here today to encourage you to nurture the science that will help, if not my son, then at least my little girl's future children.

Funding, of course, is a very good way to show support. I appreciate the significant increases in NIH funding for autism research. I am grateful for CDC's investment in vaccine research. Generous and sustained funding for short-term and long-term studies is the most powerful help the government can offer my family. Please do more.

I have also a list of please don'ts. Please don't overemphasize the investigation of some factors because they seem so risky, while ignoring other potentially important factors. We know, for example, that because vaccination is unpleasantly memorable, we tend to perceive it as riskier than, say, exposure to mercury in fish, which is not very memorable. Please don't exhaust your investigation on the mercury in vaccines and ignore the subtler and potentially more significant sources of neurotoxicants. Please don't ignore factors because they are complex or seemingly unalterable. I would prefer answers that are correct to answers that are quick and expedient.

Please don't imagine that shaking public confidence in vaccines won't lead to the death of some children. We know that previous pronouncements on thimerosal led some U.S. birthing centers to discontinue the use of hepatitis B vaccine and this in turn led to

cases of chronic infection in newborns. These babies have had about a 9 percent chance of going on to die of liver cancer or cirrhosis, neither of which are enviable deaths.

We know that in the UK and Japan, pertussis vaccines scares led to decreases in vaccination and consequent increases in whooping cough, a disease that wracks a baby's body. We cannot forget that just 10 years ago, we saw a measles epidemic in this country that killed 123 children. That's not theoretical. We can count the death certificates. Though Hib disease essentially vanished once the vaccine was out, I will never forget it—fathers carrying limp, lethargic toddlers into the emergency department. Your actions have consequences. Please don't forget.

Please don't miss the opportunity to study the results of removing thimerosal from vaccines. As the manufacturers change to mercury-free formulations, I hope someone is doing a definitive study to see if autism rates plummet.

And finally, please don't ever frame this as a battle of parents against scientists. Generating hypotheses is a first step to finding causes and cures, and this committee has heard many conflicting hypotheses. The next step, testing these hypotheses, is painfully slow and costly, but I hope you will commit yourself to this scientific process. I believe it holds the greatest hope for my son and the many children like him. Thank you.

[The prepared statement of Dr. Humiston follows:]

Testimony of Sharon Humiston, M.D., M.P.H.

Before the
Committee on Goverment Reform

U.S. House of Representatives

July 18, 2000

Mr. Chairman and members of the committee, I applaud your efforts to bring parents, scientists, and policy makers together around the issue of autism. I am grateful for the opportunity to share my perspective as a parent, pediatrician, and public health researcher.

Last week my baby Quinn demonstrated developmental skills that thrilled my husband and me: he pulled his father's hand toward a pile of rocks, used his other hand to point toward a puddle, and said "Daddy, ock bla-bla," which meant, "Daddy, throw this rock in the water." Unfortunately, Quinny is seven and a half years old.

The worst day of my life was not the day the developmental pediatrician told me, almost apologetically, that my son was autistic. The worst day came later when the specialist told me that Quinn's progress was minimal after a year and a half of intense therapy and that this made his prognosis grave. My family's response was very typical – we reached out and embraced a succession of therapies, each touted as a lifesaver. We heard that gluten allergy was the cause and we changed Quinn's diet. Later we tried, for example, a phenol-free diet, megavitamins, anti-yeast medications, and cranio-sacral massage. Each therapy was supposed to get at the cause of Quinn's autism. Each therapy was expensive and each, for my son, was a failure.

You may wonder what would make a reasonable person pursue such an array of untested, unproven approaches. Well, I am a desperate mother. I am desperate to help my son *quickly* during his early years when we'd expect rapid brain development. I am desperate because the science lags so far behind my son's needs. My family has been blown by every wind, every theory to explain this pervasive developmental disorder, and we are tired. We are physically tired, financially tired, emotionally tired. So I am here today to encourage you to nurture the science that will help – if not my son – then at least my little girl's future children.

Funding, of course, is a very good way to show support. I appreciate the significant increases in NIH funding for autism research. I am grateful for CDC's investment in vaccine safety research. Generous and sustained funding for short-term and long-term studies is the most powerful help the Government can offer my family. Please do more.

I also have a list of "please don'ts."

Please don't over-emphasize the investigation of some factors because they *seem* so risky while ignoring other potentially important factors. We know, for example, that because vaccination is unpleasantly memorable we tend to perceive it as riskier than, say, exposure to mercury in water, which is not very memorable. Please don't exhaust your investigation on the mercury in vaccines and ignore the subtler and potentially more significant sources of neurotoxicants.

Please don't ignore factors because they are complex or seemingly unalterable. I would prefer answers that are correct to answers that are quick or expedient.

Please don't imagine that shaking public confidence in vaccines won't lead to the death of some children. We know that previous pronouncements on thimerosal led some U.S. birthing centers to discontinue the use of the **hepatitis B** vaccine and this in turn led to cases of chronic infection in newborns. These babies have about a 9% chance of going on to die of liver cancer or cirrhosis, neither of which are enviable deaths. We know that in the U.K. and Japan **pertussis** vaccine scares led to decreases in vaccination and consequent increases in whooping cough, a disease that wracks a baby's body. We cannot forget that just ten years ago we saw a **measles** epidemic in this country that killed 123 children. That's not theoretical – we can count the death certificates. Though **Hib disease** essentially vanished once the vaccine was out, I will never forget it – fathers carrying limp, lethargic toddlers into the emergency room. Your actions have consequences. Please don't forget.

Please don't miss the opportunity to study the results of removing thimerosal from vaccines. As the manufacturers change to mercury-free formulations, I hope someone is doing a definitive study to see if autism rates plummet.

And finally, please don't ever frame this as a battle of parents against scientists. Generating hypotheses is a first step to finding causes and cures, and this Committee has heard many conflicting hypotheses. The next step – testing those hypotheses -- is painfully slow and costly, but I hope you will commit yourself to this scientific process. I believe it holds the greatest hope for my son and the many children like him.

Mr. BURTON. Thank you for your comments. I'd just like to say at the outset that nothing that this committee has ever said would indicate, at least from the Chair, that we are opposed to vaccines. We are very much in favor of vaccinations. What we are concerned about is whether or not the contents of those vaccinations are safe and whether or not they're being properly followed and looked into by the agencies of jurisdiction, the FDA and the CDC. And we're also very concerned about whether or not there are conflicts of interest between the people on the advisory panels that are making recommendations to FDA and the CDC and the pharmaceutical manufacturers.

I'd like to ask you, Dr.—how do you pronounce your name—Aposhian. They started using thimerosal in 1930.

Mr. APOSHIAN. About that time.

Mr. BURTON. I was just wondering, I know this is pure speculation, we have a tremendous increase in Alzheimer's and, because of the neurological problems that many people are seeing from thimerosal being used in the vaccinations, where this could be a contributing factor in the Alzheimer's increase.

Mr. APOSHIAN. There are some scientific papers that speculate about that. But at the present time, it cannot be said that Alzheimer's disease has been caused by mercury.

Mr. BURTON. You think that, along with the aluminum and formaldehyde and other things that have been in vaccinations for a long time, should be looked into by the health agencies as possible contributing factors?

Mr. APOSHIAN. There's no question that mercury does not belong in vaccines. There are other compounds that could be used as preservatives. And everything we know about childhood susceptibility, neurotoxicity of mercury at the fetus and at the infant level, points out that we should not have these fetuses and infants exposed to mercury. There's no need of it in the vaccines.

I think the Academy of Pediatrics has also quite firmly stated there is no need of thimerosal in vaccines.

Mr. BURTON. Why—and this is a question for any of you—why was thimerosal put in vaccines in the first place? Does anybody know? Why did they put that in there? It was supposed to be a preservative. As I read the statements that you made today, it was supposed to be something that kept bacteria out of the vaccinations, out of the vaccines.

Mr. APOSHIAN. That's correct, sir.

Mr. BURTON. And yet the information that I see here is that it really doesn't.

Mr. APOSHIAN. In the early thirties, in fact the 1940's and up until the mid-1950s, mercurials were used in medicine. They were used as diuretic agents. The medical community had no evidence—had nothing better to use. They had nothing better to use as a preservative at that time than thimerosal. And I would venture the opinion that it has just been going on because no one has objected to it. And there's no need for it any longer. And I don't know any medical community or scientific community that would agree to the need for having thimerosal in any vaccine.

Mr. BURTON. Dr. Enayati said in his statement in 1982, 18 years ago—and it's in the Federal Register—an FDA panel concluded

that thimerosal is toxic, causes cell damage, can cause allergic reactions, and is not effective in killing bacteria or halting their replication.

That was 18 years ago. Why, if we knew that 18 years ago, did they continue to let that be put into these vaccines? Does anybody know the answer to that?

Mr. APOSHIAN. I think that's what you should ask the FDA representative.

Mr. BURTON. Oh, I plan to. Now, the hepatitis B vaccine has thimerosal in it, and that's given to infants. As I understand it, infants don't really have a great deal of exposure to hepatitis B because it's—you can contract it through blood, through sex, or through, I guess, needles. Unless the parent has it. So why are we giving hepatitis B vaccines to infants? Does anybody know that? Unless the parent has it. Would you like to comment, Dr. Humiston? I see you started to move forward.

Dr. CAVE. One of the main areas that we need it is when we have a mother who tests positive for hepatitis B.

Mr. BURTON. I understand that. Aside from that, why the need to have it?

Dr. CAVE. I agree with you. I don't find the need for it on the day of birth in children who don't have mothers who are positive.

Mr. BURTON. OK. Doctor.

Dr. HUMISTON. The day of birth is different than some time during infancy. We know that in 1990, before universal vaccination with hepatitis B, that by age 10 there were 19,000 children in the United States that had contracted hepatitis B, even though their mothers were hepatitis B surface antigen negative. So they have—it's possible to have exposure to hepatitis B in ways other than perinatally. It's a small number overall. You know, if you look at the entire population of the United States less than 10 years of age, but 19,000—and, of course, when you are exposed to hepatitis B during your early life, you're more likely to go on and be a chronic carrier.

Mr. BURTON. Have there been studies—and I'll yield to Danny—or, excuse me, to Mr. Davis in just a minute—but have there been studies showing the various ages at which children contract hepatitis B? Because it seems to me inconceivable before the age of 6, or 5, that children would really have much exposure to it. I mean, you said below age 10. How about the various age increments? You don't know?

Dr. HUMISTON. I don't know how it's divided out.

Mr. BURTON. Could we check that out and find out what ages we start to see——

Dr. CAVE. It's very rare if the mother is not hepatitis B-positive that an infant shows hepatitis B.

Mr. BURTON. Up until what age, you say 5 or 6?

Dr. CAVE. I think it's far beyond that.

Mr. BURTON. Mr. Davis, you're recognized.

Mr. DAVIS OF ILLINOIS. Thank you very much, Mr. Chairman. I missed a part of the testimony from some of the witnesses, but that which I heard I found to be quite intriguing.

Dr. Aposhian, how long has the scientific community been aware of the alternatives to the use of mercury?

Mr. APOSHIAN. Sir, it depends how you define the scientific community. The academic community, I would say since 1955, has been concerned about the use of mercurials in medicine. The use of mercurials in medicine has had a long history. It used to be used as a treatment of syphilis. It used to be used for the treatment of many, many infectious diseases before we had antibiotics.

Mr. DAVIS OF ILLINOIS. I know that there's often resistance to change, even when something comes along that we can assume or we might even know to perhaps be more effective, more efficient, less dangerous, less costly or whatever. Can you think of any reasons why, if we are aware of the alternatives and if they are safer, why we have not moved assiduously in that direction?

Mr. APOSHIAN. Congressman Davis, there are three groups involved here, I think. We have an academic group, we have a government group, and we have an industrial or pharmaceutical group. Because of our society, most industrial groups, most pharmaceutical companies, are very reluctant to change anything because of the tremendous cost of getting that change through the FDA. And the other concern by pharmaceutical companies is just how dangerous is dangerous? And that, I think, is where the greatest argument comes in and that's where the FDA should be acting as a judge.

Dr. HUMISTON. I don't mean to be cynical about the pharmaceutical companies, but I don't think that they're going to take to moving toward thimerosal-free vaccines, I don't think they will be taking financial losses, because one of the things that happens is we won't be able to have vaccines in multidose vials. Multidose vials are much less expensive than single-dose vials. So going to all single-dose vials will actually bring more profits to the pharmaceutical companies. And I don't—you know, I am not saying that that's their motive, I'm simply saying that they have nothing to lose.

Mr. DAVIS OF ILLINOIS. But it is in fact, I guess, sometimes difficult to feel that certain kinds of self-interests don't creep into the ultimacy of decisionmaking. And I guess that's where it takes——

Dr. HUMISTON. Again I don't mean to be cynical, but I think that the pharmaceutical companies have moved quite quickly, and partly, probably, because they don't have a great deal to lose.

Mr. DAVIS OF ILLINOIS. I guess what you're saying is no matter how you cut it, you can't get around the whole concept of ultimate involvement of all of us in arriving at public policy, and that if there is enough action and activity, then one part balances out or one side balances out the other and we arrive at the public interest.

I assume—I also listened to your testimony in terms of your own personal experience, and I was obviously moved, as anybody would be by it. Given your own training as well as the experiences, do you feel or would you have reason to believe that there might be any connection between immunization and autism?

Dr. HUMISTON. What Mr. Davis is referring to is that I was formerly with the National Immunization Program. Now I'm a pediatrician at the University of Rochester. I have to say that I try very hard to keep an open mind scientifically, and I think that that is the most important stance that we can take now. What I am advo-

cating for is good science. And again, I was present during the ACIP meeting, the Advisory Committee on Immunization Practices. I was happy to see that the science is going forward quickly. I hope that the science can go forward quickly. We've—this committee has heard other theories as well. And I hope that we come to better understanding—also the genetics. I mean, there's so many factors here. I think that immunization is just a tiny part, but it sticks in our mind because it's so memorable.

Mr. DAVIS OF ILLINOIS. I thank you very much. Plus, Mr. Chairman, I must say I was pleased to hear your comment in terms of the position of the committee relative to the fact that there are no conclusions having been determined or reached, but what the committee is really hoping to do is to try and probe as deeply, as widely as it can, to try and find out as much as we possibly can about the issue. And I appreciate that comment that you made.

Mr. BURTON. Thank you, Mr. Davis. Ms. Chenoweth.

Mrs. CHENOWETH-HAGE. Thank you, Mr. Chairman. As a grandparent of an autistic child, I've been fascinated with your testimony. I want to thank all of you for the method of your delivery. I know it's difficult. In the last hearing I had difficulty even giving my own opening statement, and I'm not a patient, I'm a grandparent. But they're precious, precious little children. And my heart goes out to you. But also I thank you very much for your courage in being here today.

I wanted to begin my questioning with a question to Dr. Cave. I've been fascinated with your treatment procedure. And your procedure involves nutritional repletion of cellular chemistry and normalization of gastrointestinal bacterial balance, dietary problems, restoration of liver detoxification systems. What do you think about chelation also as a treatment? Have you considered that?

[The prepared statement of Hon. Helen Chenoweth-Hage follows:]

Statement of Congressman Helen Chenoweth-Hage
Committee on Government Reform and Oversight
2157 Rayburn House Office Building
July 18, 2000

Thank you, Mr. Chairman. I would like to thank the Committee for holding this hearing on "*Mercury in Medicine - Are We Taking Unnecessary Risks?*" I am unable to overstate the importance of this issue. I look forward to hearing the testimony of the witnesses today.

Mr. Chairman, you know as does the rest of the committee, that I have very real concerns about the current vaccination programs and the way they are administered. Over the past year, this committee has held a series of hearings regarding vaccines and their effect on the populace. However, today's hearing is about the mercury content of vaccines and the possible dangers they present to America's most precious resource, its children.

I was seriously disturbed to hear about the mercury content of certain vaccines in prior hearings, so I am glad that we will examine this issue in depth today. The question of whether mercury genuinely affects human health has been indisputably answered. It does. Recently, the Food and Drug Administration recognized the possible hazard that mercury presents in vaccines and concluded that eliminating thimerosal, an additive to vaccines that metabolizes into a type of mercury, should be implemented.

This is an important finding, due to the fact that many experts now believe that mercury may be linked to the radical increases in the rates of autism. If it is true that this additive metabolizes into mercury, could this be the root cause of such a high rate of autism? Several counties and states have noticed substantive and disproportionate increases autism rates over the past several years. We have a duty to investigate whether federal vaccine policy has contributed to these rates.

Mr. Chairman, autism is a neurodevelopmental syndrome or disorder. Some of us on this very Committee, including myself, are personally aware of the devastating effects that autism has on families. However, I will also be the first to say that grandchildren who are autistic are also a source of great joy. Too often society hides autism in a closet, out of site.

With this said, I would like to say that I look forward to the testimony of the witnesses and learning about the frightening possibility that our vaccines are causing mercury poisoning in our children.

Mr. Chairman, let me thank both you and the Committee again for holding this hearing. It's of critical importance to not only the families here, but those around the nation that have been affected by the consequences of mercury poisoning and autism. We simply must deal with this.

Thank you, Mr. Chairman.

Dr. CAVE. We are using oral chelation with a sustained release DMSA. The DMSA is a drug approved by the FDA for lead intoxication in children. We've used a sustained release form which has given us a totally different picture. We're pulling on a 24-hour basis now, and we're seeing the metal come out. And the children are changing in the first week that we start treating.

We have another layer of treatment in which we add alphallipoic acid which does take it to the central nervous system. When we start pulling it from the central nervous system, we get sentences and speech in children who have not spoken. It's been phenomenal.

Mrs. CHENOWETH-HAGE. That was going to be my next question. Can you pull it from the central nervous system?

Dr. CAVE. Yes, we can.

Mrs. CHENOWETH-HAGE. Is chelation the best method of doing that, have you found?

Dr. CAVE. It's the only method. You have to pull the metal with something that will hook on to the metal. And these have—sulfhydryl groups, which will hook on to mercury.

Mrs. CHENOWETH-HAGE. Dr. Cave, I was also interested in knowing what your thoughts were about why some children are affected this way while others perhaps have a physiologic system that's developed to the point that the toxins don't reside in the brain. What happens there?

Dr. CAVE. We are measuring the detoxification systems in the children's livers and we're finding variability. In the children that we're seeing that are developmentally delayed, there is very little—they're not able to detoxify very well. There's very little ability. The normal child has a better system. And we can measure that. There are some genetic factors. We have some ideas about that, too. And we're looking at several lipoproteins; that's very early right now. But it can be explained—it can't be fully explained, but it can be partially explained at this point, and there are genetic factors for sure.

Mrs. CHENOWETH-HAGE. I see. Mrs. Birt, I found it very interesting in your testimony that you testified to the fact that there were some questions back in 1988 and then finally—about thimerosal—and then finally in 1997 they issued a final rule, the FDA did, that disallowed thimerosal or indicated that products containing thimerosal were neither effective and may not be safe for over-the-counter——

Ms. BIRT. Correct.

Mrs. CHENOWETH-HAGE [continuing]. Treatments. And also in your testimony, you talked—you testified to the fact that the FDA asked the vaccine companies to give them information on this. And could you elaborate more on that? I found that section of your testimony fascinating.

Ms. BIRT. I think the problem is that the manufacturers aren't held accountable, so nobody is responsible in the ultimate product. It's like a big circle. It goes from the manufacturer to the FDA to the CDC to the public. But nowhere in there is anybody legally or financially accountable if there's a problem. And the way our society is geared is that profitability is the highest thing.

And I think that in order for the vaccine manufacturers to make the product thimerosal-free, they had to change their methods of

production. And this is only speculation—they may have known there was a problem earlier and just didn't want to say anything. Nobody knows that for sure.

But I think this whole process of finding out the truth will lead us to the truth eventually. But I think the fundamental problem is that we don't have accountability in the system, so the people who have the most to lose really aren't protected, which is basically the job of the government, to protect people who are at risk. And that has not been done in this process.

Mrs. CHENOWETH-HAGE. Mr. Chairman, I see my time is up. I just wish I had about 3 hours to engage with these witnesses. My congratulations to you and your staff for the outstanding information we've received.

Mr. BURTON. Thank you, Congresswoman Chenoweth. We'll have one more round, if you would like to ask some more. Mr. Gilman, Chairman Gilman.

Mr. GILMAN. Thank you, Mr. Chairman. I regret that I was tied up on the floor with legislation that we're involved in. And I want to thank you, Mr. Chairman and the committee, for conducting this series of hearings on vaccine safety, and I want to thank our panelists for coming to voice their concerns and to give us their information. As we examine the various additives that are present in vaccines, it's extremely important that we note the role that they play and what, if any, other compounds may be available to fulfill their roles as appropriate substitutes.

Today's hearing focuses on thimerosal, the preservative that contains small amounts of mercury. And that's the first that I've been made aware of how mercury is part of these vaccine substances and what they can do to our youngsters. I've been informed that these preservatives are used to inhibit the growth of bacteria fungus that might contaminate a multidose vial of vaccine where a physician reenters the same vial several times to inoculate several children. Apparently, without preservatives, there is a risk that a vial of vaccine could become contaminated and a physician could inadvertently inject a living organism into a child. Since 1968, I've been informed preservatives have been required by law in multidose vials.

Thimerosal has been used for more than 60 years in a variety of vaccines. The fact that it's been used that long, of course, does not attest to its safety. It's been effective as a preservative in very low doses and highly stable—it is highly stable throughout the shelf life of that vaccine, and works across a broad spectrum of microbial agents. As such, it's been considered the best preservative that was available. And while its value in keeping vaccines free of contamination has been unchallenged, serious questions have now arisen as to the possible side effects in infants from exposure to mercury, the mercury that's available in thimerosal.

It's my understanding that aside from 60 years experience in the field, there has been little directly applicable data on this concern until very recently. CDC has now looked at the level of exposure to mercury of immunized infants in three HMOs versus the appearance of symptoms such as renal failure, a hallmark of mercury poisoning, and various neurological deficits, including autism. This data has indicated what there is no association between the

amount of mercury an infant is exposed to from vaccines in the development of any neurologic or renal problem. And that's why it's so important we're examining this issue today.

And another type of additive to vaccines is the adjuvant. Adjuvants in vaccines help boost the child's immune response to bacteria or virus that is a poor stimulant of its own accord. Adjuvants therefore provide the ability to decrease the amount of bacteria or virus needed in a vaccine and/or to decrease the number of doses needed in an immunization series. Aluminum salts, I've been informed, are the only licensed adjuvant in our Nation. They've been safely used in vaccines for a number of years.

Today, taking testimony from our panelists who are before us now regarding adjuvants and additives in vaccines and alleged associations between these additives and various illnesses, is extremely important to us. We must be vigilant in matters of vaccine safety. We've just gone through extensive hearings on anthrax and trying to make certain that any utilization of anthrax by the military is not going to affect their well-being. At the same time, it's important we focus our attention on scientific evidence. We must be careful we don't jump to conclusions based on anecdotes and speculations, but that's why it's good you're here to present specific cases to us. We must not lose sight of the fact that vaccines have saved millions of people from debilitating and deadly diseases, but we don't want the vaccine itself to cause side effects that are just as deadly.

The effect of needlessly scaring parents away from immunizing their children is a real concern, and that's why we must tread very carefully as we go through this maze of trying to find out just what has affected our children by the substances that are present in the vaccine.

So again I thank Mr. Chairman, thank you for being here, and I want to thank our panelists who are here today to give us the benefit of their thinking.

[The prepared statement of Hon. Benjamin A. Gilman follows:]

Rep. Benjamin Gilman
Opening Statement for Vaccine Hearing on Mercury in Medicine
Government Reform
July 18, 2000

I would like to thank the Chairman for holding this series of hearings on vaccine safety and I look forward to hearing from today's panel members.

As we examine the various additives that are present in vaccines, it is important to note the role they play and what if any other compounds are available to fulfill those roles. Today's hearing will focus on thimerosal (thigh-mare-oh-soll), a preservative that contains small amounts of mercury. Preservatives are used to inhibit the growth of bacteria or fungus that might contaminate a multi-dose vial of vaccine where a physician re-enters the same vial several times to innoculate several children. Without preservatives, there is the very real risk that a vial of vaccine could become

contaminated and a physician could inadvertently inject a living organism into a child. Since 1968, preservatives have been required by law in multi-dose vials.

Thimerosal has been used for more than 60 years in a variety of vaccines. It is effective as a preservative in very low doses, is highly stable throughout the shelf life of the vaccine, and works across a broad spectrum of microbial agents. As such, it is considered the best preservative available. While its value in keeping vaccines free of contamination is unchallenged, questions have arisen as to possible side effects in infants from exposure to mercury in thimerosal. It is my understanding that, aside from 60 years experience in the field, there was little directly applicable data on this matter until recently. CDC has now looked at the level of exposure to mercury of immunized infants in three HMO's versus the appearance of symptoms such

as renal failure, a hallmark of mercury poisoning, and various neurologic deficits, including autism. This data indicated that there is no association between the amount of mercury an infant is exposed to from vaccines and the development of any neurologic or renal problem.

Another type of additive to vaccines is an adjuvant (add-juve-vent). Adjuvants in vaccines help boost a child's immune response to a bacteria or virus that is a poor stimulant of its own accord. Adjuvants, therefore, provide the ability to decrease the amount of bacteria or virus needed in a vaccine and/or to decrease the number of doses needed in an immunization series. Aluminum salts are the only licensed adjuvant in the U.S. and they have been safely used in vaccines for 70 years.

Today we will hear testimony regarding additives in vaccines and alleged associations between these additives and various illnesses. We must always be vigilant in matters of vaccine safety. At the same time, it is important that we focus our attention on valid scientific evidence and not jump to conclusions based on anecdotes and speculation. We must not lose sight of the fact that vaccines have saved millions of people from debilitating and deadly diseases throughout the years and as such, we should proceed with caution. The effect of needlessly scaring parents away from immunizing their children is very real and the results of not immunizing children can be far more dangerous than any speculative risks associated with vaccinations.

Mr. BURTON. Thank you, Chairman Gilman.

Ms. Ros-Lehtinen.

Ms. ROS-LEHTINEN. Thank you so much, Mr. Burton, for this hearing and for your constant leadership on this terrible issue of autism. I don't have autistic children, but I have a very good friend who has, as you may remember, because I've spoken about them before in this committee, two autistic children. Because of them, these hearings are of great importance to me personally and to many constituents in my district. Due to my association with her and her family I have come to know so much about autism and how many families are affected and indeed devastated by this problem.

I'm always delighted to go back home with all of your material—and I want to commend your staff for preparing such fine materials for us at each hearing—how happy the parents of autistic children are with the literature, and then when I have the meeting with the so-called experts, how alarmed they are with the papers.

I find that there's a great disconnect in the scientific community about what parents have come to know and understand through their own research and through their own set of circumstance. And I hope that both sides come closer together because I know that I will have that same reaction when I come back to Miami this weekend; that parents will be very happy with this information and the experts won't.

And we do have some very good centers for autism in south Florida. I don't know if there's a geographical connection, but certainly south Florida has been very impacted by the effects of autism. We have the Card Center at the University of Miami, Center for Autism and Related Disabilities, a great center, and the Dan Marino Institute in Broward County. So my community has been blessed with good information. Yet I find that scientists and many within the medical community, the people with whom I deal with, they are not satisfied with the information that we give them. I find that disturbing, because I would think that these experts would be happy to see others doing research and promising information.

I wanted to followup with a view of the great information that was given to us today. You were saying that in one of the publications, I'm not sure which one, that mercury levels can be detected in urine, hair, and blood.

I'm interested in knowing how many autistic children you believe have been tested for mercury levels? As I said. I have two children of my own, they're 14 and 13 now. I don't recall whether that was a normal set of tests, but whatever it was, it was at a normal range. Is testing for mercury something that is usually done by pediatricians? Do you think that that is something that they should be looking at? Would it involve a more intrusive examination than is already given to children? Are you advocating that parents should have their children tested for mercury levels?

That's my first question. Let me just throw them all out and whoever wants to, answer. Also, chelation—is that how you say it? Chelation methods, do they come in pill form or a shot or liquid that the child swallows, and how many children have undergone this chelation therapy or method? Finally, what was it formulated

originally to treat? I'm interested in understanding more about that therapy.

Thank you, whoever would like to answer those questions about mercury testing and chelation therapy and address the disconnect between parents and so-called medical authorities.

Dr. CAVE. Mercury is not something that is usually tested, and we were not really taught to test hair samples or to give chelation doses and test urine samples. If you look at some of the material I've provided in the handout on the hair samples that I have, you cannot find mercury in these children. We find mercury in the hair of children who are receiving the vaccines, but these children are beyond the first dose of vaccine. So the mercury has moved beyond this level. It stays in hair only a certain period of time. It doesn't actually stay in blood.

But when we give the dose of a chelator, it brings it into blood and then into the urine, and then we can measure it in urine. This is something that we started doing 4 or 5 years ago when we started treating the children. And I noticed that we were finding metals in the small children and in children who were receiving the—well, a vaccine like hepatitis B later on in life. I found it in the hair sample of a young man who had the hepatitis B series in college. He was left with severe depression, and his brother was left with seizure disorder. And I found it in the hair of both of these young men.

But you have to be able to look for something. You have to know how to look for it in order to find it. When we were using the drug as it's given in the regular drugstore, without technology-sustained release, we were not even finding very much in the urine. Now that we're using a sustained release, we're bringing it out into the urine.

If you notice on the handout that I have there, it's very high in the urine as submitted, even though it was negative in the hair. In the hair, we look for aluminum and we find aluminum and we find antimony in the hair. And we are treating that—we're not treating that with the same medication. We're using an over-the-counter to treat the aluminum and it's working well, with no toxicity that we can see.

Mr. BURTON. Anyone want to comment briefly on the chelation she was talking about, the various forms of chelation?

Mr. APOSHIAN. Let me say that our laboratory for the last 18 years has been the primary laboratory dealing with the use of DMSA, the development of DMSA, the approval of DMSA by the FDA. It's a chelating agent. That means it competes with other materials in the body for a particular metal or group of metals, makes that metal more soluble, and therefore excretes it.

The controversy has always been, just because you get rid of a metal does not necessarily mean you improve the clinical position of—the clinical condition of the patient. This is always controversial.

Chelation therapy is certainly not accepted by the vast majority of established medicine. It is accepted quite greatly by alternative medicine people. I think it's just a subject of controversy at the present time. There is no question at all that it helps children that

have been exposed to lead. It gets rid of the lead and decreases their chances of getting any worse.

The National Institutes of Environmental Health Sciences at the present time have a $35 million program to see whether giving DMSA to children who have been adversely affected by lead will improve their condition. As yet there is no solid information that their condition has been improved, but all the information is not present yet.

Chelation therapy has always been a method of getting rid of toxic metals. There are various chelating agents that can be given by mouth, like DMSA. There are other ones that can be given by mouth or injection. And there are also very toxic ones. I also want to point out, the problem is that you can't take an autistic child, give him any kind of an agent, and then test his brain to see whether that particular toxic metal has been removed. We can do that in animal studies; we cannot do it in human studies, of course.

Does that answer your question, Congresswoman?

Ms. ROS-LEHTINEN. Yes.

Dr. CAVE. But clinically they're improving. We're bringing them back 80 percent, 90 percent, in terms of social interaction with speech, with eye contact, and that's proof that the central nervous system is functioning at a higher level. We can't go in and biopsy the brain, but we can certainly look at the child.

Mr. BURTON. Mr. Cummings, you have questions?

Well, we have a number of questions I would like to submit for the record to each one of you. You have been very, very informative in your statements and I really appreciate that. I would like to ask you a whole host of questions, but the hour is getting late, and I know we're going to have votes on the floor and we're going to be down there for awhile. So would you all be willing to answer questions for the record that we submit to you? We'll put those in the record as soon as we get them.

I want to thank you all for being here. I hope you can stay around to hear the testimony from the agencies of the government. Thank you very much.

We will now have panel No. 2. Ms. E. Ramona Trovato, Director of the Office of Children's Health Protection, Environmental Protection Agency; Dr. William Egan, Acting Office Director, Office of Vaccine Research and Review, the Center for Biologics Evaluation and Research; Dr. Roger H. Bernier, Associate Director for Science at the National Immunization Program, Centers for Disease Control and Prevention; and Dr. Marie Bristol-Power, National Institute of Health and Human Development, the National Institute of Health.

Could I have you all stand so we could have you sworn, please?

[Witnesses sworn.]

Mr. BURTON. Be seated. We'll start with Ms. Travato. Did I pronounce your name right?

Ms. TROVATO. You sure did. May I begin?

Mr. BURTON. Yes.

STATEMENTS OF E. RAMONA TROVATO, DIRECTOR, OFFICE OF CHILDREN'S HEALTH PROTECTION, U.S. ENVIRONMENTAL PROTECTION AGENCY; DR. WILLIAM EGAN, ACTING OFFICE DIRECTOR, OFFICE OF VACCINE RESEARCH AND REVIEW, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH [CBER], FDA; DR. ROGER H. BERNIER, ASSOCIATE DIRECTOR FOR SCIENCE, NATIONAL IMMUNIZATION PROGRAM, CENTERS FOR DISEASE CONTROL AND PREVENTION; AND DR. MARIE BRISTOL-POWER, NATIONAL INSTITUTE OF HEALTH AND HUMAN DEVELOPMENT, NATIONAL INSTITUTE OF HEALTH

Ms. TROVATO. Good afternoon. I am Ramona Trovato, Director of the Office of Children's Health Protection at the U.S. Environmental Protection Agency. I appreciate the opportunity to appear before you today to talk about the problem of mercury, particularly as it affects fetuses and very young children.

Mr. Chairman, while I appreciate the primary interest of this committee today is the role that mercury may play in causing health effects in children when used as preservatives in vaccines, EPA does not have regulatory authority to address vaccines and their preservatives. EPA does have authority to address releases of mercury to our air, land, and water, and is actively addressing such releases through both regulatory and nonregulatory actions.

Mercury is a naturally occurring metal which persists in the environment and has long been known to have toxic effects on the nervous systems of humans and wildlife. The most significant releases of mercury to the environment in the United States are man-made emissions to the atmosphere from combustion sources, including waste and fossil fuel combustion. Mercury from such emissions as well as naturally occurring mercury and mercury from past uses, such as in fungicides on crops, is deposited into the soil and water. Concentrations of mercury in air and water are usually low and of little direct health concern. Once mercury enters water, however, it may be converted to methylmercury which can then accumulate in fish and marine animal tissue. Methylmercury levels in fish at the top of the food chain are, an average, 7 million times higher than the concentrations of dissolved methylmercury found in the surrounding waters. As a result, human exposure to methylmercury occurs primarily through eating contaminated fish. The amount of methylmercury that people are exposed to depends on the species of fish consumed, the concentration of methylmercury in the fish, and how much and how often fish are consumed.

While most U.S. consumers need not be concerned about their exposure to methylmercury, some exposures may be of concern. Those who frequently consume large amounts of fish or who eat fish from water contaminated with mercury may be more highly exposed. Populations such as pregnant women and their fetuses may be at risk if they consume large amounts of contaminated fish or fish with relatively high levels of methylmercury.

Because the developing fetus is the most sensitive to the effects of methylmercury, women of childbearing age may be at particular risk. These women should pay attention to the fish advisories

issued by their States that suggest limiting the consumption of fish containing higher levels of methylmercury.

Methylmercury is toxic to adults, children, and the fetus but prenatal and postnatal exposure can adversely affect the nervous system. Dietary methylmercury is almost completely absorbed into the blood and distributed to all tissues, including the brain. It also readily passes through the placenta to the fetus and fetal brain. Effects on the fetal nervous system occur at lower exposures than do effects on the adult nervous system. Mercury interferes with the development and function of the central nervous system, with health consequences ranging from subtle to severe, depending on the amount and timing of exposure.

In 1995, EPA published a reference dose of 0.1 micrograms per kilogram of body weight per day, based on the effects seen in children following methylmercury consumption by the mother during pregnancy.

Just last week, the National Academy of Sciences released their findings on the health effects of methylmercury based on its evaluation of recent epidemiological studies. The NAS affirmed EPA's reference dose is a scientifically justifiable level for public health protection for the most sensitive subpopulation—mothers and their unborn fetuses. The NAS has also indicated that the majority of U.S. population has low risk of adverse effects from current methylmercury exposures. However, the NAS also estimated that more than 60,000 children are born each year at risk of adverse neurodevelopmental effects such as overall cognitive ability, language development, spatial perceptual skills, and motor skills due to in utero methylmercury exposure.

EPA is taking action to reduce mercury in the environment. EPA has issued standards that limit air emissions of mercury. The agency has developed regulations for boilers, process heaters, solid waste combustors and chlor-alkali plants. The remaining largest identified source of mercury emissions are coal-fired utility boilers.

In summary, it is clear that women of childbearing age should take steps to minimize their exposure to methylmercury from eating contaminated fish. People who regularly eat fish should be aware of any State fish advisories. Because of the beneficial effects of fish consumption, the long-term goal needs to be reduction of the concentration of methylmercury in fish rather than the replacement of fish in the diet by other foods. EPA will continue to take steps to further improve public health, especially to protect children and fetuses, our most susceptible population.

Thank you very much, and I'll be happy to answer questions.

Mr. BURTON. Thank you, Ms. Trovato.

[The prepared statement of Ms. Trovato follows:]

Testimony of E. Ramona Trovato
U.S. Environmental Protection Agency
to the
Committee on Government Reform
U.S. House of Representatives

July 18, 2000

Introduction:

Good Morning. I am Ramona Trovato, Director of the Office of Children's Health Protection in the U.S. Environmental Protection Agency and I want to thank you, Chairman Burton, Ranking Member Waxman, and members of the Committee, for inviting me to talk about mercury.

What is EPA's Role?

EPA has authority to address releases of mercury to the environment, including its presence in our air, water, and soil. EPA undertakes both regulatory and non-regulatory actions to reduce the release of mercury to the environment and thus, the human health consequences of mercury exposure. EPA does not have regulatory authority over vaccines, and Section 3(2)(B)(vi) of the Toxic Substances Control Act (15 U.S.C. 2602(2)(B)(vi)) specifically excludes drugs from the definition of "chemical substance."

What is Mercury?

Mercury is an element and, as such, it is neither created nor destroyed. The same amount of mercury has existed since the earth was formed. As a naturally occurring metal, mercury takes several forms: elemental, inorganic, and organic. Mercury combines with other elements, such as chlorine, sulfur, or oxygen, to form inorganic mercury compounds or "salts" which are usually white powders or crystals. Mercury also combines with carbon to form organic mercury compounds. Methylmercury is the form of organic mercury in the environment, while an ethylmercury salt (thimerosal) has been used as an additive to biologics and vaccines since the 1930's to combat bacterial contamination. The scientific community knows a lot about the human health and ecological effects of mercury and mercury exposure, and has agreed, in spite of remaining scientific uncertainties, that mercury, in certain forms and levels of exposure, is an important human health and environmental problem.

Mercury has long been known to have toxic effects on the nervous systems of humans and wildlife. Inorganic mercury enters the air from coal and waste combustion, industrial plants,

and from mining ore, and is then transported through the air finally being deposited on land and in waters. As previously noted, mercury persists in the environment. In water, elemental mercury may be biotransformed through the action of bacteria into methylmercury which is a more toxic and bioaccumulative form. Methylmercury can bioaccumulate in predatory fish and marine mammals to concentration levels that are hundreds of thousands of times higher than concentrations in surrounding waters. People who routinely consume large amounts of contaminated fish or consume fish with relatively high levels of methylmercury are at risk of adverse effects. Fetuses exposed to methylmercury through their mother's consumption of contaminated fish may be at risk of adverse effects because the developing nervous system is more vulnerable to mercury toxicity.

What are the Health Effects of Mercury?

Methylmercury is toxic to adults, children, and the fetus. Both prenatal and postnatal exposures can adversely effect the nervous system. Among adults, methylmercury can produce neurological damage ranging from fatalities at high doses to effects including neurological damage only identifiable through specialized clinical testing (e.g., visual field evaluation, neuromotor dysfunction) at low doses.

Some recent large epidemiological studies of children have identified cognitive deficits as a result of *in utero* methylmercury exposure, including impairment in attention, language processing, and memory.

Fetal nervous system development is a particularly vulnerable period that may be adversely effected by methylmercury exposure. Many of the same biological events that occur in the fetal brain continue postnatally in children. Specifically, methylmercury impairs migration of neurons, synapse formation, and myelination, processes that occur both prenatally and postnatally. Susceptibility to the developing fetus has been demonstrated by the fact that in several mercury poisoning incidents worldwide, minimally affected mothers gave birth to severely affected infants. Thus, EPA concludes developing fetuses are more vulnerable to methylmercury toxicity than adults.

Delayed neurotoxicity from methylmercury exposure is also a concern. Data from both human and animal models reveal an interaction between earlier methylmercury exposure and impaired function during aging. For example, data from Japan (the site of severe poisoning episodes in the 1950s and 1960's in Minamata and Niigata), found that people with earlier methylmercury exposure experienced a greater likelihood of being unable to independently care for themselves including the ability to dress, bathe, and use the toilet independently. There is a plethora of potential effects ranging from intellectual deficits to sensory and motor impairment that may result from methylmercury exposure during different phases of life.

How are we Exposed to Mercury?

Concentrations of mercury in air and water are usually low and of little direct health concern. Once mercury enters water, either directly or through air deposition, it may be converted to methylmercury and, as such, can bioaccumulate in fish and animal tissue. As a result of this bioaccumulation, the concentration of mercury in predators at the top of the food web (for example, predatory fish and fish-eating birds and mammals) is a cause for both human health and ecological concern.

Human exposure to methylmercury occurs primarily through eating contaminated fish. The amount of mercury that people are exposed to depends on the species of fish consumed, the concentration of the methylemercury in the fish, and how much and how often they eat fish.

Seafood is an important part of a healthy, balanced diet for everyone. While most U.S. consumers need not be concerned about their exposure to methylmercury, some exposures may be of concern. Those who regularly and frequently consume large amounts of non-commercial fish -- either marine fish that typically have much higher levels of methylmercury than the rest of seafood, or freshwater fish that have been affected by mercury pollution -- may be more highly exposed. Certain populations, such as pregnant women and their fetuses, may be at risk, if they consume large amounts of contaminated fish, or fish with relatively high levels of methylmercury.

What are the Sources of Mercury?

Global mercury emissions from all sources (natural and anthropogenic) are estimated to be about 5,000 to 5,500 tons per year (tpy). Of this total, approximately 1,000 tpy are estimated to be natural emissions, which result from the mobilization or release of geologically bound mercury by natural processes such as volcanos. Approximately 2,000 tpy are estimated to have originated from past anthropogenic activity, while current anthropogenic emissions account for the remaining 2000 tpy.

Mercury released to the environment via the atmosphere may be transported, then deposited onto soil and water. Such emissions can be anthropogenic, natural or re-emitted emissions. Table 1 presents annual U.S. emissions from the largest categories of anthropogenic sources.

Table 1* Estimated Annual National Emissions of Mercury to the Air from the Largest Anthropogenic Sources; 1994 -1995

Source Category	Tons Per Year	Percent of Total
Utility boilers-coal combustion	52	32.6
Municipal waste combustors	29	18.7
Medical waste incinerators	16	10.1
Chlorine production	7	4.5
Hazardous waste incineration	7	4.4
Portland cement, excluding hazardous waste-fired	5	3.1

*1997 Mercury Study Report to Congress

The Agency does not have national estimates for mercury releases to water. However, water discharge permits generally require monitoring for mercury before discharge and we anticipate these releases to be low relative to air emissions.

While the Agency does not have comparable inventories at this time, there is enough information to say with confidence that emissions have decreased from some categories since 1990. Incineration emissions (especially from MWCs and MWIs) have decreased considerably because of reduced mercury content of batteries, pollution prevention activities, state regulations, and the early impacts of federal regulation (i.e., early compliance, and shutdown of marginal incinerators). Chlor-alkalki emissions have also likely decreased because of the decrease in the number of operating facilities (from about 20 in 1990 to 12 in 2000) and the decrease in their mercury use. Utility emissions likely haven't changed much since the amount of coal burned has slightly increased; however, this increase has been partially offset by increased use of control technologies such as scrubbers.

What is EPA doing to Reduce Exposure to Mercury in the Environment?

EPA is taking action to reduce mercury in the environment. These actions include issuing regulations for industries that significantly contribute to mercury releases. To date, EPA has issued standards that limit air emissions of mercury from municipal waste combustors, medical waste incinerators, and hazardous waste combustors. The Agency is developing regulations now for industrial, commercial, and institutional boilers; process heaters; industrial, commercial, and other non-hazardous solid waste combustors; gas turbines; and stationary internal combustion engines; and for chlor-alkali plants. By December 15 of this year, EPA intends to make a finding under the Clean Air Act as to whether it is appropriate and necessary to regulate mercury emissions from electric power plants.

EPA also supports the efforts of state and local governments to achieve mercury discharge reductions through outreach and technical assistance for mercury pretreatment programs at sewage treatment plants.

Releases of mercury compounds must be reported on the Toxics Release Inventory (TRI). Beginning with reports this year (2000), the threshold for TRI reporting of mercury releases has been lowered to capture releases from many more facilities.

EPA is encouraging voluntary efforts to control mercury releases with industry groups such as the American Hospital Association who have agreed to eliminate the use of mercury containing products at their facilities.

Federal, State and Tribal governments publish fish advisories to assure the public's right to know about whether and which fish are safe and in what amounts. To date, there are 1,931 fish consumption advisories in 40 states that have been issued, and ten states have issued statewide advisories for mercury in their lakes and/or rivers. In fact, almost 68% of all advisories issued in the United States are a result of mercury contamination.

The National Academy of Sciences (NAS) report released on July 11, 2000 regarding the toxicological effects of methylmercury reinforces the importance, especially for women who may become pregnant, of heeding consumption advisories for noncommercial fish. The NAS findings also reaffirm EPA's existing guidance to states on the appropriate levels to be used in developing consumption advisories as "scientifically justifiable." While the NAS indicated that the majority of the US population has low risk of adverse effects from current methylmercury exposures, they also indicated that individuals who often consume fish (a primary exposure pathway) with relatively high levels of methylmercury may experience methylmercury exposures close to those that have demonstrated observable adverse effects. They estimated that over 60,000 children are born each year at risk of adverse neurodevelopmental effects (i.e., overall cognitive ability, language development, spatial perceptual skills, and motor skills) due to in utero methylmercury exposure.

Since it was just released, EPA has not yet had an opportunity to review the NAS report and all of it's recommendations.

Conclusion

EPA will continue to take steps, both on its own and through partnerships with other federal agencies and the states, to further improve public health, especially for the most vulnerable segments of our population, by reducing releases of mercury in our environment.

Thank you for the opportunity to testify today.

Mr. BURTON. Dr. Egan.

Mr. EGAN. Thank you, Mr. Chairman and members of the committee. I am William Egan, the Acting Director for FDA's Office of Vaccine Research and Review. I appreciate this opportunity to discuss additives in childhood vaccines. I will focus my current remarks on thimerosal. I ask that my full written statement be entered into the record.

Mr. BURTON. Without objection, so ordered.

Mr. EGAN. Let me say that I am sympathetic to the concerns of the parents expressed by the previous panel. FDA will continue to work with parents and other public health agencies to foster the research and data necessary to determine the causes, treatment and hopefully prevention of autism.

Vaccines licensed by FDA have been protecting children in the United States from deadly infections for well over 50 years and have been credited for saving more lives and preventing more illnesses than any other medical treatment. The risk of childhood diseases from failure to vaccinate far outweighs exposure to thimerosal in vaccines. Prior to licensure each vaccine undergoes a thorough review, and FDA considers all vaccines currently available to be both safe and effective.

Preservatives are added to vaccines to help minimize the consequences of inadvertent microbial contamination, and with certain exceptions the use of preservatives is required by regulation for all multidose formulations. Thimerosal is an effective preservative which has been used in vaccines and other products since the 1930's.

Requirements for preservatives in multidose vaccine formulations exist in many countries, not just in the United States, and have arisen as a result of tragic experience when bacterially contaminated vaccines were inadvertently administered to children. While the use of thimerosal does not absolutely eliminate the possibility of bacterial contamination, it markedly reduces its likelihood.

The FDA has been actively addressing the issue of thimerosal as a preservative in vaccines. A review of thimerosal by FDA and other Public Health Service agencies last year found no evidence of harm from its use in vaccines. Nevertheless, because of concerns about the potential exposure of infants to mercury from all sources, in July 1999 the Public Health Service, in concert with the American Academy of Pediatrics, urged vaccine manufacturers to reduce or eliminate thimerosal in vaccines. Much progress has been made to this end over this past year.

Let me focus on the routine recommended immunizations given to children in their first 6 months of life. Last year at this time thimerosal was present in both of the licensed hepatitis B vaccines; in some, type B Haemophilus influenza, DTaP vaccine, and that is the vaccine for diptheria, tetanus and pertussis. Since last summer, thimerosal has been eliminated or reduced by more than 96 percent in the pediatric hepatitis B vaccines. With regard to the Haemophilus vaccines, Wyeth-Lederle has announced that they will be manufacturing only their thimerosal-free single-dose Haemophilus formulation. The other Haemophilus vaccines are already thimerosal-free as is a combination vaccine for Haemophilus

and hepatitis B. All of the Haemophilus vaccines now being manufactured are thimerosal-free.

Let me now turn to the four DTaP vaccines. The DTaP vaccine from SmithKline Beecham does not contain thimerosal as a preservative, and both Wyeth-Lederle and Aventis Pasteur have announced that they will be submitting license supplements to FDA for thimerosal-reduced vaccines either this month, later this month, or in August. North American Vaccines has begun discussions with the agency on a thimerosal-free formulation. FDA is committed to the expedited review of these applications, and hopefully in early 2001 will have additional thimerosal-reduced DTaP vaccines.

Various Federal agencies, including FDA, the Environmental Protection Agency and the Agency for Toxic Substances and Disease Registry, have been addressing the health risks of mercury, particularly methyl mercury. Thimerosal is a derivative of ethyl mercury, a closely related compound. It is important to note that there are no convincing data or evidence of any harm caused by the level of exposure that some children may have encountered following the existing immunization schedule. FDA's Office of Vaccines continues to urge manufacturers to develop new vaccines without thimerosal as a preservative and to remove or reduce thimerosal content in existing license vaccines.

Based in part on the substantial progress that has been made in the reduction of thimerosal for vaccines in this past year, the American Academy of Family Physicians, the American Academy of Pediatrics and the Public Health Service in consultation with its Advisory Committee on Immunization Practices recently reaffirmed its goal set last year to greatly reduce or remove thimerosal from vaccines as rapidly as possible. The group also stated that the risk of not vaccinating children with DTaP or the remaining HIB vaccine is believed to far outweigh the risk, if any, of the thimerosal in them.

Childhood vaccines have been a success story. Without vaccinations, children would be at a high risk of contracting many serious preventable childhood diseases. It makes good sense to remove thimerosal from vaccines, and we are committed to that goal, and we are rapidly reaching that goal. While we are continuing to work to remove thimerosal from childhood vaccines, we need to do this safely.

Thank you for the opportunity to testify, and I will be glad to answer any questions.

[The prepared statement of Mr. Egan follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

STATEMENT OF

WILLIAM EGAN, Ph.D.

ACTING OFFICE DIRECTOR

OFFICE OF VACCINE RESEARCH AND REVIEW

CENTER FOR BIOLOGICS EVALUATION AND REVIEW

FOOD AND DRUG ADMINISTRATION

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM

U. S. HOUSE OF REPRESENTATIVES

JULY 18, 2000

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Committee, I am William Egan, Ph.D., Acting Office Director, Office of Vaccine Research and Review (OVRR), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA or Agency). We appreciate the opportunity to discuss the issue of additives in childhood vaccines, in particular thimerosal.

Vaccines, licensed for use in the United States (U.S.) by FDA, have been protecting our nation's children from deadly infectious diseases for over fifty years. In fact, immunizations represent one of the most significant public health achievements of the 20th century. Vaccines can be credited for saving more lives and preventing more illnesses than any medical treatment. Without question, continuing to ensure our children are vaccinated with licensed vaccines is critical to protect their health and to prevent disease outbreaks. Prior to licensure, each vaccine undergoes a rigorous review process to establish its safety and effectiveness. FDA considers all vaccines currently available to be safe and effective.

It is essential that children continue to receive all vaccines according to currently recommended schedules. The risk of the emergence of devastating childhood diseases like whooping cough, bacterial meningitis, tetanus, polio and diphtheria is real. The risk of these devastating childhood diseases from failure to vaccinate far outweighs the minimal, if any, risk of exposure to levels of thimerosal or mercury in vaccines.

Nevertheless, FDA has been actively addressing the issue of thimerosal as a preservative in vaccines. An FDA review of this issue one year ago found no evidence of harm from the use of thimerosal as a vaccine preservative but raised questions about the potential exposure of infants to mercury from thimerosal in vaccines. Based on this review, the Public Health Service (PHS) acted quickly, urging vaccine manufacturers to reduce or eliminate thimerosal in vaccines. Much progress has been made to date. The Agency has been working with other PHS agencies, the American Academy of Pediatrics and manufacturers, particularly those that manufacture childhood vaccines, to eliminate thimerosal from vaccines and to further evaluate the potential health effects of thimerosal.

PURPOSE OF VACCINE ADDITIVES

In addition to the actual immunogen, vaccines may contain preservatives (e.g., thimerosal), adjuvants (e.g., the aluminum salts), and stabilizers (e.g., gelatin). The vaccine may be a liquid preparation in a suspending fluid such as buffered saline. Adjuvants are materials that, when used in combination with vaccine immunogens, increase the strength and/or duration of the immune response. At present, the only adjuvants that are found in U.S. licensed vaccines are the aluminum salts.

Preservatives are added to vaccine preparations to help minimize the consequences of inadvertent microbial contamination; with certain exceptions, they are required by regulation for multi-dose formulations. There are four preservatives that are currently

contained in U.S. licensed vaccines. These are: thimerosal, phenol, 2-phenoxyethanol, and benzethonium chloride.

THIMEROSAL AND MERCURY

Thimerosal is an effective preservative and has been used in some vaccines and other products since the 1930s. Thimerosal contains mercury in the form of ethyl mercury. Thimerosal is the most widely used preservative in vaccines. FDA estimates that it is used in more than 30 licensed vaccines and biologics currently marketed in the U.S. Thimerosal is used as a safeguard against microbial contamination. Disease outbreaks have occurred following contamination of multi-dose vaccine vials. While use of thimerosal as a preservative does not eliminate the possibility of bacterial contamination (multi-dose vials with thimerosal have become contaminated), the likelihood of contamination can be markedly reduced.

Mercury is a metal that is found in elemental form (such as the mercury used in thermometers), as inorganic salts, and as organomercurials (such as thimerosal). Humans may be exposed to organic mercury in the form of methyl mercury from eating contaminated fish. The magnitude of exposure to mercury (especially methyl mercury) and the degree of risk from fish consumption depend on the level of mercury in the fish consumed and the amount of fish an individual consumes. Very high levels of mercury are toxic. Because mercury is found naturally in the environment, it is not possible to prevent all exposure to mercury, however, the industrial uses and releases of mercury

have been reduced very substantially in recent decades in the U.S. and most other industrialized countries.

Although mercury is found in the environment, in food and in household products, exposure to mercury is of concern and, when possible, should be avoided. For this reason, various Federal agencies have been addressing the health risks of mercury. One type of mercury, called methyl mercury, is found in fish and has received particular attention because high doses have been associated with adverse health effects. FDA, the Environmental Protection Agency (EPA) and the Agency for Toxic Substance and Disease Registry each have developed guidelines for intake of methyl mercury. As noted thimerosal contains a related mercury compound called ethyl mercury.

It is very important to remember that safety margins are incorporated into all acceptable mercury exposure limits. **There are no convincing data or evidence of any harm caused by the low levels of thimerosal that some children may have encountered in following the existing immunization schedule.**

Nearly all recommended pediatric vaccines available today in the U.S. are thimerosal-free. In 1999, FDA conducted a review of vaccines being used at that time. The review suggested that some infants, depending on which vaccines they receive and the timing of vaccination, may have been exposed to levels of ethyl mercury that could build up to exceed one of the Federal guidelines established for the intake of methyl mercury. There are no guidelines established for ethyl mercury, but experts agree that methyl mercury

guidelines are appropriate to use in this situation. It is important to remember that there are safety margins incorporated into all Federal guidelines on methyl mercury exposure. Again, any mercury exposure from these vaccines is within the safety margin incorporated into the guidelines. **No children or infants were receiving toxic levels of mercury from vaccines, but FDA still believed it appropriate to pursue alternatives to using thimerosal as a preservative in vaccines.**

It should be noted that other than the occurrence of local hypersensitivity reactions, no harmful effects have been reported from thimerosal at doses found in vaccines. Some individuals experience local skin reactions such as redness and swelling that may suggest a delayed type of hypersensitivity reaction following injection with products containing thimerosal. While one study found that most patients do not develop reactions to thimerosal given as a component of vaccines, even when they tested positive for thimerosal hypersensitivity, a prior history of hypersensitivity to thimerosal, or any component in a vaccine, is considered a contraindication to further vaccination with thimerosal-containing vaccines.

PROGRESS AND CONTINUING ACTIONS ON REMOVAL OF THIMEROSAL

Under section 413(a) of the Food and Drug Administration Modernization Act (FDAMA) of 1997 (Pub. L. 105-115), entitled "Food and Drug Administration Study of Mercury Compounds in Drugs and Food," FDA was required to: (1) Compile a list of drugs and foods that contain intentionally introduced mercury compounds, and (2) provide a

quantitative and qualitative analysis of the mercury compounds in this list. The statute did not differentiate between mercury as an active or an inactive ingredient. The provision also required the study of the "adverse effects on health of children and other sensitive populations from exposure to . . . mercury."

CBER conducted a review of the use of thimerosal in childhood vaccines as well as other biologics. As part of this review, U.S. vaccine manufacturers responded to a December 1998 and April 1999 FDA Federal Register request to provide more detailed information about the thimerosal content of their products which included thimerosal as a preservative. It should be noted that the approved labeling of all biologicals including vaccines requires the listing of preservatives and the concentration on the label. (21 CFR 610.61)

While the review found no evidence of adverse effects caused by thimerosal in vaccines, except for minor local hypersensitivity reactions (as explained above), the assessment determined that the use of thimerosal as a preservative in vaccines might result in the intake of mercury during the first six months of life that exceeded recommended guidelines from EPA. **The amounts, however, do not exceed the recommended guidelines set by FDA, the Agency for Toxic Substances and Disease Registry, and the World Health Organization.** Of note, such guidelines contain safety factors and are meant as starting points for evaluation of mercury exposure, not absolute levels above which toxicity can be expected to occur.

Even though no major safety concerns resulting from use of thimerosal in vaccines were found, FDA concluded that reducing or eliminating exposure to thimerosal in vaccines was merited. Given the goal of reducing human exposure to mercury from all sources and the feasibility of single dose vials in the U.S., for which preservatives are not mandated, this action was justified. This review recognized the limitations of available data and recommended further studies to provide a more precise characterization of the potential risk from thimerosal in vaccines. These conclusions led FDA and others within PHS to announce the July 1999 recommendation that, as a precautionary measure, thimerosal be reduced or eliminated from childhood vaccines to make already safe vaccines even safer.

On July 1, 1999, CBER notified all vaccine manufacturers by letter that the use of thimerosal in biologic products would continue to be evaluated. As part of the evaluation, CBER requested that all manufacturers of thimerosal-containing vaccines provide information to CBER regarding their plans for thimerosal as a preservative in U.S. licensed vaccines.

The letter requested that if the manufacturer intended to remove thimerosal from their product(s), the following information needed to be discussed:

- proposed studies to assess the effect of removing thimerosal on sterility, potency, stability, and immunogenicity of the product;
- feasibility of eliminating or reducing the amount of thimerosal, using alternative preservatives, or reformulating the product solely for single dose containers;

- anticipated manufacturing changes as a result of removing thimerosal, if any; and,
- approximate time-line necessary to evaluate and implement removal.

If the manufacturer intended to continue using thimerosal in their product(s), an explanation was requested as to why that decision was made. (The letter can be found at www.fda.gov/cber/ltr/thim070199.htm.)

In August 1999, the available scientific information on thimerosal in vaccines was reviewed at a public workshop sponsored by the National Vaccine Advisory Committee (NVAC). The NVAC workshop was convened to examine the evidence for risks associated with possible exposures, however, there was no current evidence of a significant public health problem from thimerosal in vaccines. The meeting participants did urge that thimerosal be removed from vaccines as a prudent measure and that further research continue.

FDA's OVRR has been encouraging manufacturers to develop new vaccines without thimerosal as a preservative and to remove or reduce the thimerosal content of existing, licensed vaccines. Substantial progress has been made in the removal of thimerosal from vaccines. In August 1999, FDA approved a license supplement from Merck for a thimerosal-free hepatitis B vaccine. In March 2000, FDA approved a license supplement from SmithKline Beecham Biologicals for a thimerosal reduced hepatitis B vaccine (with more than 96 percent of the thimerosal removed from the vaccine, from a level of 25 micrograms of thimerosal per dose to less than one microgram per dose). Additionally, Wyeth-Lederle Vaccines and Pediatrics is now marketing only a single-dose, thimerosal-

free formulation of their *Haemophilus influenzae* type b (Hib) vaccine (they are no longer marketing the thimerosal containing multi-dose formulation). The other U.S.-licensed Hib vaccines are thimerosal-free. Thus, all pediatric hepatitis B and Hib vaccines currently being marketed are thimerosal-free or greatly reduced. Vaccines for polio, chicken pox, and mumps-measles-rubella already were thimerosal-free. Based on the progress in the past year, the maximum amount of ethyl mercury that an infant may be exposed to from the routine immunization schedule has been reduced by sixty percent (60%).

At present, there are four U.S.-licensed DTaP vaccines. The DTaP manufactured by SmithKline Beecham Biologicals (SBB) does not contain thimerosal as a preservative, while the DTaP vaccines from Wyeth-Lederle Vaccines and Pediatrics, Aventis Pasteur, and North American Vaccine do contain thimerosal.

Recently both Wyeth-Lederle Vaccines and Aventis Pasteur announced plans to submit supplements to their respective DTaP licenses in either July or August of this year for thimerosal-reduced DTaP vaccine formulations. FDA is committed to the expedited review of these supplements.

To further encourage the development of thimerosal-free vaccines, CBER sent another letter to vaccine manufacturers on May 31, 2000. CBER requested an update on progress toward the goal of thimerosal-free vaccines, particularly for vaccines administered to

infants and children. For each manufacturer's product noted in the reply to CBER, the following information was requested:

- actions taken to date to develop thimerosal-free or thimerosal-reduced vaccine;
- time lines for implementing proposed changes to reduce or eliminate thimerosal from the product(s); and,
- identification of which products, if any, the manufacturer intended to continue using thimerosal and an explanation of why reduction or removal of thimerosal is not feasible.

Responses were requested from manufacturers within 45 days. (The letter can be found at www.fda.gov/cber/ltr/thim053100.htm.)

In June 2000, the National Immunization Program (NIP) of the Centers for Disease Control and Prevention (CDC) convened another meeting intended to further address the potential for health problems associated with exposure to thimerosal in vaccines. CDC had recently conducted an initial study to screen for any possible association between a variety of neurologic, developmental, and renal outcomes and the amount of thimerosal in vaccines. The consensus of the group reviewing the data was that the findings were insufficient to support any causal relations between exposure to thimerosal-containing vaccines and selected neurological development disorders, but did urge that additional research be continued.

FDAMA REPORT

As discussed above, under section 413(a) of FDAMA, FDA was required to: (1) compile a list of drugs and foods that contain intentionally introduced mercury compounds, and (2) provide a quantitative and qualitative analysis of the mercury compounds in this list. FDA published requests for data and information on mercury compounds in drugs and food. The Agency asked all manufacturers of any food, including dietary supplements, and human and veterinary drug products (prescription or over-the-counter (OTC)) containing any intentionally introduced mercury compounds, whether used as an active or inactive ingredient, to provide information about the products to the Agency.

The Agency received 41 responses to the request-for-data notices; 38 from manufacturers of products, one from an association of homeopathic pharmacists, and two from consumers. Of the 38 responses from manufacturers, 15 were from manufacturers of homeopathic drug products, and 23 were from manufacturers of drug and/or biologic products (13 drug manufacturers, eight biologic manufacturers, and two manufacturers of both types of products). Five of the drug manufacturers informed the Agency that they had no products containing any mercury compounds. One drug manufacturer was an animal health corporation providing information on a veterinary drug product, and two manufacturers of homeopathic products included information on five veterinary drug products as well as human drug products.

In November 1999, FDA made available the document prepared in response to the FDAMA section entitled "Mercury Compounds in Drugs and Foods." The document discusses drugs (including biologics) and foods that contain intentionally introduce mercury compounds. The document provides a quantitative and qualitative analysis of the mercury compounds in the products. (The document can be found at www.fda.gov/cder/fdama/mercuryreport.htm.)

CONCLUSION

On April 17, 2000, Secretary Donna E. Shalala, Department of Health and Human Services (DHHS), kicked off National Infant Immunization Week by releasing a new public awareness campaign urging all parents to immunize their children. The key message is that childhood vaccines have been a success story in American public health initiatives. Childhood immunization rates have reached all time highs with more than 90% of America's children receiving the most critical doses of vaccines for children by age two. Reported rates of diseases, for which childhood vaccines were developed, were at or near record lows in 1998. Without vaccinations, children would be at a very high risk for contracting many of these preventable childhood diseases.

While FDA and other components of DHHS work to remove thimerosal from childhood vaccines, parents should continue to have their children vaccinated. The risks of not vaccinating children far outweigh the unknown and much smaller risk, if any, of exposure to thimerosal in vaccines.

Thank you for the opportunity to testify.

Mr. BURTON. We have some votes on the floor. How many votes are there? Three. We have three votes on the floor, and I really apologize, but we will probably have to run down there for those votes. Rather than have you start your testimony, Dr. Bernier, I think we will go ahead and recess now, and we will be back in 25 minutes. We stand in recess.

[Recess.]

Mr. BURTON. If we can get the doors closed, please, and get everyone to return to the hearing. I apologize for being away for so long.

Dr. Bernier.

Dr. BERNIER. Good afternoon, Mr. Chairman and members of the committee. I am Dr. Roger Bernier, Associate Director for Science of the National Immunization Program at the Centers in Disease Control and Prevention.

In opening, I would like to emphasize that we in the National Immunization Program have deep empathy for all of the parents who have experienced the devastating disorder that is autism. It is impossible for us who have devoted their lives to the health and well-being of children not to be affected and touched by the personal stories and hardships that lie behind every child and family affected by autism.

Because of their enormous contributions to the health and well-being of children, vaccines have been frequently cited as one of the greatest public health achievements in the 20th century. The introduction and widespread use of vaccines have prevented millions of cases of childhood diseases and millions of premature deaths. Thanks to vaccines, there are few visible reminders of how serious and deadly vaccine-preventable diseases can be. The graphic impact of pertussis, another disease that was quite prevalent prior to the development and use of an effective vaccine, is detailed in my written testimony, and I would like if my written testimony can be part of the record.

As a world leader in the licensing of new vaccines, the United States places a high priority on safety and efficacy. The steps that we have taken with respect to thimerosal illustrate how much we value vaccine safety. The Public Health Service in collaboration with the American Academy of Pediatrics and the American Academy of Family Physicians set a goal for the removal or significant reduction of thimerosal as a preservative for all vaccines routinely administered to children in the first year of life. We took this action even though there was no scientific data showing such exposure caused any harm.

The risk of harm from thimerosal in vaccines remains largely theoretical. However, because it is feasible to produce vaccines that don't need thimerosal-based preservatives, we set the goal of moving as swiftly as possible to a thimerosal-preservative-free childhood immunization schedule while ensuring that children continue to receive the immunizations necessary to prevent disease. Since last June we have made significant progress toward achieving that goal. Six of the seven vaccines recommended for routine use do not contain thimerosal as a preservative, including the four vaccines that never did. By early 2001 we expect to have an adequate thi-

merosal-preservative-free vaccine supply for all of the routinely recommended childhood vaccines.

Since last July, the CDC has also undertaken a number of studies to understand the potential human health effects, if any, from exposure to thimerosal in vaccines. Using medical histories from the Vaccine Safety Datalink, investigators screened more than 100,000 children. They wanted to see if any statistical associations could be found between exposure to ethyl mercury in thimerosal-containing vaccines and those conditions most likely to be related to this type of exposure, that is kidney or neurologic conditions found in the medical records. The researchers looked at 17 different diagnostic codes. They found five inconclusive correlations between thimerosal exposure and the codes for language delays, speech delays, attention deficit disorder, unspecified developmental delays and tics. Importantly, however, this screening study did not find any evidence of any increased association between these conditions among premature infants, nor did it find any associations between thimerosal exposure and autism.

An independent expert review of the screening study with the five inconclusive correlations was also undertaken. Twelve experts from outside the CDC evaluated the methods used and the results obtained. The consultants were unanimous in agreeing that the available evidence taken as a whole failed to meet the set of criteria necessary to establish that thimerosal caused the adverse health effects examined in these studies.

We did not stop here, however. Good science involves trying to reproduce findings. We thus arranged to analyze information from another managed care organization to see if the five inconclusive correlations in the initial screening study could be duplicated in a similar yet completely separate data base. The second study found no statistically significant positive correlation between speech, language and attention deficit disorders and exposure to mercury from thimerosal-containing vaccines. The direction of the findings is reassuring as it does not confirm the earlier observations.

To help us continue to address concerns about vaccine safety, CDC and NIH are contracting with the Institute of Medicine to establish a standing committee on vaccine safety. And I believe, Mr. Chairman, this is partly in response to the request that you had made with Congressman Waxman from the last hearing. There are steps very far along to move toward working with IOM to look at these vaccine safety concerns. This IOM committee will meet several times each year to assess any new evidence about possible adverse health effects from vaccines and to determine which vaccine safety concerns are a priority for further followup. The first issue we will seek to be taken up by the committee will be to review the available information about vaccines, including thimerosal and autism.

Mr. Chairman, I recognize that a call for more research can be discouraging for parents with autistic children who feel that they cannot wait another day before doing something about this illness, but information which is not the right information only sends parents and families down the wrong paths. The history of science is replete with hypotheses and touted cures that have not panned out. If we hope to accurately identify and effectively address the causes

of diseases and disorders, we must continue to trust the tools that have served us well, in this case the most rigorous scientific methods possible.

In summary, I would like to reiterate three key points from my testimony. First, the introduction and widespread use in the United States of vaccines against many childhood diseases have prevented hundreds of millions of cases of disease and millions of deaths.

Second, vaccine safety has been and is a high priority at the CDC and other Federal agencies. The vaccines produced and licensed in the United States meet the highest standards of safety and efficacy in the world.

Third, there is currently no persuasive scientific evidence which establishes a causal link between vaccines and autism or vaccines and any neurodevelopmental outcome. It is imperative that children continue to receive all of the recommended vaccines in the most timely manner possible. Doing so will assure the greatest possible level of protection from the still circulating viruses and bacteria that cause serious and potentially deadly childhood diseases.

Mr. Chairman, I would be happy to answer any further questions that you or the other Members may have.

Mr. BURTON. Thank you.

[The prepared statement of Mr. Bernier follows:]

TESTIMONY OF ROGER H. BERNIER, Ph.D., M.P.H.

ASSOCIATE DIRECTOR FOR SCIENCE

NATIONAL IMMUNIZATION PROGRAM

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM

U.S. HOUSE OF REPRESENTATIVES

JULY 18, 2000

Bernier

Good afternoon Mr. Chairman and members of the committee.

I am Dr. Roger Bernier, an epidemiologist and Associate Director for Science of the National Immunization Program at the Centers for Disease Control and Prevention (CDC). Thank you for the opportunity to testify today about vaccines, which are among the safest pharmacologic interventions for disease prevention available. I will also discuss some of the achievements and issues which arise from the widespread use of vaccines among children in our country and, more specifically, concerns about a possible relationship of mercury in vaccines and autism.

Before I begin my testimony on vaccines, I would like to emphasize the solidarity that we at CDC feel with all of the parents and families who have experienced or are experiencing the devastating illness that is autism. The National Immunization Program's goal is first and foremost about the protection of children and promoting the health of children. No one who cares about children as much as we do, and no one who devotes their lives to children's well being as we do every day, can feel untouched by the personal stories and hardships that lie behind every child and family with autism. As long as the causes of autism remain uncertain, we encourage and applaud the efforts of our scientists, parents, and advocates to work together to identify the causes of autism and hopefully to one day prevent it just as we have successfully been able to prevent other childhood diseases such as smallpox and polio. Mr. Chairman, even though we work in immunization, we are not immune to autism. This condition has struck our homes, our staff, and their families, just as it has struck everywhere else in America.

Regarding all of the groups which testified or will testify here today, let me reiterate that we in immunization are no less anxious than they are to help find the cause and cure of autism.

I would like to begin my testimony by putting a vivid face on at least one of the vaccine preventable diseases that we are seeking to prevent with today's immunization schedule. I believe this vivid description is important since we have been very successful in controlling vaccine preventable diseases in the United States, and without these diseases as reminders in our daily lives, we can easily forget how serious and even deadly these diseases can be. The short passage I wish to cite is from a 1975 medical article by a physician from Indiana University describing pertussis or whooping cough. It reads:

> "The child possessed of the coughing fit is a pitiful sight, all the more so as the observer is helpless to alleviate or terminate the attack. Each attack consists of 10-30 forceful coughs per spasm, and into each cough the patient appears to concentrate all his energy. He leans forward, or, if standing, stands with legs spread, grasping the nearest object and leaning far forward, tongue protruded to the utmost, saliva and mucus streaming from nose and mouth, eyes bulging with tears streaming, his entire body wracked with the total exertion of each cough. The coughing continues in a staccato series. The face becomes more and more cyanotic, the neck bulges with venous congestion and still the attack continues. Finally, when it seems certain that death is imminent, a final cough appears to clear offending secretions or mucus from the upper airway and the first opportunity to inspire is offered. With a massive effort, inspiration ensues, air rushes into the lungs

against a still narrowed glottis and the characteristic whoop is produced....

Apart from the complicating conditions which occur in some patients with pertussis, the major danger from the disease is during severe coughing paroxysms, during which prolonged hypoxia may lead to irreversible changes in the central nervous system or even death. The greatest mortality via this mechanism occurs in infants."-Olson, LC, Pertussis, Medicine 1975, 54:427-458

Estimates are that approximately 70% of the U.S. population experienced pertussis before adulthood in the prevaccine era. Fortunately, through routine childhood vaccinations, pertussis cases have dropped more than 95% from previous levels and we now prevent thousands of cases of pertussis like this each year.

Vaccines are often cited as one of, if not the greatest, achievement of biomedical science and public health in the 20th century. To understand why this statement is true, we can point to the remarkable success we have had in controlling not only pertussis, but many other infectious diseases which used to be widely prevalent in the United States.

Smallpox, which caused almost 50,000 cases of disease and more than 1,500 deaths each year at the beginning of this century, was eradicated in 1977.

Wild polio viruses, which caused an average of more than 16,000 cases and 1,800 deaths per year

in the early 1950's just prior to the introduction of the vaccine, have been eliminated from the Western Hemisphere since 1991.

Measles, which caused more than a half million cases each year just prior to the introduction of the vaccine in the early 1960's, has been eliminated from the United States except for international importations that result in limited domestic spread.

Haemophilus influenzae type b (Hib), which caused an estimated 20,000 cases of invasive disease each year, was the leading cause of childhood bacterial meningitis and the most common cause of mental retardation acquired after birth. Because of vaccination, Hib has been nearly eliminated in children.

Diphtheria, which caused more than 175,000 cases and almost 15,000 deaths in the three years just prior to vaccine licensure in 1923, has virtually disappeared from the United States with fewer than 10 cases per year since the 1980's. Deaths have become rare with less than one per year on average. During the 1990's, the health benefits from our successful use of diphtheria toxoid in the U.S. have been strikingly contrasted by the experience of the former Soviet Union. The failure of the newly independent states to maintain adequate vaccination coverage levels resulted in more than 146,000 cases of diphtheria and more than 4,000 deaths. In the United States, immunization efforts have not faltered and estimates of the impact of diphtheria toxoid in the United States indicate that vaccination has averted more than 58 million cases and has saved almost six million lives during this century.

Tetanus toxoid was introduced in the United States in 1927 and tetanus deaths have declined consistently throughout the 73 year history of toxoid use in the United States, reaching an all time low of a single death in 1996.

Mumps vaccine was licensed in 1969 and there were more than 150,000 cases and 25 deaths in the year preceding licensure. A long-term decline in mumps cases has occurred since licensure with a record low number of 606 reported cases in 1998 with many years having no mumps deaths.

Rubella cases began to decline in 1970 and have continued to do so for the 30 years since vaccine licensure. Congenital rubella cases have followed a similar pattern, and the six to nine year epidemic cycle whereby thousands of children were born with serious congenital defects such as cataracts, hearing loss, and mental retardation has been completely eliminated.

The United States has been a world leader in the development and licensing of new vaccines and has placed a high priority on producing vaccines which meet the highest standards for safety and efficacy. These standards pertain not only to the active ingredients, which elicit protective immune responses, but also to the preservatives such as thimerosal. Thimerosal, an ethylmercury containing preservative used since the 1930's, is added to some vaccines because it is very effective in preventing bacterial contamination and resulting infections in vaccine recipients.

In mid-1999 administration of a combination of vaccines that contained thimerosal as a

preservative was recognized as exceeding one federal guideline for mercury exposure. It is important to note that the form of mercury used in thimerosal is ethylmercury. Although toxicity data are lacking for ethylmercury, it is currently assumed that methylmercury guidelines are appropriate to use in this situation. Even though there was no evidence of possible harm caused by ethylmercury exposure from immunizations, the United States Public Health Service agencies, including NIH, FDA, HRSA, and CDC took action, working collaboratively with the American Academy of Pediatrics and the American Academy of Family Physicians. Last summer a goal was set for the removal or significant reduction of thimerosal as a preservative from all vaccines routinely administered to children in the first year of life. While the risk of harm from this source was only theoretical, the decision to set a goal to remove thimerosal was made as a precautionary measure. Given the concern about the health effects of mercury of any sort, the elimination of mercury from vaccines was judged a feasible means of reducing an infant's total exposure to mercury in a world where other environmental sources of exposure may be more difficult or impossible to eliminate.

During the year since the goal was set, progress in removing or reducing thimerosal in vaccines has been outstanding. The United States has now achieved a pediatric hepatitis B vaccine supply from two manufacturers that is free of thimerosal as a preservative, and, as of this month, a *Haemophilus influenzae* type b vaccine supply from all four manufacturers is available that is free of thimerosal as a preservative. For DTaP vaccines, there are four manufacturers, one of which has produced a vaccine that is already free of thimerosal, and at least one other is expected to produce a vaccine without thimerosal as a preservative within six to nine months. Measles,

mumps, rubella, varicella, inactivated polio, and the recently licensed conjugate pneumococcal vaccines have never contained thimerosal. Based on our progress over the past year, the maximum amount of mercury an infant may be exposed to from routine immunizations has been reduced by 60 percent.

Thus, by early 2001, the United States is expected to have obtained an adequate vaccine supply for the routine pediatric vaccines that is completely free of thimerosal as a preservative.

Since July 1999, efforts have been made not only to reduce the thimerosal content of vaccines, but also to carry out further research to better understand the potential human health effects, if any, from exposure to thimerosal in vaccines. Two avenues of research have been pursued, one involving the use of clinical and laboratory information to examine the blood levels of mercury in children shortly after vaccination, and a second involving the use of epidemiologic information to examine health outcomes in children who have received thimerosal containing vaccines.

In the first avenue of research, investigators at the University of Rochester, Bethesda Naval Hospital, and NIH have looked for mercury in blood and urine in a small number of infants shortly after vaccination. Initial results from these studies indicate that infants vaccinated with thimerosal containing vaccines have blood and urine levels of mercury that are at or below the levels that are considered background levels or those levels found in unvaccinated children. If confirmed by the addition of more children in the study, these results suggest that mercury levels

after vaccination are very unlikely to be related to any adverse health outcomes. Because of the further reduction in the use of vaccines containing thimerosal over the next year, additional studies of this type will no longer be feasible in the near future.

In the second research approach, using epidemiologic information from the Vaccine Safety Datalink (VSD), a network of managed care organizations on the west coast funded by CDC to examine questions of vaccine safety, investigators screened more than one hundred thousand children for numerous health outcomes thought to be potentially associated with the ethylmercury in thimerosal containing vaccines. The purpose of this research was to determine if these children who received vaccines containing thimerosal were any more likely to develop abnormalities than children not exposed to thimerosal through vaccination, and, if so, whether the risk increases with exposure to larger amounts of thimerosal. Initial analyses which looked at children's exposure both above and below the EPA reference levels for methylmercury failed to show any relationship between exposure and any adverse health effects. Despite the lack of any findings suggesting any adverse health outcomes, additional analyses were undertaken. Results for 17 kidney and neurologic conditions that were looked at showed an inconclusive correlation between exposure to thimerosal containing vaccines for five of these conditions, including those coded as language delays, speech delays, attention deficit disorder, unspecified developmental delays, and tics. However, there was no evidence of any increased risk for these conditions among premature infants. This finding is important because premature infants would theoretically have been the most likely to show any health effect if one existed since as the smallest babies they would have the highest body exposure to mercury per unit of body weight.

None of the other 12 kidney and neurologic conditions investigated showed any association with exposure to thimerosal containing vaccines.

As for autism, investigators did not find any indication among the 127 children in the Vaccine Safety Datalink diagnosed with this disorder of an association with ethylmercury at any level. When assessing how increasing doses of ethylmercury from thimerosal containing vaccines affected the risk of developing autism, investigators did not find that increasing dose significantly increased the risk.

To obtain an independent review of these observations on thimerosal exposure and adverse health effects, CDC asked expert consultants from outside of CDC to evaluate the methods used and results obtained. The consultants made use of a frequently used set of criteria which scientists refer to in trying to assess a causal relationship. Among the criteria considered were 1) whether or not the exposure occurred before the disease of interest, 2) the strength or magnitude of the association between exposure and disease, 3) the consistency of the findings with other results, 4) whether or not a dose response relationship was manifest, and 5) the plausibility of the results in light of what is already known about the biology of disease in human beings. The consultants were unanimous in agreeing that the available evidence as a whole failed to meet the set of criteria necessary to establish that thimerosal causes the adverse health effects examined in these studies. Because of the potential implications of the results however, the consultants urged further investigation.

Prompted by the preliminary VSD findings indicating an inconclusive correlation between exposure to thimerosal-containing vaccines and five of seventeen conditions, CDC quickly arranged to analyze information from another managed care organization on the east coast to see if the findings from the VSD study could be duplicated in a completely separate study. We found no statistically significant positive correlation between three of the five conditions (speech, language, and attention deficit disorders) and exposure to mercury from thimerosal-containing vaccines. The number of children that developed tics and unspecified neurologic disorders was too few to do a repeat analysis. These results require further scrutiny before reaching any final conclusions, however the direction of the findings is reassuring as it does not confirm the earlier observations.

Last month, individuals from the organization Cure Autism Now (CAN) presented to CDC a review it conducted of information in the medical literature about mercury poisoning and autism. We appreciated the opportunity to examine this comprehensive report and are grateful to CAN for bringing it to our attention. Their review concluded that autism is a form of mercury poisoning and that vaccines containing thimerosal, an ethylmercury based preservative, should be eliminated immediately. In reviewing this report, we have applied a similar set of criteria for causality as were used by CDC consultants in evaluating the information from the Vaccine Safety Datalink. The evidence assembled by the Cure Autism Now report presents a very intriguing set of similarities between the clinical characteristics of autism and mercury poisoning. However, the evidence assembled does not satisfy the criteria for strength, consistency, dose-response, coherence and other criteria. In our view, the Cure Autism Now report offers

intriguing comparisons that should be investigated further, but which at this time are insufficient to establish a causal association between mercury exposure and autism or between vaccines containing thimerosal and autism.

In terms of next steps, I wish to again emphasize that the number of vaccines without thimerosal as a preservative has greatly increased in the past year and it is expected that by early 2001, it should be feasible to use a routine vaccination schedule that includes only vaccines free of thimerosal as a preservative. We are on course to transition to these new vaccines as smoothly as possible without creating any abrupt changes in the vaccine delivery system. It is essential that children continue to receive all vaccines according to the recommended schedules. We have the right goal–to remove thimerosal as a precautionary measure, we are making outstanding progress, and we need to stay the right course we are on for next several months until our vaccine supply has been successfully replaced with vaccines free of thimerosal as a preservative.

In terms of next steps in research, CDC is conducting a study in the metropolitan Atlanta area of nearly all children known to have autism and a matched group of control children to determine if vaccination with MMR vaccine has been different in the two groups. Although the focus is on MMR vaccine, information on all routinely recommended infant and childhood vaccines is being collected and it may be possible to evaluate potential associations between exposure to thimerosal-containing vaccines and autism.

CDC and NIH are collaborating to support a study of autistic regression and vaccination to be

conducted in the NIH-funded Centers of Research Excellence in Autism. The focus of this study will be on MMR vaccine and onset of regression, but it may be possible to evaluate associations between exposure to thimerosal-containing vaccines and regressive autism, as well as earlier onset autism.

Finally, in order to better sort through the numerous public concerns about vaccine safety and to respond appropriately to the most compelling questions, CDC and NIH are contracting with the Institute of Medicine (IOM) to have IOM establish a standing committee on Vaccine Safety which will meet three or four times each year to assess any new evidence about possible adverse health effects from vaccines and determine which concerns are most deserving of further follow-up. The first issue to be taken up by the committee will be to review the available information about vaccines, including thimerosal, and autism. The IOM committee will also be asked to review the evidence, including results of the studies listed above, on the possible association between thimerosal and other neurodevelopmental problems. Depending on the findings of the IOM committee, additional studies may be undertaken to evaluate possible associations between thimerosal-containing vaccines and neurodevelopmental disorders.

Mr. Chairman, I recognize that often the call for more research by government officials and scientists can be disappointing and discouraging to parents and families with children who have autism now and feel that they cannot wait another day before doing something about this terrible disorder. But information which has not been obtained using the most rigorous scientific methods only sends parents and families down the wrong paths to ever more frustrating dead

ends that do not help children in the long run. We must entrust our future course to the best information we can collect, and that is information collected using the most rigorous scientific methods possible. This will take more time and will challenge everyone's patience to the utmost. But perhaps we can take some consolation from the fact that the information we do generate will be information that parents can count on, and not information that will disappoint because it raised false hopes.

In summary, I would like to reiterate three key points from my testimony.
First, the introduction and widespread use in the United States of vaccines against many childhood infectious diseases have prevented hundreds of millions of cases of disease and millions of deaths. Vaccines are one of our most valuable weapons against disease and have afforded us one of our proudest achievements in public health.

Second, vaccine safety receives the very highest priority from CDC and other federal agencies. The vaccines produced and licensed in the United States meet the highest standards of safety and efficacy. CDC, other federal agencies, manufacturers, regulators, scientists, and the doctors and nurses who make these vaccines available to children are constantly monitoring the performance of vaccines to assure that only the safest and best vaccines remain in use.

Third, recent concerns which have arisen about the potential relationships, if any, between mercury in vaccines and adverse neurologic health effects or between vaccines and autism are under active review and study by the US Public Health Service agencies. At present, there is no

persuasive scientific evidence which establishes a causal link between vaccines and autism or vaccines and any neurodevelopmental outcomes, but we pledge that any change in this assessment resulting from further research will be communicated in timely fashion to parents, doctors, and nurses. In the meantime, it is imperative that children continue to receive all of the recommended vaccines in the most timely manner possible to assure the greatest possible level of protection from deadly childhood diseases that are still lurking.

Mr. Chairman, I would be happy to answer any questions that you or the other committee members may have.

Mr. BURTON. Dr. Bristol-Power.

Ms. BRISTOL-POWER. Mr. Chairman, members of the committee, I am Dr. Marie Bristol-Power, coordinator of the Network on the Neurobiology and Genetics of Autism at the National Institute of Child Health and Human Development at the NIH. I am pleased to address the committee on the topic on NIH autism research and vaccines.

Autism is a complex disease, and a variety of influences, genetic, infectious, immunological, metabolic and possibly environmental, have been implicated as causes or triggers for autism. We believe that no single cause can account for all cases of autism, nor that any one treatment or cure will prevent or treat effectively all of its manifestations. Autism might be better understood as a class of disorders. Solving the puzzle of autism will be like peeling an onion, one layer at a time.

Current consensus is that autism probably involves multiple genes interacting in some complex way that makes individuals susceptible to autism or autism spectrum disorders. The scientific challenge is to identify both the genetic basis underlying the disorder and the environmental influences that might precipitate autism in a genetically susceptible individual.

Autism has two modes of presentation: One, the symptoms are apparent from birth. In the second the child apparently develops normally and then loses functional speech and socialization somewhere between 18 and 24 months of age. At this time there is no proven explanation for why children who develop normally lose speech and communication or speech and socialization. However, like the overall etiology of autism, there is likely to be a variety of causes for autistic regression.

Recent reports both in the literature and testimony from this committee have raised the possibility of a link between autism and vaccinations, particularly the MMR vaccine, and between autism and vaccine additives. Since it is clear that vaccines are safe and effective for the vast majority of children, such reports raise the question of whether or not some children may suffer adverse events from vaccines which are helpful to the vast majority of children who receive them.

The results of current study are inadequate to draw conclusions which would have far-reaching effects on children vaccination programs so important to the health of America's children. NIH is taking a number of different approaches to get information as soon as possible that will determine the merit of these recent concerns.

In addition to pursuing our ongoing research on a variety of different causes for autism, NICHD, with cofunding from the CDC, is beginning a study of regression in autism. A thousand persons with autism will be evaluated through the Network on the Neurobiology and Genetics of Autism of the Collaborative Programs of Excellence in Autism which are supported by Child Health and the Institute on Deafness and Other Communication Disorders. We will identify a number of—200 children with documented regressive autism, and they will be compared with matched groups of children with early onset autism and with normally developing children. We will then compare across these groups early onset autism, regressive autism, and normal development; the presence, absence, duration of normal

development; age of regression; vaccination history of children and of mothers over the course of the pregnancy; measles antibody levels and any association of vaccine additives and autism. The assessments will be done independently with blind assessments, and we will reexamine the hypotheses raised by investigators such as Drs. Singh, Wakefield and O'Leary. No one study can be definitive.

Recent work by CDC is important and informative. We are also eagerly awaiting reports from the American Academy of Pediatrics and a report from the group founded by the National Academy of Sciences and the National Institute of Medicine, which is important because it will be an ongoing committee. This retrospective research and the reviews will provide valuable information. However, what is really needed is a prospective longitudinal study that will follow a minimum of 100,000 to 150,000 children and youth from pregnancy through at least 21 years of age so we can find out what the interaction of genes and environment are that result in autism.

We stand ready to work with you, with Congress, with parent advocacy groups, scientists and individual families so that no stone is left unturned for us to uncover the causes of autism, including the causes of autistic regression.

I am pleased to answer any questions you might have.

Mr. BURTON. Thank you.

[The prepared statement of Ms. Bristol-Power follows:]

STATEMENT OF

MARIE M. BRISTOL-POWER, Ph.D.

COORDINATOR, NETWORK ON THE NEUROBIOLOGY
AND GENETICS OF AUTISM

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

NATIONAL INSTITUTES OF HEALTH

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM

U.S. HOUSE OF REPRESENTATIVES

JULY 18, 2000

Bristol- Power

Mr. Chairman and Members of the Committee, I am Marie Bristol-Power, Ph.D., the Coordinator of the Network on the Neurobiology and Genetics of Autism for the National Institute of Child Health and Human Development (NICHD) at the National Institutes of Health (NIH). In addition, I am the NICHD program staff representative to the NIH Autism Coordinating Committee (NIH/ACC). At your invitation, I am pleased to address this Committee on the topic of NIH autism research and vaccines.

INTRODUCTION

Autism is a developmental disorder that affects the most central of human behaviors—the ability to communicate, to interact socially and emotionally with others, and to have the broad repertoire of skills and knowledge needed to easily take one's place in the worlds of work and leisure. The great variability in expression of autism and related disorders indicates the complexity of the puzzle this disorder presents. Genetic, infectious, metabolic, immunologic, and possible environmental influences have been implicated as possible causes or triggers of autism.

We believe that no single cause will account for all cases of autism (and the range of Autism Spectrum Disorders), nor will any one intervention or treatment prevent or "cure" all its manifestations. Autism might be better understood as a class of disorders. Solving the puzzle of autism will be like peeling an onion, one layer at a time. To date, the gene, protein product, and some understanding of mechanisms have been found for Fragile X, once defined as a form of autism. This past year, a major gene for Rett's syndrome, one of the Autism Spectrum Disorders, was identified. Genetic "hotspots" for autism have

been discovered by independent, international groups of researchers using common diagnostic criteria. Promising work also continues on candidate genes such as on chromosome 15q11-13, and the serotonin transporter gene. The current consensus is that autism probably involves multiple genes that interact in some complex way to make individuals genetically susceptible to Autism Spectrum Disorders. The scientific challenge is to identify both the genetic basis for the disorder and the other influences that might lead to or precipitate autism in susceptible individuals.

REGRESSION IN AUTISM

There are two modes of presentation of autism—one, thought to be true for the majority of children with autism, in which the child has symptoms from birth, and a second, historically considered to constitute 20-30% of all cases, in which the child apparently develops normally and then loses functional communication and social skills, usually between 18-24 months. Recent reports suggest that the relative proportion of early onset to later onset regressive autism may be changing. Further research is needed to verify these reports. In any case, at this time, there is not a proven explanation why some children appear to develop normally and then regress. As with the overall etiology of autism, there is likely to be a variety of causes of autistic regression. In fact, a number of other developmental disorders, caused by a number of different mechanisms—genetic, metabolic, neurologic, immunologic and combinations of these mechanisms -are characterized by periods of normal development followed by regression. At the NIH, scientifically defensible mechanisms will be investigated so that the tragedy of various forms of regressive autism can be understood and ultimately prevented. The NIH

supports research in these areas, and encourages the submission of research applications on these different mechanisms. Currently supported studies in these areas include research at the University of Utah/Utah State on a possible immuno-genetic basis for autism and at the University of Rochester on the interaction of genes and environment in at least a subset of cases of autism.

VACCINES AND AUTISM

Recent reports in the literature and testimony before this Committee have raised the possibility of a link between vaccines, especially the MMR vaccine, and regressive autism, a particular concern given the importance of vaccines to the health of America's children. A related concern has been raised about the possibility of a link between mercury and autism resulting from exposure to preservatives such as thimersol in cumulative infant vaccinations. Since it is clear that vaccines are safe and effective for the vast majority of children, such reports raise the question of whether or not some children may suffer adverse events from vaccines that are helpful to the vast majority of children who receive them.

Even before recent letters to the Secretary of Health and Human Services were received from the Chairman and Ranking Member of this Committee, the NIH was looking very carefully at the suggestions raised by congressional witnesses and others on what causes autistic regression. The results of current studies are inadequate to draw conclusions that would have far-reaching effects on children's vaccination programs. However, these results are of sufficient concern that they must be addressed. The NIH is taking a number

of different approaches to get information needed as rapidly as possible to determine the merit of these recent concerns.

In addition to pursuing ongoing research on the various causes of autism, the NICHD, with co-funding from CDC, has begun a study of regression in 1,000 persons with autism through the Network on the Neurobiology and Genetics of Autism of the Collaborative Programs of Excellence in Autism supported by the NICHD and the National Institute on Deafness and Other Communication Disorders. A minimum of 200 children with documented regressive autism will be compared with matched groups of children with early onset autism and 200 normally developing control children. Group comparisons (early onset autism, regressive autism, and normal development) will include presence/absence/duration of normal development, age at regression, vaccination histories of children and of mothers (i.e., maternal vaccination before, during, or after pregnancy), measles antibody levels, and association of vaccine additives and autism. The study provides for independent, blind assessment of laboratory samples. Analyses will re-examine the hypotheses of Drs. Singh, Wakefield, and O'Leary. Initial laboratory assessments will include comparisons of immunity to measles using ELISA and other related tests of antibody levels and presence of measles virus nucleic acids in peripheral white blood cells using Real Time (RT) PCR. Subsequent assessments may include immunity to other components of the MMR vaccine, immune responses to DTP vaccine (including thimerosal), immune responses to host proteins, and transcript profiling using expression arrays representing infectious agents.

Since no one study will be definitive, the NIH is also eagerly awaiting the reports and research recommendations on this topic expected to come from an established blue ribbon panel at the American Academy of Pediatrics, and another panel of experts about to be established by the National Academy of Sciences/Institute of Medicine.

Retrospective research and literature reviews will provide valuable information. However, a prospective, longitudinal study is ultimately needed to determine the contributions of both genes and environments to healthy development and to the onset of developmental disorders such as autism. A national initiative, involving the NICHD and other NIH institutes, CDC, EPA, other federal agencies, and independent research laboratories is needed to study the developmental course of autism and other disorders in the context of normal development. Such an effort would involve following a minimum of 100,000 to 150,000 children and youth from pregnancy through at least 21-years of age, collecting both biological and behavioral measures, including vaccination history and exposure to other environmental toxins, diet, and other influences. The NICHD is working with the other agencies to initiate the planning for such a study. The recent announcement of the imminent completion of the description of the human genome signals the beginning of a new era of genetic medicine. We must pursue knowledge of the role of environmental influences in the course of autism and other developmental disorders with the same diligence we are applying to understand the underlying genetic susceptibility to autism.

At the same time, we must be vigilant that we do not overlook alternative explanations for autism and for regression. For example, recent research by Dr. Karin Nelson of the National Institute of Neurological Disorders and Stroke has identified potential biological markers present at birth that distinguish infants with autism or mental retardation from infants with cerebral palsy and from normal infants. This research, as well as work by Dr. Patricia Rodier at the University of Rochester that suggests onset of autism as early as the first three weeks of gestation, raises questions about the impact of postnatal influences on the onset of autism. Similarly, possible metabolic or other infectious sources of autism etiology must also be explored. All hypotheses must be open to independent testing and researchers held accountable to the rules of evidence and peer review.

The NIH is committed to working with the Congress, parent advocacy groups, other federal agencies, scientists, and individual families so that no stone will go unturned in our search for the causes of autism, including the causes of autistic regression after normal development.

I will be pleased to respond to your questions.

Mr. BURTON. Would you put that slide up there, please.

I don't know if you can see that slide or not, but it shows the growth of autism in America, and if you can look at that real closely, you will see that in the 1940's up through the 1970's, there was a gradual growth, and then it started to climb. The HIV vaccine was introduced in the late 1980's, and the hepatitis B vaccine was introduced, and we used to have somewhere between 1 child in 2,000 was autistic, and now it is close to 1 in 150. Some people would say that is darn near an epidemic.

What I would like to ask is if this thimerosal is not a problem, why are you phasing it out of the vaccines?

Mr. EGAN. Although I am not aware of any convincing data on harm from the thimerosal that is in vaccines——

Mr. BURTON. Mercury.

Mr. EGAN [continuing]. From mercury in vaccines, we are nonetheless committed to removing mercury, all sources of mercury, from children. And we are also concerned about potential risks and I guess some of the data that are making people more concerned in recent years about the effect of low levels of mercury.

Mr. BURTON. My grandson in 1 day got 62 times what was an acceptable level. In 1 day.

Let me ask you about this quote. In 1982, 18 years ago, as detailed in the Federal Register, and you can look this up, Federal Register volume No. 42, an FDA panel concluded that thimerosal is toxic, causes cell damage, can cause allergic reactions and is not effective in killing bacteria or halting their replication. That was 18 years ago, and yet you keep saying there is no conclusive evidence. Why is that?

Mr. EGAN. That report in the Federal Register was referring to the use of thimerosal, these organicmercurics, in topical materials.

Mr. BURTON. Not given internally?

Mr. EGAN. Like mercurochrome.

Mr. BURTON. It is bad on the outside, so you give it on the inside?

Mr. EGAN. In high concentrations. Yet it is effective as a preservative in biologics. It has continued to be used as a preservative in some of the eye drops.

Mr. BURTON. You know, one of the things that concerns me, Doctor, is that—you say that mercury in vaccines has not been proven to be a problem. How do you account for this dramatic rise? Do you think that is all genetics?

Mr. EGAN. I don't know the causes of the rise.

Mr. BURTON. You will admit it is a dramatic rise?

Mr. EGAN. It is dramatic, and I would agree with your assessment as epidemic.

Mr. BURTON. And mercury is a poison?

Mr. EGAN. Yes, it is. It is neurotoxic.

Mr. BURTON. And the FDA and the CDC are committed to phasing it out. Why not take it out today; 8,000 children are going to be immunized today. We understand that there is a supply for every child in America of nonmercury-oriented drugs. Why is it that we are not phasing it out today?

Mr. EGAN. There are a couple of things. If I can first address its use as a preservative, it is an effective preservative, and it is dem-

onstrated to be an effective preservative. All of the preservatives that are used in vaccines are required to meet the USP definition of a preservative, meaning that the test article, the vaccine with the preservative in it, is taken. There are five challenge organisms that are added, there are three bacteria and two fungi, and these are added at 0.1 milliliter of each of the bacteria and fungi in a concentration between 100,000 and a million organisms, and within 14 days the preservative is required to reduce the bacterial count by 99.9 percent.

Mr. BURTON. Let me interrupt you there. As I understand it, if you take a vaccine that is a single vaccine, not a multiple vaccine, in one shot, that the preservative that you are talking about either isn't necessary, or you don't have to use something like mercury; is that correct?

Mr. EGAN. That's correct.

Mr. BURTON. It is a single shot.

Mr. ENAYATI. A single-dose vial.

Mr. BURTON. Why don't we do that?

Mr. EGAN. That is primarily what is being done. Most of the changes that have been brought about since last summer have been the conversion of vaccines from multidose vials or even single-dose that did contain——

Mr. BURTON. If we have a supply on hand to take care of the needs of the American people and the children, why are we continuing to put mercury in their bodies? Why don't we stop now? Dr. Bernier.

Dr. BERNIER. I would like to try to answer that question, Mr. Chairman.

Mr. BURTON. Sure.

Dr. BERNIER. It is a good question, and it is one that we believe we would answer in the following way. We have set a goal to remove thimerosal from vaccines. We do not disagree with anyone who believes that this material should be taken out as rapidly as possible. We have set that goal. And I think we are pleased by the substantial progress that has been made and documented here today. Last year at this time a child could receive 187.5 micrograms of ethyl mercury from vaccines. Today that maximum is down to 75 micrograms. We have, since last summer, now reached a point where six of the seven vaccines are free of thimerosal as a preservative, and we believe the seventh one will be as soon as 6 to 9 months now, which is in early 2001.

Mr. BURTON. Seventy-five micrograms, 1.5 is considered safe.

Dr. BERNIER. I am not sure where you get that value, Mr. Chairman.

Mr. BURTON. For a 33-pound child, according to what we have found through our research, 1.5 micrograms is what is acceptable.

Dr. BERNIER. I need to emphasize that there is no data, there is no compelling evidence at this time of any harm that has come to any child from vaccines that contain thimerosal as a preservative.

Mr. BURTON. How do you account for that graph over there? Do you think that is a coincidence?

Dr. BERNIER. I would like to defer that to Dr. Bristol-Power. I think this is a question about autism and the increasing rates of autism, and she is best qualified to comment on that.

Mr. BURTON. Let me make one more comment. Of the 11 members on the Advisory Committee on Immunization Practices, of the 11 members, 6 of them have financial interests of one kind or another in the pharmaceutical companies that manufacture these vaccines. That doesn't look good to the public. Now, it may or may not be something that we should be concerned about, but it does concern a lot of people that we are keeping mercury that isn't necessary in vaccines when we have a supply that doesn't have to have those—that mercury in there. At the same time, the committee that is making the advisory panel that makes recommendations to CDC, over half of them have financial interests in the pharmaceutical companies. We checked for the past 10 years, and every one of the recommendations by the advisory panels has been accepted by FDA and CDC; so what they say is pretty much law. Now, how do you account for that?

Dr. BERNIER. I think there are several questions in your last statement. Let me tackle the issue about conflict of interest which I think you are raising.

I am not responsible primarily for the management of that committee or have any direct responsibilities. The only thing I can say to you is, as I understand it, there are laws and regulations about who can serve on committees, and CDC is currently, as I understand it, following those procedures and has gotten a vote of confidence about how they are doing on that. I am not qualified to comment about that. In our society it is possible under the law to have conflicts of interest, and there are procedures for dealing with those.

On the issue of whether or not we could move more quickly, we believe substantial progress has been made. We have set the goal, and we think that we have the right goal. We think that we have made substantial progress. If we were to move too precipitously, there would be consequences to pay. We know from the hepatitis B experience that occurred last summer that children fall through the cracks and that there is disease that is resulting as a consequence. So we don't want to move to this transition in a way that in some way jeopardizes the health of children, because we are confident that that will happen if we move too precipitously.

So we are on the right course. We have made tremendous progress, and we are going to get there in the foreseeable future. We should stay the course.

Mr. BURTON. Ms. Chenoweth, and could you yield to me for about 10 seconds?

Mrs. CHENOWETH-HAGE. Yes.

Mr. BURTON. Let me just say that 8,000 children are immunized today. You are phasing out thimerosal. You know there is a problem. You are not saying it, but you know there is a problem. You have a supply on hand that does not require having mercury in it, and yet you continue to use mercury, mercury-oriented vaccines. It makes no sense. You have a supply to do it, and the FDA is not stopping this immediately, I submit, because there is a financial interest by a lot of pharmaceutical companies that have a large supply of this mercury-oriented vaccine still in stock.

Mrs. CHENOWETH-HAGE. Thank you, Mr. Chairman, and I may ask you for a second and maybe a third round of questions. I have a lot of questions to ask these witnesses.

I do want to open up my questioning by making a statement that I have a staffer who is in the Navy Reserve right now, but he used to be active with the airborne divisions, and he was in for a test in one of the medical military hospitals, and upon taking his temperature, they broke a thermometer, and mercury splattered across his glasses and some got in his eye. Well, the first thing they did was cutoff his clothes. The second thing was call in OSHA to clean up the mercury. And then they worked on him to make sure his eyes were irrigated, and you guys, you witnesses, absolutely amaze me. I wonder where the disconnect is, for Pete's sake.

You listened to the testimony just as I did, and you are willing to, with a straight face, tell us that you are eventually going to phase this out after we know that a small baby's body is slammed with 62 times the amount of mercury that it is supposed to have, and OSHA reacts like they did in the case of this accident of this naval man. It doesn't make sense. No wonder people are losing faith in their government. And to have one of the witnesses tell us it is because mothers eat too much fish? Come on. We expect you to get real.

We heard devastating testimony in this hearing today, and we heard it last April. And this is the kind of response we get from our government agencies?

I am sorry.

When I was a little girl, my daddy talked to me about something about a duck test. I would ask each one of you to read this very excellent work by Sallie Bernard and Albert Enayati, who testified here today. My daddy used to say if it walks like a duck and talks like a duck and sounds like a duck, for Pete's sake it is a duck.

I recommend that you read this. Side by side, page after page of analysis of the symptoms of people who are affected with mercury poisoning compared to autism, this is the duck test, and you folks are trying to tell us that you can't take this off the market when 8,000 children are going to be injected tomorrow; 80 children may be coming down, beginning tomorrow, with autism? What if there was an E. coli scare? What if there was a problem with an automobile? The recall would be like that.

We are asking you to do more than analyze it. We are asking you to tell this body and the American people that it is more inconclusive. It passes the duck test, and we need you to respond. We need that to come off the market now because you think that this is—do you think that we are elevating the case today? Just wait until it gets in the courts. This case could dwarf the tobacco case. And we would expect you to do something now before that circus starts taking place. Denial is not proper right now.

I yield back the balance of my time, Mr. Chairman.

Mr. BURTON. Mr. Waxman.

Mr. WAXMAN. Dr. Bristol-Power, you are an expert on autism, someone well versed on the literature of autism. Can you tell us your position on the possible connection between vaccines and autism?

Ms. BRISTOL-POWER. Based on the evidence right now, we are looking at any evidence linking vaccines and autism, particularly the MMR vaccine and autism and additives in autism. Some very serious concerns have been raised both in recent literature reports and in evidence and testimony before this committee. So we are beginning a study right now to look very seriously at whether or not there is a link that should be—that can be substantiated in a large group of 1,000 patients with well-documented autism. We will be collecting behavioral measures and biological measures that will be tested in an independent laboratory that will reexamine the hypotheses that have been raised here. We are taking seriously the testimony of this committee and are reacting, we hope, with most haste to get answers to the questions that you have raised.

Mr. WAXMAN. I think that is worthwhile because we want to make sure that we have checked everything out and evaluate whether this hypothesis is accurate or not that there is some connection, but up to now haven't you and other scientists looked at the connection between vaccines and autism, and have you found evidence to connect the two? Or are the reports accurate that say that autism might occur very early on in fetal development and that the connection appears because the time of autism manifesting itself in the child is pretty close to the time that immunizations are given?

Ms. BRISTOL-POWER. There are a couple of aspects. Historically, the vast majority of children have symptoms of autism from birth, so for that group certainly the later onset associated with any vaccines would not be compatible.

We have a group of children that do regress that we know develop normally and lose speech and social interaction. At this point we don't have a satisfactory answer why they regress. But there are a variety of developmental disorders which are characterized by a period of normal development and regression. For example, there is a disorder called glutaricacidemia. It is a metabolic disorder. The children develop normally, and without treatment essentially it blows out their basal ganglia, and they become very disabled, and that is a metabolic cause.

There are genetic disorders. Rett syndrome, those children develop normally, and then only gradually develop autistic characteristics. We now know there is a genetic basis for that. We have to be careful in assuming that because the onset is later, it necessarily is associated with something that happened later.

Mr. WAXMAN. I appreciate that, but I want to ask another question of Dr. Bernier. On this issue of mercury, mercury is being taken out of vaccines, and I think that is a good thing because we should always err on the side of safety. The question that I would like to ask, and I am sure parents want to know, is this being done because there are known adverse related events or as a precautionary measure? CDC convened an expert panel to examine data that showed a possible weak link between thimerosal and certain developmental delays. The panel presented its findings to CDC's Advisory Committee on Immunization Practices and concluded that data were insufficient to show a causal connection between thimerosal and certain developmental delays. Is that true? Is that the position that CDC has taken?

Dr. BERNIER. That's correct, Mr. Waxman. At the present time CDC has no evidence of harm to any children from thimerosal in vaccines. We have constantly acted to look at the safety. Following the episode last summer, CDC did begin to look at the data in the Vaccine Safety Datalink, and one of the outcomes that we looked at was autism, and there was no suggestion of any association between thimerosal exposure and autism in the Vaccine Safety Datalink study.

Mr. WAXMAN. Dr. Egan, is the FDA removing thimerosal from vaccines in response to evidence of actual harm or as a precautionary measure?

Mr. EGAN. It is done as a precautionary measure and to reduce mercury exposure from all sources, vaccines included.

Mr. WAXMAN. I see my time has expired.

Mr. BURTON. You say that you are doing it as a precautionary measure. When did FDA and CDC first start being concerned about mercury in vaccines?

Mr. EGAN. I guess the major concern started somewhere around May 1999.

Mr. BURTON. May 1999. When you look back at the statement, and you were talking about a topical mercury a while ago, but in 1982, the FDA panel concluded that thimerosal is toxic, causes cell damage, can cause allergic reactions and is not effective in killing bacteria or halting their replication. If that was true for a topical mercury substance, why would you not be concerned about that if it was ingested?

Mr. EGAN. Those topicals refer to high concentrations.

Mr. BURTON. I understand, but we are talking about pretty high concentrations; are we not?

Mr. EGAN. I will have to look up and get back to you exactly what the concentrations were.

Mr. BURTON. I wish you would, because it doesn't say what the concentrations were. Like I said, we had testimony today from people that said that their children were getting 125 times, 75 times what EPA and others say is—and CDC says is a safe amount of mercury into their bodies. If in 1982 you knew there was a problem and you didn't know the amounts for a topical, why would you continue to allow vaccinations to be given to children by the millions when there was a concern? I mean, I just don't understand. You say in 1999 you became concerned about it, but in 1982 in the Federal Register you had an FDA panel that said, hey, this is a problem. They said it is toxic. It causes cell damage and can cause allergic reactions. This was a topical. Why would you allow it to be inside a vaccination?

Mr. EGAN. It was allowed because it is effective as a preservative for those vaccines, and the dose was markedly reduced relative to those topicals.

Mr. BURTON. But you knew mercury was toxic, and there had been an FDA panel that said it was a problem, yet nobody over there said, we ought to take a look at this as far as vaccinations are concerned?

Mr. EGAN. I don't know. I don't know what people said.

Mr. BURTON. When this panel reached its conclusions and put it in the Federal Register, did anybody say, hey, if it is bad for the

outside, why are we giving it to them on the inside? Or was maybe the pharmaceutical companies that made it as a preservative and it was in the vaccines saying that they had to keep it in there. Can you do some research and find out what happened during this timeframe? I can't imagine in 1982, 18 years ago, realizing that this was a real problem, continuing to keep it in vaccinations.

Mr. EGAN. It was kept in other materials at that time as a preservative, not as an active ingredient.

Mr. BURTON. When did they start taking it out of over-the-counter stuff?

Mr. EGAN. I will have to get back to you on all of those. I believe it is still in ophthalmics——

Mr. BURTON. Many of the over-the-counter——

Mr. EGAN [continuing]. As preservatives.

Mr. BURTON. Many of the over-the-counter drugs they have taken it out of at FDA request. In 1998, they said that it was no longer generally recognized as safe, and yet here we are 2 years later, and you are phasing it out. You are phasing it out.

This is the thing that Mr. Waxman and I may not agree, but I cannot understand, maybe you can explain, if there is any question about mercury in vaccine, if there is even a question, you are phasing it out because there is a question. You have a supply of all the vaccines that are necessary to immunize children of this country. You have that. You have them now. Why in the world are you continuing to immunize kids with something that is questionable? Give me an answer. I don't understand it.

Mr. EGAN. To date there is no—we have no evidence, convincing evidence, of harm from the thimerosal in vaccines.

Mr. BURTON. Doctor, I understand you have said that. The point is that you have a supply that you don't have to worry about, and you have a supply that you are phasing the mercury out of because there is concern. You don't agree that there is scientific evidence. If you are phasing it out, why in the world not use what you know to be safe so that the kids of this country can be safe?

Mr. WAXMAN. Mr. Chairman, I ask unanimous consent that you be given an additional minute, because I think you have asked a key question. Why not take it off now?

Dr. BERNIER. I think a couple of things need to be pointed out. First of all, we have concerns about reliance on a single manufacturer. There are issues about whether or not that single manufacturer could gear up rapidly enough to move from being a partial provider of our national need to being the exclusive provider for the entire country. We have concerns about wether or not they can really do what they say they can do. That is No. 1.

No. 2, we have concerns when we rely on a single manufacturer about problems that can occur in production, in meeting the requirements of the FDA. There have been episodes where there have been a fire in a plant. There have been episodes where there has been disruptions in the manufacture, and there have been shortages. So we have concerns that if we transition our vaccine supply too abruptly, we are taking a gamble. We are afraid we might lose and risk the health of children.

There is also an issue about public policy, and we believe that whenever possible we should try to promote a situation where we

have several manufacturers. In the long run that serves the interest of children best if we can have multiple producers of vaccines and not have to rely on a single one.

So, Mr. Chairman, I think we are exaggerating the disagreement here this afternoon. We agree that we do not need to have thimerosal in vaccines. If it doesn't need to be there, we should take it out. And we should take it out as rapidly as possible. We have agreed to that. The Public Health Service, the vaccine manufacturers, and the academies are all in agreement. We have two, in my career, historic documents which are joint statements by the American Academy of Family Physicians, the American Academy of Pediatrics, and the Public Health Service, which includes NIH, FDA, HRSA and CDC all signing one statement. That is not easy to accomplish, believe me. We have all said that this material should come out as soon as possible. We don't disagree.

There has been substantial progress made in just the last 12 months for hepatitis B. As Dr. Egan has said, there are two vaccines that are free. There is no more hepatitis B with thimerosal for pediatric use. Children can have an entire supply free of thimerosal. For HIB, there are four vaccines. Three always were free, and now the fourth one is going to be free this month. So now we can say the entire supply of HIB vaccine is going to be thimerosal free.

That leaves DTaP. There are four companies, one of which has already achieved thimerosal-free status. Three others are working on it. Two of them have told us publicly that they will have the supplements into Dr. Egan this summer, and we have gone on the record publicly stating this. We discussed this, during this last month. We put in writing that we anticipate that we are going to get there by early 2001. Some argued don't put the date in there. That will force us to be accountable in a way that we may regret, but people agree to do that because they agreed that it is a priority, and they saw the light at the end of the tunnel, and they were confident about it.

In summary, No. 1, we agree with you that thimersol should come out. No. 2, it is coming out rapidly. And the third point is we have to do it in a way that we feel will not jeopardize the health of children, and we have seen their health jeopardized in the case of hepatitis B. We don't want to jeopardize their health this way.

Some may think that is a gamble worth taking because there is not disease right now, but I can say this. When the three options were given at the ACIP meeting in June, the ACIP was not willing to take that gamble. The American Academy of Family Physicians would not take that gamble. NIH would not take that gamble. HRSA would not take that gamble. CDC would not take that gamble, and FDA would not. They all signed the joint statement.

Mr. BURTON. You have made your point.

Mrs. Chenoweth, would you yield to me for just a minute?

Mrs. CHENOWETH-HAGE. Yes, Mr. Chairman.

Mr. BURTON. The point is today you have a supply of vaccine that could be used to vaccinate every child in America that does not contain mercury.

Now, the 8,000 children that are going to be vaccinated today, tomorrow and the next day are going to have mercury in the vaccine.

Now, if you are wrong, if you are wrong, those kids could become autistic as a result of that. Like my grandson, they could become autistic and be ruined for life. And no matter how much hyperbole you use, if you have a safe supply of vaccine over here, why are you using the other?

You said we only want to have one supplier. Well, you know, get the others up to speed as quickly as possible. You have a supply now. You have people supplying it now, and this hypothesis begs the question if you don't have a supply, then you still have a supply of the mercury-oriented vaccine as a backup if you have to use it, but why not use the safe stuff right now?

Mrs. Chenoweth.

Mrs. CHENOWETH-HAGE. Thank you, Mr. Chairman.

You know, I still go back to the fact—I still want to talk about the duck test. Mr. Egan, I will address this to you. You know, it was shown in the last panel that autistic symptoms emerge after vaccination. It was shown that vaccines contain toxic doses of mercury. It was shown that autism and mercury poisoning, the physiological comparison is striking. There is altered neurotransmitter activity, abnormal brain neuronal organization, immune system disturbance, EEG abnormalities. It goes on and on and on, the comparisons. That is why I say, I back up what the chairman and the ranking member are all asking you, that we cannot wait until 2001 to have this pulled off.

You know, if a jury were to look at this, the circumstantial evidence would be overwhelming. Let's do something before we see it in the courts.

Mr. Egan, you stated it is very important to remember that safety margins are incorporated in all acceptable mercury exposure limits, right? Could you tell me what those exposure limits are for a 1-month-old, a 3-month-old, a 6-month-old, a 9-month-old and a 1-year-old?

Mr. EGAN. Various government agencies have arrived at different guidelines for mercury exposure.

Mrs. CHENOWETH-HAGE. I am asking you, representing your agency, Doctor. Can you tell me based on your testimony what those exposure limits are that you referred to for a 1-month, 3-month, 9-month, 6-month and 1-year-old?

Mr. EGAN. Well, last summer when this was discussed within the Public Health Service, all of the agencies of the Public Health Service concurred on the ATSDR recommendation, guidelines, which is 0.3 micrograms of mercury per kilogram body weight per day.

Mrs. CHENOWETH-HAGE. Well, would you provide that in detail to the committee in a report?

Mr. EGAN. Yes, I will, ma'am.

Mrs. CHENOWETH-HAGE. How were those exposure limits arrived at? Could you also provide that in the report? I'd also like to know what the demographics of the population was that were tested. And could you forward that data to support your claim that you made in your testimony?

Mr. EGAN. Yes, ma'am.

Mrs. CHENOWETH-HAGE. OK. And all the background data. What studies, Dr. Egan, were submitted to the FDA to prove that thimerosal was safe?

Mr. EGAN. When—OK. When thimerosal was, you know, was first used in vaccines in the—I guess starting around the 1930's when vaccines were not regulated by FDA but by other organizations, there were some toxicology studies, you know, acute toxicology studies in animals and very, very limited amount of data in people that there was no acute toxic effect.

Mrs. CHENOWETH-HAGE. And these were studies that were done in 1930, that were submitted to——

Mr. EGAN. They were also done in, I guess, the late 1920's and reported by researchers at Eli Lilly in 1930.

Mrs. CHENOWETH-HAGE. OK. With regards to the induction of HIB vaccine and hepatitis B vaccine, could you advise the committee on what studies were done with regards to these new vaccines that would prove that thimerosal was safe? These were done, introduced, in the eighties and nineties.

Mr. EGAN. I believe it was in 1990. There was a long history of the use, safe use of thimerosal, you know, in vaccines since they were—since it was first introduced. And at that time, there was no data to suggest that the added mercury from the introduction of those new vaccines would be harmful.

Mr. BURTON. The gentlelady's time has expired. I'm sorry. Mr. Waxman.

Mrs. CHENOWETH-HAGE. I do have other questions that I would like to submit in writing.

Mr. BURTON. Yes. We'll give you some questions we'd like for you to answer if you wouldn't mind after the hearing is over.

Mr. EGAN. Yes, sir.

Mr. BURTON. Mr. Waxman.

Mr. WAXMAN. As I understand your testimony, you're not sure there's a problem from thimerosal, but you're taking the prudent course of getting it out of the vaccines. Dr. Bernier, as I understand your statement before in answer to the question why we're not taking it out of all vaccines immediately, you worry about the supply of vaccines that will be available, although the chairman made the statement that we have enough supply now to immunize every child in the country with vaccines without the thimerosal. Is that an accurate statement?

Dr. BERNIER. I would have to refer that to the manufacturer. We have been told publicly that yes, they do have an adequate supply of vaccine, but we're concerned—I wouldn't want to—I guess my first answer was perhaps a little too long; I didn't get to the second part. We have concerns about the supply. But the second thing is we have concerns about the harm that might come from an overly abrupt change. To answer the question it's a harm we believe is more real than the harm that we think would be associated with thimerosal.

Mr. WAXMAN. What is that harm?

Dr. BERNIER. We know the harm from pertussis, we know the harm from hepatitis B. We know the harm from Haemophilus influenza B. We can, for example, just look at USA Today. Two days ago, there was this story of a mother who made a decision not to immunize her child against Haemophilus influenza B because it was a new vaccine. It sounded scary to her. And when asked by her pediatrician, should I take this Haemophilus B influenza vac-

cine, or do you want this Haemophilus B vaccine for your child, the mother made a decision "no." The child is now deaf, the child has mental difficulties that requires Ritalin every day, and obviously this mother has deep regret about that. We believe——

Mr. WAXMAN. I'm going to have to interrupt you because it sounds like you've answered the question and you're going on, but I only have a limited time. That would take up all my time.

Dr. BERNIER. I understand. I have that tendency.

Mr. WAXMAN. I understand. I have the same tendency. But just so I can frame the issue: Nobody wants to have thimerosal, because it has mercury, in the vaccines, whether we think it does harm or whether we're sure it does harm or whether we just think maybe it does and let's be safe about it, so we ought to get it out of the vaccines as quickly as possible. But what I hear you saying is that if we move too precipitously, we might not have a full supply of all the immunizations available of all these illnesses that we know can be prevented, and we know we're going to get all these diseases back and we don't know, if we have the use of the vaccines that still have thimerosal in them, that there's ever going to be any harm for sure about the mercury. Is that your position?

Dr. BERNIER. That's right. We would be trading a harm that we know for one we don't know. We know the harm will come if children are not immunized, and we know that it happened just in the last 12 months. So we're facing a harm we know versus a theoretical harm—which at this time is still only theoretical from the best evidence that we have.

Mr. WAXMAN. I think that's a good on-point statement, answer to my question. I think all of us would like to have this thimerosal out as quickly as possible. But on the other hand, I must agree with you. I don't want the supply upset, because I believe in immunizations, and I worry that people are going to be frightened because of the theory that has not yet been established of a connection to autism, that they might not get their kids vaccinated. We know for sure when that happens, we're going to get a whole long list of terrible diseases that I can feel as passionate about as anybody else.

But the chairman showed a graph that showed an increase in autism. The chart showed a steep rise in the number of cases of autism. Ms. Bristol-Power, the chairman says there's a dramatic increase in autism, but some experts have told us that this could be due to better detection. I wonder if you have a view about that and if there really is an epidemic, a sudden increase, because Dr. Egan seemed to agree there was an epidemic, but you're the expert on whether there was.

Mr. EGAN. I'm sorry, but what I meant was apparently there's a very large number of cases.

Mr. WAXMAN. Being detected.

So my question, Dr. Bristol-Power: Are there more cases being detected because there's a dramatic increase in cases or better detection mechanism?

Ms. BRISTOL-POWER. We don't have the information to answer that question. We know that part of the increase is better diagnosis, more public awareness, and better services, frankly, so more children are being presented at service locations.

In the United States right at the moment, we don't have adequate studies that would let us know about whether there is an increase in prevalence. We do know worldwide epidemiological studies show that—any studies done since 1987—there's about a double the rate of previous results from previous studies. But again it's not clear how much of that increase is from better diagnosis and greater public awareness, where these children have been diagnosed in other categories before.

Mr. WAXMAN. Do you agree with that position, or do you agree with that position of Dr. Bristol-Power?

Mr. EGAN. Dr. Bristol-Power is the expert on autism, not I.

Mr. WAXMAN. So you would have no disagreement with her.

Mr. EGAN. I would have absolutely no reason to disagree with her.

Mr. WAXMAN. Thank you, Mr. Chairman.

Mr. BURTON. I think we're reaching the end of the hearing. I do have a couple final questions I'd like to ask here. How long will children continue to receive mercury vaccines if there's not a recall? How many years will they continue to receive those?

You know, you mentioned the DTaP vaccination, but you have not mentioned the DPT vaccination which is still in use, which does use thimerosal. And the DPT shot, there's a lot of concern about that vaccination. That's why they went to the DTaP shot. Yet the FDA has not recalled the DTP vaccination and it's still being used. So how long will mercury vaccines containing mercury be used if there's no recall?

Mr. EGAN. For the routine immunization schedule that's recommended by ACIP and AIP, the recommendation is for DTaP.

Mr. BURTON. I know, but they still use the DTP shot. We had people from CDC and Health and Human Services testify that they still are using it. It's still being used.

Mr. EGAN. Again I'll have to get back to you on some of that. There have been some lots of DTP, primarily I believe Tetramune which is the DTP-HIB combination vaccine, but I believe that the few lots of that that have been released are for sale overseas.

Mr. BURTON. Well, in any event——

Mr. EGAN. It's not being used the United States.

Mr. BURTON. You're saying you don't believe there's use in this country?

Mr. EGAN. I'll have to check on it.

Mr. BURTON. But in any event, the question I'm asking is mercury containing vaccines, how long will they be in use if there's not a recall?

Mr. EGAN. Well, the majority of the vaccines, the Haemophilus vaccine and the hepatitis B vaccines are already thimerosal free. This has been accomplished since last summer.

Mr. BURTON. My question is—those vaccines that contain mercury, even though you're phasing it out. How long will they be used if you do not recall them?

Mr. EGAN. The—in their public statement, Pasteur and Wyeth, who are the other major manufacturers, two other major manufacturers of DTaP, said that they will be submitting supplements to their license for thimerosal-reduced vaccines either the end of July or the beginning of August.

Mr. BURTON. But the existing supply will be used until it runs out, and you don't know how long that would be?

Mr. EGAN. No. Perhaps my colleague from CDC can, you know, comment on the——

Mr. BURTON. I'd just like to know, because even though you're transferring over to vaccines containing no mercury, if there's a supply out there, if it's not recalled they're going to continue to be given to children. And that's a concern. Yes, sir.

Dr. BERNIER. May I try to answer that question? I don't think I can be definitive about it, because you're right that there is a pipeline, there is a supply, and it doesn't disappear overnight. But I think the handwriting is on the wall for vaccines that contain thimerosal in the United States, Mr. Chairman, I think we all agree with that. And as soon as the supply is considered adequate and secure, I believe you will find committees and others beginning to recommend many preferences for these vaccines. How quickly will all of this take place? The recommendation—it will depend on how the recommendation is stated. If you'll go back to the July 1999 statement of—joint statement—it said that this goal was to be achieved as rapidly as possible. And we're now publicly on record as predicting that it will occur early next year. But——

Mr. BURTON. OK. This is my last question, and if Mr. Waxman has any questions he can ask them as well. The FDA seems to be saying that vaccines that were licensed from 1970 to the year 2000 were not required to do testing on thimerosal. Is that correct? None of those—I mean, because thimerosal was used from the 1930's on, they really haven't done any testing since the seventies on whether or not there's a side effect from that; is that correct?

Mr. EGAN. I'm not sure if any—what test was or wasn't done on those specific vaccines, but I will get back to the committee on that.

Mr. BURTON. We'd like to know if there was any testing done on thimerosal. So anything you can give us on that we would appreciate.

Henry, do you have any last questions? If not, I want to thank you very much for being here. We'll submit some more questions to you for the record.

We appreciate you being here. We hope that you'll carry back to the agencies which you represent, the concerns of these parents that were here today regarding vaccines. We're for vaccinations, Henry and I agree on that, but we want to make sure they're completely tested and they're safe. Thanks a lot.

[Whereupon, at 5 p.m., the committee was adjourned.]

[Additional information submitted for the hearing record follows:]

July 26th, 2000

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Congressman Dan Burton, Chairman
Attention: Beth Clay. Esq.
Committee on Government Reform
2157 Rayburn House Office Building
Washington DC 20515

Dear Congressman Burton,

In my letter to you of July 18th, I submitted my case history to you as evidence of the damaging effects mercury has to the human body. I am sending this letter again today with another copy of my case history to ensure that my letter is made a part of the public comment on the Committee's July 18th hearing on Mercury in Medicine, and is entered into the Congressional Record.

My letter of July 18th was written to inform you of my horrible experience with Mercury poisoning in hopes it will influence you to take legislative action to eliminate the use of Mercury in Dentistry, as well as in pharmaceuticals and household goods. I have enclosed my case history as anecdotal evidence that Mercury is harmful to the heath of some people.

What saddens me most is that back in December of 1990, after CBS' 60 Minutes aired a segment on "Mercury, Poison in your mouth?" my mother contacted me to suggest my Multiple Sclerosis came from Mercury. Because, at the time, I had no fillings in my mouth, and then as now, the information about the dangers of Mercury remain unreported and out of the mainstream, I dismissed the possibility outright.

Had I but known how insidious and nefarious the metal can be to a human body, I could have sought help sooner (or chosen never to have used it in the first place), thereby saving myself years of pain and suffering. I find it morally reprehensible that a substance never having been classified, nor approved by the FDA is used freely in Dentistry and that the American Dental Association is allowed to suppress information about its harmful, if not deadly effects on some people.

Given the restrictions already placed on its use in Sweden, Austria, Germany and Australia, and in light of the class action lawsuit in Canada, I am amazed the United States is not also taking steps to control, if not eliminate, the use of Mercury. As an example of how sick Mercury can make a person, it is my sincerest wish my story will help others avoid the same fate.

Sincerely,

Amy Pasche

enclosure

A MIRACULOUS RECOVERY – a case history of mercury poisoning.

Between the ages of four and six, I had six mercury amalgams placed in my mouth to fill cavities in my baby teeth. Just after placement of the first amalgams, I developed severe allergies to milk, terrible gas pains in my chest, persistent upper respiratory infections, and chronic eczema. These troubles continued until the age of sixteen, when I began to experience severe constipation and amenhorrea. At eighteen, I developed bleeding hemorrhoids, and by twenty, I had acid reflux, and occasions of projectile vomiting.

At 23, I experienced two bouts of optic neuritis, and subsequent testing confirmed a diagnosis of Multiple Sclerosis (MS). At 25, I began to have tonic seizures - a burning, freezing sensation spread down my left side to my waist, my legs grew numb, and I became paralyzed from the waist down. The seizures, lasting one to two minutes, occurred anywhere from 5 to 15 times a day, and within eight months, had disappeared. For the next five years thereafter, I had the constant sensation my rectum was falling through my pelvic floor, and my problems with constipation and hemorrhoids worsened.

At 30, I started having urgency incontinence and terrible muscle spasms throughout my lower back and pelvic floor, which pinched surrounding nerves, causing terrible pain. My digestive problems worsened, and I began to lose weight. My gastroenterologist diagnosed me with Irritable Bowel Syndrome. Finally, at 31, in constant pain and with swollen abdomen, I started to have severe diarrhea, fever, and rectal bleeding. I was given a fissurectomy, but my condition worsened. Hospitalized, tests revealed I had bleeding ulcers throughout my lower intestines, fistulas forming abscesses in my abdominal cavity, and severe anemia. I was diagnosed with Crohn's Disease, and treated with steroids and antibiotics. Standing 5'5" tall, in just one year, my weight had dropped from 125 to 95 pounds.

In November of 1997, a month after starting treatment for Crohn's, I developed shingles. After the sores cleared, I suffered from post-herpetic neuralgia for another two years. Four months into treatment, I had a complete rectal prolapse – eight inches of my lower intestines fell from my anus and dangled inside out between my legs. Doctors surgically removed twelve inches of diseased colon and explored my abdominal cavity for cancer, but found nothing. While in the hospital, I suffered a grand mal seizure, which doctors were unable to explain.

After surgery, my health continued to deteriorate. My pain intensified, as constant muscle spasms pinched nerves, and neuralgia wracked my body. I had pains in my chest, back, and abdomen, and I became jaundiced. I suffered from chronic insomnia, short-term memory loss, and again, severe constipation. I developed terrible food allergies to dairy, wheat, gluten, eggs, soy, preservatives, spices, sugar, and caffeine, which made the pain I felt after eating, and during digestion, excruciating. I lost even more weight. I also became allergic to my medications and was forced to stop taking them.

Desperate, I turned to alternative therapies, and found an acupuncturist and Doctor of Oriental Medicine (OMD) in Los Angeles, who has developed a sensitive diagnostic technique to detect hidden pathogens causing illness. I began flying back and forth to Los Angeles from San Francisco for treatment and, for the first time in five years, began to

improve. In October of 1998, after two months on Chinese herbs, I felt better overall, but I started to experience numbness in my legs and difficulty walking.

A week after the numbness started, I began having violent seizures involving my entire body. I lost all muscle control and thrashed wildly about the floor. My jaws ground back and forth, and I yawned repeatedly. During the third seizure, my jaw dislocated and I was rushed to the emergency room to have it reset. After two days, the seizures were constant and I was hospitalized in an attempt to control them; none of the medications worked. The neurologists had never seen anything like it and could offer no remedy. After three days under heavy sedation, my insurance company denied me further benefits, and I was discharged into the care of a psychiatrist, who tried an experimental antipsychotic drug on me not yet approved by the FDA. The drug's side effects exacerbated my existing symptoms.

I begged that my family return me to the OMD in Los Angeles, and I moved into a hotel near his office where, no longer in any condition to travel or take care of myself, I lived for eight months, the first three under the constant care of a family member. Soon after the move, I became paralyzed from the neck down, retaining only partial use of my right arm. I lost control of my facial features, tongue, and mouth so that speech was nearly impossible. Sometimes, I was unable to even open my eyes or to speak and could move only the pinky on my right hand to indicate I had not lost consciousness. Day and night, I kept a piece of wood between my teeth to prevent my jaw from dislocating again. The pain from neuralgia was exquisite. I felt as if my skin had been burned away, and I were being probed with an electric cattle prod.

After clearing multiple layers of bacterial, viral and fungal infections, high levels of mercury were detected in my brain, spinal cord, and intestinal tract, causing auto-immune reactions. The source of mercury poisoning had come from the dental amalgams placed in my baby teeth, thirty-two years before. Although my last filling had fallen out by the age of eight, the mercury remained, having entered my system through my lungs, sinuses, and intestinal tract, eventually permeating my entire body. The MS and Crohn's Disease were caused by my immune system attempting to eliminate both the mercury and the multiple bacterial, viral, and fungal infections.

Blood tests and hair analysis by a Western M.D., specializing in heavy metal poisoning, confirmed I had not only accumulated high levels of mercury from my tooth fillings, but also nickel, another heavy metal used in dental amalgams. Because his treatment for clearing mercury, DMPS IV, increased the risk of seizure, he advised me to continue using Chinese herbs.

As I began to clear mercury, I developed even more symptoms. Mercury activated the Herpes Zoster virus, causing my optic neuritis to flare again, and I developed painful hearing sensitivities and ringing in my ears. I became extremely sensitive to odors of any kind, the slightest smell making it difficult for me to breathe, and provoking a seizure. At other times, in episodes lasting between ten and twenty seconds, my diaphragm froze. I could neither inhale nor exhale, although I consciously directed myself to. Mercury in my lungs was blocking the nerve impulse transmissions between my brain and diaphragm. Two weeks after a modification to my herbal prescription, the difficulties with my diaphragm

disappeared, and gradually, as I cleared more mercury, my problems with vision, hearing, and smell were also resolved.

After two months of taking herbal prescriptions to clear mercury, the paralysis began to recede from my upper torso and I could use my arms to lift myself up out of my wheelchair. I regained some feeling in my legs and could drag myself across a room, or help myself in and out of bed. The constant movements I was having in my limbs, and loss of control of my tongue and facial muscles were symptoms of Tardive Dyskinesia, a condition of the central nervous system found in individuals having taken high dosages of antipyschotic drugs over long periods of time. These drugs chelate manganese; however, in my case, mercury had interfered with the function of both molybdenum and magnesium in my brain. Magnesium regulates neuromuscular contractions and has important anti-seizure effects on the body. I began taking supplements of both, while continuing with herbs to clear mercury, and soon the symptoms of Tardive Dyskinesia disappeared completely, my nerve pain improved, and my seizures became less violent.

The seizures also changed character. Instead of grand sweeping movements, I became either rigid, or twitched incessantly, as my body shook with tremors. My joints swelled and became stiff, throbbing with arthritic pain and my hands and feet curled up into claws. The painful muscle spasms in my back, legs, and pelvic floor returned. Mercury was found blocking both calcium channels and hormone receptors, and mercury antibodies had triggered an autoimmune attack on joint tissue.

Finally, after four months of clearing mercury, the neurological issues began to abate. The paralysis in my hips and legs slowly receded, and after five months, I could walk with a cane, and soon after, with no assistance at all. My seizures and tremors stopped, the numbness and nerve pain diminished, and my joint pain relented. By May of 1999, the neurological issues had cleared, but instead, I began another exacerbation of Crohn's Disease. The debilitating diarrhea with fever returned, as I had 40 to 50 attacks a day, and abdominal cramping left me doubled over in pain. Mercury related microfistulas were found along my entire digestive tract, from my esophagus to my rectum, once again causing pockets of infection in my abdominal cavity.

Though still terribly weak, I moved home to San Francisco in late June of 1999, and again traveled to Los Angeles to continue treatment. Gradually, as I improved, my food allergies abated and my weight came up to 99 pounds. Because the fistulas were slow to heal, in September and October of 1999, under the supervision of my gastroenterologist, I underwent three infusions of Remicaide, a new Crohn's medication that specifically targets treatment resistant fistulas. The results were positive.

Today, after twenty months of clearing mercury, my intestinal issues are mild, my neurological difficulties, non-existent, my food allergies, gone (although, I continue to avoid all dairy), and, at 115 pounds, my weight has returned to normal. I take a yoga class every other day, and thirty-minute walks, three times a week. At 34, I am feeling better than I have in fifteen years. Although I am still clearing residues of mercury, and continue my trips to Los Angeles for treatment, I anticipate once I am completely free of mercury and its related antibodies, I will enjoy a full and permanent recovery.

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July 13, 2000

Dental amalgam ("silver") fillings contribute more mercury to the body burden in humans than all other sources (dietary, air, water, vaccines, etc.) combined. These fillings contain 50% mercury - which is more neurotoxic than lead, cadmium, or even arsenic.

To put this in perspective, the amount of mercury contained in one average size filling exceeds the U.S. E.P.A. standard for human exposure for over 100 years. Put in other terms - if the mercury from one average size filling were dispersed into a 10 acre lake, an advisory would have to be posted prohibiting the consumption of any fish pulled from that water because it would be contaminated with unsafe levels of mercury.

Mercury vapor escapes from dental amalgam fillings and is rapidly absorbed into the body. It accumulates in all body tissues and has been shown to cause pathophysiology. Scores of studies have verified this. Furthermore in the case of pregnant women with amalgam fillings the mercury readily passes from her bloodstream through the placental barrier and accumulates to even higher levels in the developing fetus' organs than it does in the mother's. Mercury from dental amalgam has also been shown to concentrate in the mother's milk, providing not only a prenatal, but perinatal and postnatal exposure for the developing child, whose immune system and central nervous system are exquisitely vulnerable to this poison.

Scrap amalgam mercury, that unused portion of the mixed filling material left over after the filling is placed into a tooth, must by law be handled as a toxic waste disposal hazard. That is to say, I cannot throw it in the trash, bury it in the ground or incinerate it. It must be stored in an air-tight vessel until properly disposed of. How in the world can we justify storing this same material in people's mouths and proclaim it as safe? And without even securing their informed consent?

Governments of other countries (Canada, Germany, Sweden, France, Norway, and the United Kingdom) have already seen the folly of such a practice and have placed restrictions and/or issued advisories against the use of mercury fillings in dentistry - particularly in young children and in pregnant women.

In addition to the direct mercury exposure to humans from dental fillings, there exists a secondary route of exposures from dental offices. Published research shows that between 14% and 27% of the mercury found in municipal waste waters originates from dental offices. Mercury in this form ultimately finds its way into our rivers, lakes, bays and oceans where it undergoes a bioconversion by bacteria into methyl mercury - the form commonly found in fish and shellfish. In this form when eaten, 90-100% of the mercury is absorbed. This is the form of mercury which caused the tragedy in Japan's Minimata Bay in the 1970's when hundreds of people were poisoned and died from eating mercury laded fish.

In conclusion: there is no scientific debate over the following facts regarding mercury from dental fillings:

1 - Mercury is more toxic than lead, cadmium or arsenic

2 - Mercury escapes from dental amalgam fillings primarily as a vapor

3 - 74-100% of inhaled mercury vapor is readily absorbed into the human body
4 - Mercury from dental fillings accumulate in the body to harmful levels which cause pathophysiology
5 - Dentistry is the only health profession which has refused to abandoned the use of mercury on patients

I have been practicing dentistry for 27 years. For the first 8 years I placed amalgam fillings, believing that I was providing a good service for my patients, just as most dentists still do today. I truly believed what I had been taught in dental school - that the mercury was "locked in" the amalgam and could not escape into the patient's body. Then some 19 years ago I discovered the scientific truth of the matter - that mercury vapor is constantly released from dental amalgam fillings and is absorbed into patients bodies. At that time we didn't know how much was absorbed or whether that amount was enough to cause any harmful effects. However as a member of the health profession I felt obliged to err on the side of caution and abandoned the use of amalgam until its safety could be scientifically proven.

Today, 19 years later I know that such proof is non existent. It's time we in dentistry become proactive in face of the science surrounding this issue. I hope Congress will do the same if necessary to give organized dentistry a nudge in the right direction.

Richard D. Fischer, D.D.S., F.A.G.D.
Past President, International Academy of
Oral Medicine and Toxicology

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- Germany -

Congressman Dan Burton
Attn: ..th Clay
Committee on Government Reform
2157 Rayburn WOB
Washington, DC 20515
USA

27/7/00

Public comment on the Committeee's july 18th hearing on Mercury in Medicine

Dear Mr. Burton,

I (46 years) am suffering of a mercury-intoxication because of amalgam. (see the enclosed doctor's attests) Since almost 5 years I am seriously disabled (60%), unable to work and get therefore an invalid-pension. Every day, every minute is like hell – pain, pain, pain in my body, in my soul. Medical: toxic encephalopathy grade IIb with diplopy, nystagmus, vertigo, disturbance of equilibrium, sickness, disturbance of concentration, mind and sleep. And more: an injury of the heart, gut and immun-system. My life is destroyed by amalgam, a friend of mine even died.

Make sure, that this never happens again in the world! Fight for the human rights, fight for those who are to weak!

God bless you!

Yours sincerely

Gunda Hoeke

Gunda Hoeke
- Arztin -

10961 Berlin
Blücherplatz 2
Tel. 030 - 252 11 13

24.Mai 1999

Ärztliches Attest

Betreff: Nowack, Regina, *24.9.53,
wohnhaft: Nachodstr.24, 10779 Berlin

Diagnosen: Strabismus convergens alternans, Abducensparese bds., Zentral-vestibuläre Störung, chron.Müdigkeitssyndrom, Quecksilberallergie, Quecksilberintoxikation; chron.Vertigo,

Sehr geehrte Damen und Herren,

obige Patientin befindet sich seit 22.2.96 in meiner ärztlichen Behandlung.
Sie stellte sich wegen multipler Beschwerden wie Schwindel, Benommenheit, Sehstörungen inform von Doppelbildern, Migräne, chron.Müdigkeit, Gedächtnis-und Konzentrationsstörungen, Schwächezuständen, Herzrhythmusstörungen, abdominellen Beschwerden sowie Gelenkbeschwerden, Parästhesien und Wirbelsäulenbeschwerden vor. Nachgewiesen ist ein Strabismus convergens alternans und eine Abducensparese, die fast konstant zu Doppelbilderschen führen, sowie eine zentral-vestibuläre Störung, ebenso eine Quecksilberallergie und Quecksilberintoxikation. Zur Klärung der Ursache wurde eine umfassende Diagnostik gemacht. Sämtliche Untersuchungen waren unauffällig, übrig blieb nur der Verdacht auf Schadstoffbelastung. Mittlerweile (s.o.) wurde eine Quecksilberintoxikation nachgewiesen.
Unter der Behandlung, u.a. einer Entgiftungstherapie, besserten sich einzelne Symptome und das Allgemeinbefinden. Die Hauptsymptomatik wie Sehstörungen, Gleichgewichtsstörungen und Schwindel blieben aber unverändert. Bei jeder Entgiftung lassen sich erhöhte, z.T. hohe Ausscheidungswerte von Quecksilber nachweisen. Bis zu deren Verschwinden oder dem Verschwinden der Symptome muß diese Therapie unbedingt fortgesetzt werden.

Mit freundlichen Grüßen

Gunda Hoeke
Ärztin
Blücherplatz 2, 10961 Berlin
72 80723 Telefon
252 11 13

(Gunda Hoeke)

Ärzte für [illegible]

EMG, EMG, AEP, VEP, SEP
Dopplersonographie
(Extra-transcraniell)

10627 Berlin
Telefon 324 10 59
Telefax 323 99 82
14.04.99

Ärztliches Attest

Frau Regina Nowack, geb. 24.09.1953,

10779 Berlin, Nachodstr. 24,

ist in unserer ärztlichen Behandlung.

Diagnose:

Schwermetallintoxikation

Vestibularisausfall

bds. Abducensparese

hirnorganisches Psychosyndrom

Frau Nowak leidet seit 1995 (damals Amalgamentfernung) unter einer erhöhten Müdigkeit, unter Konzentrationsstörungen, unter Gedächtnisstörungen, auch unter Kopfschmerzen, unter Sehstörungen, Schwindel und Gleichgewichtsstörungen.

Fax: 844 712 72

Ärztliche Bescheinigung zur Vorlage bei der Krankenkasse

Hiermit bescheinige ich, daß Frau Regina Nowack, geb. 24.09.1953 im Jahre 1997 wegen der Folgen einer Quecksilberintoxikation mit zentral-vestibulären Störungen, Sehstörungen, Gleichgewichtstörungen, Herzrhythmusstörungen, Chronischer Müdigkeit, Gedächtnis- und Konzentrationsschwäche, chronischen Arthralgien und Cephalgien in meiner regelmäßigen ärztlichen Betreuung war.
Die Krankheitssymptome reduzierten sich unter der Einnahme von Entgiftungstherapeutika.

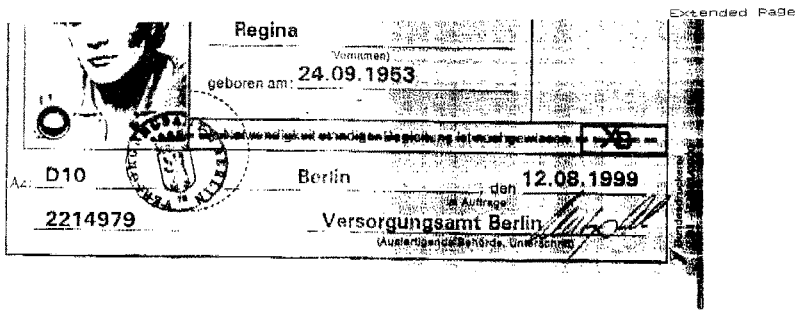
Dr. med. Peter Hauber
Praktischer Arzt
Florowmeße 1
[illegible] Steglitz

Berlin, den 8. März 1999

Dr. med. Peter Hauber



für Nowack
Regina


Extended Page
Regina
(Vornamen)
geboren am: 24.09.1953
X
Az: D10
Berlin
den 12.08.1999
2214979
Versorgungsamt Berlin

Faxabsender: +49 2324 72551 WEINERT 28/07/00 23:04 S.: 1

Initiativgruppe Zahn und Gesundheit
Hattingen
Gemeinnütziger Verein

Gesine Weinert

D-45549 Sprockhövel, 28th July, 2000
Finkenweg 10
Tel. no. 0049 2324 72551

Congressman Dan Burton
Attn.: Beth Clay
Committee on Government Reform
2157 Rayburn HOB

Washington, DC 20515

Ref.: Health hazards of dental amalgam fillings

Dear Sir,
I send you this letter as part of the public comment on the committee's July 18th hearing on Mercury in Medicine which is to be entered into the Congressional Record. I wish to inform you to which extent I suffered for more than 25 years by 8 amalgam tooth fillings.

My health problems started 30 years ago first with

- headaches and migraine, often 3-times per week,
- troubled sleep caused by sudden awakening, heavy pulpitations of the heart and ear thumping, so that I had in general only 2 4 hours of sleep,
- hay fever, allergies against different kinds of pollen and food, 2 desensitizations without success,
- rucking visual disorders and nystagmus which made it impossible to endure even a short drive by car,
- for 14 years tinnitus left side,
- heavy lumbar pain with disc prolaps, twice with hospitalization,
- hypertension,
- thyroid nodule with operation.

My disease comprised finally the following symptoms:

- a steady feeble condition with strong nervousness, heart-attacks, cardiac arrhythmias, heart racing,
- circulatory disorders, collapses, vertigo, drowsiness,
- susceptibility to infection, irritable cough,
- concentration difficulties, thought disorders,
- difficulties to speak or to control the hand when writing,
- epileptic attack, two attacks of delusion,
- frequent cramps in the legs, in the head and neck muscles,
- sleep apnoea syndrome, intestinal fungus candida.

Because of this diseased state I tried for more than 15 years to find medical help. I consulted about 35 doctors and spent altogether 16 weeks at various hospitals without getting the right diagnosis: amalgam intoxication. Only after removal of my 8 amalgam fillings and a gradual detoxification of the mercury deposits in my body I recovered little by little.

Since 5 years I have now been working in a patients' association to warn other people against amalgam tooth fillings.

Yours truly,

G. Weinert

July 17, 2000

To Committee Chairman Dan Burton

Regarding Committee on Government Reform of the U.S. House of Representatives hearing on "Mercury in Medicine."

It is Sunday morning and I am writing this quickly so I can fax it to you in time for the hearing on 7/18/00.

I married a wonderful man in 1990 and we experienced 4 years of happiness until March, 1994 when Dirk began to experience symptoms such as:

- glitches in his handwriting
- both short term and long term memory loss
- physical impairment of his right side
- cognitive impairment

His physician suspected a stroke and scheduled an MRI. The physician said he found nothing wrong. Two years later, my husband's symptoms had worsened to the point, he stopped driving. He could no longer write and he needed help with reading. He became withdrawn and we stopped going to social functions. In September, 1996 a Santa Fe physician tested my husband for heavy metal intoxication and the results showed extremely high levels of mercury which is a neural toxin. Mainstream medicine does not test for heavy metals. The physician who did, practiced alternative medicine (chelation therapy) and routinely tested all his patients for heavy metals.

We have spent the past 4 years trying to remove the mercury from my husband's body. Because there was no specific protocol for mercury detoxication, we got some of the mercury out of his body, but found out that more remained which showed up months later. In the meantime, the brain atrophy continued.

Today, my husband requires 24 hour care. He still has some mercury in his body. He has just about given up spiritually, and emotionally. He is Dutch and now his language skills have deteriorated. He speaks little English and mostly poorly pronounced Dutch. I speak no Dutch, so our conversations are limited. He needs assistance climbing stairs or walking on rough surfaces. He cries a lot these days because he is so discouraged and afraid. He needs help with eating. He cannot at this point relearn lost skills of daily living.

It is too late for us but hopefully your committee can begin to deal with this monster. Too many people are diagnosed with Alzheimers, when perhaps there is heavy metal intoxication such as mercury. I hope to see the following:

- No more amalgams which contain 50% mercury. If we were told years ago to avoid eating swordfish because of high levels of mercury found in this fish, then why are we putting such a poison in our mouths.

- Mainstream testing for heavy metals whenever, there is any evidence of unexplained dementia or brain damage. I would prefer that this testing be done automatically as part of routine physicals. I have been tested and discovered that I too have high levels of mercury. I am presently going through detoxification through alternative medicine.

- Integrate alternative medicine with mainstream medicine, so that affected people can be detoxed of heavy metals.

I was 47 when I married for the first time to Dirk. Four years later the nightmare began. It has been very painful to watch this man's deterioration. When I met Dirk, he was Director of Vocational Training for the Federal government (Western states). He was a vital man whose retirement years have been a nightmare. He is 70 years old and I don't know if he will reach 71.

Thank you for taking time to read my words. I hope they help.

Most sincerely,

Noel Schuurman

Noel Schuurman
1832 Cerros Colorados
Santa Fe, NM 87501
FAX (505) 820-0349

Anne Ferreira
22 Neff Drive
Hampton, VA 23669-1153

July 20, 2000

Congressman Dan Burton
2153 Rayburn House Office Building
Washington DC 20515

Dear Congressman:

Thank you for conducting the hearings on "Mercury in Medicine". In particular, I deeply appreciate you including the dental amalgam issue in this hearing. It is an issue that has been long overdue in receiving congressional attention. Please enter this letter into the congressional record.

I am writing to you in regard to dental amalgam fillings, commonly called "silver fillings", which are literally so close to the brain of millions of Americans. The public is health conscious, but unaware of what is being placed on their teeth when they have a cavity filled. Silver fillings or amalgams have never been approved by the Federal Drug Administration (FDA) although they have been used for over 160 years. There have been thousands of scientific research papers written and published worldwide on the toxicity of amalgams. The contents of amalgams is approximately 50% mercury, 35% silver and the remaining 15% consisting of copper, tin, and zinc. The mercury is used because of its binding properties. However, mercury is one of the most toxic substances known to man, more toxic than lead, arsenic and cadmium. There is no safe level of mercury. It is not a question of being allergic. It is extremely poisonous. This is even more crucial with children. How can we tolerate the poisoning of our children – the future of our country?

I would like to share my personal experience and how mercury/silver fillings have affected my health and how difficult it was to have it diagnosed. I experienced long and intense sensations of tingling and numbing on top of my head, eyes, face, and a sharp shooting pain in my head. A neurologist ordered a MRI of the brain. It revealed brain lesions. The doctor told me that it was normal and that he saw it in lots of patients. According to him, it was due to the aging process (I was then 48 years old). He could not explain what was causing the problem. I was left untreated and forced to go to another doctor who gave me beta blockers after reviewing the MRI. I was given high blood pressure medicine to carry oxygen to the brain. I actually had low blood pressure. Nothing helped! I felt weak, sick and unable to function. Doctors were unable to diagnose the problem. I had several other symptoms: heart palpitations, fibromyalgia, cold extremities, high sensitivity to noise, sudden episodes of nervousness and anxiety, candidas, severe digestive problems, low immune function, food and chemical allergies, very low energy level, and extreme fatigue. Lying in bed, many times, I wished I could stop breathing because it was exhausting.

Doctors ordered lab work and the results were within normal range. They could not help me. I had a doctor, at Walter Reed Army Medical Center, tell me that "It is all in your head; you are making up the symptoms". What a way to add insult to injury! Doctors are not trained to diagnose mercury toxicity. They are ignorant of its symptoms. I had faith in God and prayed every day that I would get relief and be able to find a doctor who could help me.

In November 1996, I went to see a Doctor in Maryland. He ordered a hair analysis for toxic metals. When I went back one month later for a follow-up visit, I found out I had aluminum, nickel and a very high level of mercury – 11.7 parts per million (ppm). The "normal" level considered tolerable is 1.1 ppm. I had another hair analysis done two months later and the mercury level had gone up to 12.6 ppm. My Doctor recommended I have all the amalgam fillings and all other metals removed from my teeth.

I had a difficult time finding a toxic-free dentist. I was told to get educated on the issue by a dentist in Richmond and when I was ready, to tell the dentist exactly what to do. I was in tears, sick, very weak and frightened, and now I was to get educated? I learned quickly that it is "unethical" for a dentist to talk about the mercury in amalgams and that if he does, he is at great risk of losing his license. I went to a dentist in North Carolina who refused to talk to me about the dangers of amalgams, but measured the electrical charges in my teeth. I had high negative charges (-22) on the top right molar and I had positive charges. I understand, from my research, that dissimilar metals and water (saliva) have a battery effect and create electricity. One amalgam generates one thousand times more electricity than what the nerve ending needs to function. Once I had the metals removed, the tingling, numbing sensation disappeared. The electrical charges were eliminated.

My health is improving, but I still have to deal with the mercury poisoning. I still have a long way to go. One must wonder how many millions of dollars are spent and the diagnoses are missed due to mercury toxicity and high electrical current in the mouth due to dissimilar metals. I know I am one of thousands and maybe millions of people that have come to recognize that mercury amalgams have been a major contributor to health problems. Yet, the public is not aware of the magnitude of this problem and that the FDA has a medwatch to report adverse reactions to dental materials.

I ask that you do not delay, but give priority to investigate as soon as possible this major health issue, in order to achieve the following objectives:

1. Investigate the dental mercury regulatory issue. Mercury and other alloys have never been approved by the FDA to be mixed for use as dental devices.

2. A congressional committee needs to be established to directly oversee dental health. Currently, no congressional committee has direct oversight of dental health issues. Dental issues impact and are an integral part of the total health. This is generally not recognized by the medical profession and associated congressional committees which treat dental health issues separately.

3. The American Dental Association (ADA) and state dental boards need to be investigated for coercing dentists not to discuss the pros and cons of amalgams and alternative composites. Legislation needs to be passed to protect the basic doctor-patient confidentiality relation and informed consent. Dentists who have lost their licenses because of this should have them reinstated by federal legal action.

4. ADA and state dental boards' coercion violates the first amendment.

5. ADA and state dental boards' coercion of dentists not to discuss the pros and cons of amalgams and alternative composites violates anti-trust laws.

6. The ADA owned patents to amalgams. Conflict of interest issues need to be investigated.

7. The composition of the state dental boards needs reform. Currently only ADA-approved dentists make up the board. At least half of the board needs consumer and alternative dentistry representation.

8. Independent research needs to be done on amalgams to determine their safety. There is no scientific research that shows that mercury amalgams are safe. The ADA only uses opinion papers to argue its safety. It is no coincidence that virtually all of Western Europe has banned amalgams. It is just a matter of time before the US Government becomes informed by constituents like myself and follows suit.

9. Currently available composites and other dental materials need to be scientifically tested for safety.

10. Insurance companies need to be investigated for collusion with the ADA in only covering amalgam fillings. Most dental plans specifically exclude composites unless they are on frontal teeth. Replacing amalgams with composites is not for cosmetic reasons but for health reasons.

11. Disposal of new amalgam filling scraps and old removed fillings need to be treated as toxic waste. According to the Environmental Protection Agency (EPA) amalgam waste is classified as toxic waste. Who is regulating this part of dental work? The auto industry is being environmentally regulated, why not the dental industry which handles mercury – one of most toxic elements known to man?

12. Amalgam filling particles are disposed into the water sewer system during dental procedures. Who is regulating this part of dental work?

13. The quality of the air in dental offices needs to be investigated. The mixing of amalgams, removal and replacement, release mercury vapor into the air. The National Institute for Occupational Safety and Health recommends procedures for workers occupationally exposed to all organic and inorganic mercury compounds. Adherence to these standards needs to be investigated. See U.S. Dept. of HEW Public Health Service 1977-757-009/42.

14. Pollution from the dead. Crematoriums incinerate human remains that have amalgam fillings. According to Dr. Mat Hanson, a Swedish research scientist, an average of four grams of mercury is emitted into the air per human body cremated. There are no EPA mercury emission limits for crematoria. Who is regulating this health issue?

15. Many pharmaceutical products contain mercury as a preservative. Injected these products may put patients at high risk because they are highly reactive to mercury.

16. Mercury is extremely poisonous. It needs to be tightly regulated.

According to the EPA, dental amalgams are a highly toxic waste before placing it in the teeth and after removal from the teeth. What is it, when in the person's mouth? I would appreciate your help as a public servant to protect the public. I have done a lot of research on this issue, which I can provide you. My home phone is 757 – 851-4805. My e-mail is virginia@portone.com . Please advise if I can be of further assistance. Anything you can do to achieve any or all of the above objectives would be deeply appreciated.

Sincerely,

Anne Ferreira

Anne Ferreira

DOCUMENTS TO BE ENTERED OF CONGRESSIONAL RECORD

July 29, 2000

Congressman Dan Burton
Committee on Government Reform

Attn: Beth Clay, Esq.

Dear Ms. Clay:

The enclosed document, *Personal Accounts of Mercury Poisoning from Dental Amalgams*, is being submitted herewith to be entered into the Congressional record for the Committee on Government Reform hearing, "Mercury In Medicine --Are We Taking Unnecessary Risks!" which took place on July 18, 2000.

There are hundreds of additional personal accounts available for submission upon request.

We are most grateful for your commitment and diligence in your investigation of the link between mercury dental amalgams and systemic illness.

Sincerely yours,

Freya B. Koss

Consumers for Dental Choice
1400 Sixteenth Street N.W., Suite 230
Washington, DC 20036

DENTAL BOARD OF CALIFORNIA

Quarterly News & Action Report

VOLUME 7 June 30, 2000

The Dental Board of California

Members of the Board

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Roger Simonian, DDS

Vice President
Kit Neazy, DDS

Secretary
Richard Benveniste, DDS

John Berry, DDS

Llewellyn Chin, Public Member

Robert Christoffersen, DDS

Katie Dawson, RDH

LaDonna Drury-Klein, RDA

Mark Goldenberg, DDS

Peter Hartmann, DDS

Kathy Holladay, Public Member

Alan H. Kaye, DDS

Michael Pinkerton, Public Member

—

Executive Officer of the Board

Georgetta Coleman

CONTENTS

Dental Material Fact Sheet 1

New Members 1

Disciplinary Actions 1-4

Did You Know? 4

CDHA News 4-5

Telephone Medical Advice 5

Dental Board Website 6

PRESIDENT'S MESSAGE

Roger Simonian, DDS



In recent editions, this column has been reserved for the President to share information about the Board. In keeping with that tradition, I would like to discuss the action the Board took in December 1999, regarding a petition from Consumers for Dental Choice. The petition addressed five major points relative to Business and Professions Code Sections 1648.10 and 1648.20 of the 1992 Statutes. At that meeting, the Board took action on four of the five points made in the petition. Since that time, several reports have been written regarding the petition and the Board's action. This article is intended to clarify what was requested and how the Board responded to that request. Since this was a complex petition making several requests of the Board, for the benefit of the reader, the following information contains the legal basis for the petition, the specific requests, and the action taken by the Dental Board.

Business & Professions Code Section 1648.10 mandated the Dental Board of California to develop and distribute a Dental Materials Fact Sheet (Fact Sheet) which described and compared the risks and efficacy of the various types of dental restorative materials that may be used to repair a dental patient's oral condition or defect. The law required the fact sheet to contain specific information and be updated as deemed necessary by the Board. Section 1648.20 exempts any dental tool or instrument used during the dental procedure from the provisions of Section 1648.10, and clarifies the language so the Fact Sheet focuses on those dental materials that remain in a patient's mouth after completion of a procedure. These can include, but are not limited to, removable and fixed restorative materials, orthodontic appliance materials, and materials used in the restoration of teeth. In May 1993, a two-page Fact Sheet containing the pros and cons of various dental restorative materials was developed and distributed by the Board. The petitioner requested the revision of the Dental Material Fact Sheet to (1) rid the Fact Sheet of misleading language on amalgams; (2) include in the fact sheet all statutory

Continued on page 2 →

THE BOARD WELCOMES FOUR NEW MEMBERS

The Senate Rules Committee of the Legislature recently appointed Attorney Michael Pinkerton as a public member to the Dental Board of California. Mr. Pinkerton is currently the Director of the California Association of Insurance and Financial Advisors. Mr. Pinkerton has vast legal experience including having served as a Deputy Attorney General from 1985-1989.

Alan H. Kaye, DDS, was appointed by Governor Gray Davis. Dr. Kaye has been licensed in California since 1976 and practices oral and maxillofacial surgery in Beverly Hills. In addition to his California dental license, Dr. Kaye holds a license in New York and Florida.

Katie Dawson, RDH, was appointed by Governor Davis to fill a vacated auxiliary position on the Board. Ms. Dawson is past president of the California Dental Hygienists Association and has been a practicing hygienist for 23 years.

LaDonna Drury-Klein, RDA, was also appointed by Governor Davis. Ms. Drury-Klein is a faculty instructor with the Dental Assisting Department of Alameda Community College.

(Continued from page 1)

requirements regarding the dentist's responsibility to fully inform the patient of the available options of dental restorative materials. The Fact Sheet should also encourage dentists to discuss with their patients the advantages and disadvantages of the various dental filling materials; (3) the Fact Sheet update should cover the past six years of research documenting hazards of all dental filling materials and; (4) the Fact Sheet should provide dentists with guidance on properly warning patients about the reproductive toxicity of the mercury contained in amalgam. The Fact Sheet should also address ways in which practitioners may determine patient sensitivity to mercury, i.e., a comprehensive health questionnaire. Any interested party should have the opportunity to review and comment on the Fact Sheet prior to its distribution. The Board's goal is to have a new Fact Sheet for distribution by December 2000. *The Board voted to approve all the above referenced recommendations.*

The petitioner has requested the Board, as part of the licensure process, to require all participants in the dental licensure examination to complete a questionnaire on the various types of dental restorative materials. Board staff recommended that, in lieu of a questionnaire, the California Law Examination be revised to include questions on Business & Professions Code Section 1648.10. *The Board voted to approve the above recommendation.*

In addition, the petitioner requested a number of items the Board considered to fall under the general heading of informed consent. The petitioner requested that (1) the dentist advise patients of the different types of filling materials; (2) the dentist advise patients and staff that an amalgam contains mercury, a substance designated under Proposition 65 and found to be hazardous. The petitioner also requested the dentist provide copies of the revised Fact Sheet to any patient requiring a restoration.

The Board voted to include an article in the newsletter encouraging dentists to discuss with their patients the different restorative materials. The article should also suggest that dentists discuss with their patients the percentage of mercury in amalgam and that mercury and other substances used in dental offices are designated hazardous under Proposition 65. The Board encourages discussion between the dentist and patient regarding the potential sensitivity and allergic or adverse reactions to mercury by some patients. The Board further approved the distribution of the revised Fact Sheet to all licensed dentists.

The petitioner requested the Board to clarify its position on mercury-free practice. The Board agreed to publicly clarify that it has no position either pro, or con, on the various dental restorative materials. The dentist is free to decide what type of restorative materials he/she may use or not use in the practice. However, the Dental Board of California encourages dentists to discuss the choice of restorative materials with their patients. ■

July 28,2000

Dear Congressman Burton:

Re: Committee on Government Reform Hearing, Mercury in Medicine, July 18, 2000,

Please enter this document as part of the congressional record. Thank you.

Bernard Windham, Editor- Chemical Engineer 12164 Whitehouse Road
Tallahassee, FL,32311 850-878-9024

I. Introduction
II. Toxicity and Health Effects of Mercury
III. Systemic Mercury Intake Levels from Amalgam Filling Exposure
IV. Immune System Effects and Autoimmune Disease
V. Medical Studies Finding Health Problems Related to Amalgam Fillings
VI. Documented Results of Removal of Amalgam Fillings
VII. Health Effects from Dental Staff Exposure to Mercury
VIII. Scientific Panel and Government Bodies That Have Found Amalgam Fillings Unsafe

I. Toxic metals such as mercury, lead, cadmium, etc. have been documented to be neurotoxic, immunotoxic,
reproductive/developmental toxins that according to U.S. Government agencies cause adverse health effects and learning disabilities to millions in the U.S. each year, especially children and the elderly(105,160). Exposure of humans and animals to toxic metals such as mercury, cadmium, lead, copper, aluminum, arsenic, chromium, manganese, etc. is widespread and in many areas increasing. . The U.S. Center for Disease Control(276) ranks toxic metals as the number one environmental health threat to children. According to an EPA/ATSDR assessment, the toxic metals mercury, lead, arsenic, and cadmium are all ranked in the top 7 toxics having the most adverse health effects on the public based on toxicity and current exposure levels in the U.S., with nickel and chromium also highly listed. While there is considerable commonality to the health effects commonly caused by these toxic metals, and effects are cumulative and synergistic in many cases, this paper will concentrate on the health effects of elemental mercury from amalgam fillings. Studies have found considerable genetic variability in susceptibility to toxic metals as well. The public appears to be generally unaware that considerable scientific evidence supports that mercury is the metal causing the most widespread adverse health effects to the public, and amalgam fillings have been well documented to be the number one source of exposure of mercury to most people, with exposure levels often exceeding Government health guidelines and levels documented to cause adverse health effects.

II. Toxicity and Health Effects of Mercury

1. Dental amalgam contains about 50 % mercury. The average filling has 1 gram of mercury and leaks mercury vapor continuously due to mercury's low vapor pressure along with loss due to galvanic action of mercury with dissimilar metals in the mouth(182,192,292,348,349), resulting in significant exposure for most with amalgam fillings(see Section III). Mercury vapor is transmitted rapidly throughout the body, easily crosses cell membranes, and like organic methyl mercury has significant toxic effects at much lower levels of exposure than other inorganic mercury forms(38,281,287,304,329). According to the U.S. EPA & ATSDR, mercury is among the top 3 toxic substances adversely affecting large numbers of people(217), and amalgam is the number one source of exposure for most people(see III).

2. Mercury is the most toxic of the toxic metals. Mercury (vapor) is carried by the blood to cells in all organs of the body where it:

(a) is cytotoxic(kills cells) (2,21,27,36,56,147,148,150,160,210,259,295,333/333)
(b) penetrates and damages the blood brain barrier(311), resulting in accumulation of mercury

and other toxic substances in the brain(14,20,25,85, 99,175,273,301/262,274); also accumulates in the motor function
areas of the brain and CNS(48,291,327,329).

© is neurotoxic(kills brain and nerve cells): damages brain cells and nerve cells (19,27,34,36,43,69,70,147,148,175,207, 211,273, 291,295,327,329,301,303,395/39,262,274,303); generates high levels of reactive oxygen species(ROS) and oxidative stress, depletes glutathione and thiols causing increased neurotoxicity from interactions of ROS, glutamate, and dopamine(13,56,98,102,126,145,169,170,184,213,219, 250, 257,259,286,290,291,302,324,326,329,424); kills or inhibits production of brain tubulin cells (66,67,161,166, 207,300); inhibits production of neurotransmitters by inhibiting: calcium-dependent neurotransmitter release(372,432), dihydroteridine reductase(27,122,257,333), nitric oxide synthase(259), and effecting phenylalanine, tyrosine and tryptophan transport to neurons) (34,122,126,257,285,288,333/255,333)

(d) is immunotoxic(damages and inhibits immune T-cells, B-cells, neutrophil function, etc.) (17,27,31,38,44,45,46,60,127,128,129,130,152,155,165,181,226,252,270,285,316,355/272) and induces ANA antibodies and autoimmune disease(38,43,45,59,60,118,131,181,234,269,270,313,314,334,342,343)

(e) is nephrotoxic(toxic to kidneys) (14,20,203,223,260,268,334)

(f) is endocrine system-disrupting chemical(accumulates in pituitary gland and damages or inhibits pituitary glands hormonal functions at very low levels(9,19,20,25,85,99,105,273,312,327,348,369/274), adrenal gland function(84,369), thyroid gland function(50,212,369), and disrupts enzyme production processes at very low levels of exposure (9,13,33,56,111,194,348,355,410-412)

(g)exposure to mercury vapor (or methyl mercury) causes rapid transmittal through the placenta to the fetus (20,22-24,27,38,39,61,112,186,281,287,304,311,338,339,348,361,366,20/4,22,37,39,41,42) and significant developmental effects-much more damage to the fetus than for maternal exposure to inorganic mercury and at lower exposure levels than for for organic mercury(287,304,etc.).

(h)reproductive and developmental toxin (2,4,9,10,22,23,24,37,38,41,61,105,149,160,275,276,281,305,338, 361,367, 20/4,39,55,149,162,255,308,339,357); damages DNA(296,327,272,392,142,38,41,42) and inhibits DNA & RNA synthesis(114/149); damages sperm, lowers sperm counts and reduces motility. (4,37,104.105,159,160/4, 55,162); causes menstrual disturbances (9,27,146); reduces bloods ability to transport oxygen to fetus and transport of essential nutrients including amino acids, glucose, magnesium, zinc and Vit B12(43,96,198,263,264,338,339,347,427); depresses enzyme isocitric dehydrogenase (ICD) in fetus, causes reduced iodine uptake & hypothyroidism(50,91,212,222,369) & learning deficits; causes learning disabilities and impairment, and reduction in IQ(1,3,38,110,160,285c,263,264/39), causes infertility (4,9,10,24,38,121,146,357,365,367/4,10,55,162), causes birth defects (23,35,37,38,110,142,241/241).

(i)prenatal/early postnatal exposure affects level of nerve growth factor in the brain,impairs astrocyte function, and causes imbalances in development of brain(38,119,161,175,194,305/175,255,39)

(j)causes cardiovascular damage and disease: including damage to vascular endothelial cells, damage to sarcoplasmic reticula, sarcolemma, and contractile proteins, increased white cell count, decreased oxyhemoglobin level, high blood pressure, tachycardia, inhibits cytochrome P450/heme synthesis(84), and increased risk of acute myocardial infarction (35,59,202,205,212,232,306,310,351/201,308).

(k) causes immune system damage resulting in allergies, asthma, lupus,chronic fatigue syndrome(CFS),and multiple sensitivities(MCS) (8,17,45,46,52,60,75,86,87,90,97,101,128,129,131,154,168,181,212, 226, 228,230,234,265, 267,296,313,342, 388/272) and neutrophil functional impairment(285/59,etc.).

Facts about Mercury and Dental Amalgam
(with Medical Study References)

(l) causes interruption of the cytochrome oxidase system/ATP energy function(84) and progressive coproporphyrinuria, resulting in low energy, digestive problems, and porphyrins in urine (34,69,70,73,210,212,226,232,260)

(m) inhibition of immune system facilitates increased damage by bacterial, viral, and fungal infections (17,45,59,129,131,251,296,350,40), and increased antibiotic resistance(116,117,161,258,389,53).

(n) mercury causes significant destruction of stomach and intestine epithelial cells, resulting in damage to stomach lining(leaky gut)(222,Shelton,228) and accumulation of heliobacter pylori, a suspected major factor in stomach ulcers and stomach cancer(256).

(o) causes mitochondrial release of calcium induced by modification of the--SH groups of proteins (1,21,35,38,43,329,333,432),as well as damaging enzymatic process(33,96,111,194,252,338,410-412) resulting in improper cysteine regulation(194), inhibited glucose transfer(338,254), damaged sulfur oxidation processes(33,338), and reduced glutathione availability (necessary for detoxification)(13,126,54).

3. Mercury has been well documented to be an endocrine system disrupting chemical in animals and people, disrupting function of the pituitary gland, thyroid gland, enzyme production processes, and many hormonal functions at very low levels of exposure . Mercury (especially mercury vapor) rapidly crosses the blood brain barrier and is stored preferentially in the pituitary gland, hypothalamus, and occipital cortex in direct proportion to the number and extent of dental amalgam surfaces (1,14,16,19,20,25,34,38,61,85,99,162,211, 273,274,287,327,348,360,366,369) Thus mercury has a greater effect on the functions of these areas. The pituitary gland controls many of the body's endocrine system functions and secretes hormones that control most bodily processes, including the immune system and reproductive systems . One study found mercury levels in the pituitary gland ranged from 6.3 to 77 ppb(85), while another(348) found the mean level to be 30ppb- levels found to be neurotoxic and cytotoxic in animal studies. The hypothalamus regulates body temperature and many metabolic processes. Mercury damage thus commonly results in poor bodily temperature control, in addition to many problems caused by hormonal imbalances. Such hormonal secretions are affected at levels of mercury exposure much lower than the acute toxicity effects normally tested, as previously confirmed by hormonal/reproductive problems in animal populations(104). Mercury also damages the blood brain barrier and facilitates penetration of the brain by other toxic metals and substances(311).

4. Mercury's biochemical damage at the cellular level include DNA damage, inhibition of DNA and RNA synthesis(4,38,41,42,114,142,197,272,296,392/149); alteration of protein structure(33,111,114,194,252/114); alteration of the transport of calcium(333,43,96,254,329,432); inhibitation of glucose transport(338,254), and of enzyme function and other essential nutrients(96,198,254,263,264,338,339,347,410-412); induction of free radical formation(13,54), depletion of cellular gluthathione(necessary for detoxification processes) (111,126), inhibition of glutathione peroxidase enzyme(13), endothelial cell damage(202), abnormal migration of neurons in the cerebral cortex(149), and immune system damage (34,38,111,194, 226,252,272,316,325,355). Oxidative stress and reactive oxygen species(ROS) have been implicated as major factors in neurological disorders including stroke, PD, Alzheimer's, ALS, etc.(13,56,84,98,145,169,207b,424). Mercury induced lipid peroxidation has been found to be a major factor in mercury's neurotoxicity, along with leading to decreased levels of glutathione peroxidation and superoxide dismustase(SOD)(13). Only a few micrograms of mercury severely disturb cellular function and inhibit nerve growth(175,147,175,226,255,305). Exposure to mercury results in metalloprotein compounds that have genetic effects, having both structural and catalytic effects on

Facts about Mercury and Dental Amalgam
(with Medical Study References)
(4,9,38,104,105,107,140,141,275,276, 288,290,365,367,372,432).

7. An average amalgam filling contains over ½ gram of mercury, and the average adult had at least 5 grams of mercury in fillings(unless most has vaporized). Mercury in solid form is not stable, having low vapor pressure and being subject to galvanic action with other metals in an oral environment(182,192,292,348,349),so that within 10 years up to half has been found to have been transferred to the and body of the host(34,35,182, & section III).

8. Elemental mercury vapor is more rapidly transmitted throughout the body than most other forms of mercury and has more much toxic effects on the CNS and other parts of the body than inorganic mercury due to its much greater capacity to cross cell membranes, according to the World Health Organization and other studies (38,183, 282,287,360,section III). Mercury vapor rapidly crosses the blood-brain barrier(14,85,311) and placenta of pregnant women (20,22-24,27,38,105,162,186,231,281,287,304,308, 311,361) Developmental, learning, and behavioral effects have been found from mercury vapor at much lower levels than for exposure to methyl mercury(287,304). Similarly for inhibition of some essential cellular processes(333,338,329).

9. Running shoes with ½ gram of mercury in the heels were banned by several states, because the amount of mercury was considered dangerous to public health and created a serious disposal problem. Mercury from dental offices and human waste from people with amalgam fillings has much higher levels and is a major source of mercury in Florida waters. One study found dental offices discharge into waste water between 65 and 842 milligrams per dentist per day(231), amounting to several hundred grams per year per office. This is in addition to air emissions. Additionally cremation of those with amalgam fillings adds to air emissions and deposition onto land and lakes. A study in Switzerland found that in that small country, cremation released over 65 kilograms of mercury per year as emissions, often exceeding site air mercury standards(420), while another Swiss study found mercury levels during cremation of a person with amalgam fillings as high as 200 micrograms per cubic meter(considerably higher than U.S. mercury standards). The amount of mercury in the mouth of a person with fillings was on average 2.5 grams, enough to contaminate 5 ten acre lakes to the extent there would be dangerous levels in fish(151). A Japanese study estimated mercury emissions from a small crematorium there as 26 grams per day(421). A study in Sweden found significant occupational and environmental exposures at cremetoria, and since the requirement to install selenium filters mercury emission levels in crematoria have been reduced 85%(422).

10. Studies have found that levels of exposure to the toxic metals mercury, cadmium, and lead have major effects on classroom behavior, learning ability, and also in mental patients and criminals behavior(3,160).

Studies have found that both genetic susceptability and environmental exposures are a factor in xenobiotic related effects and disease propagation. Large numbers of animal studies have documented that genetically susceptable strains are more affected by xenobiotic exposures than less susceptable strains(234,425,526,etc.). Some genetic types are susceptable to mercury induced autoimmunity and some are resistant and thus much less affected(234,425,383). Studies found that mercury causes or accelerates various systemic conditions in a strain dependent manner, and that lower levels of exposure adversely affect some strains but not others, including inducing of autoimmunity. Also when a condition has been initiated and exposure levels decline, autoimmune antibodies also decline in animals or humans(234c,60,368,405). One genetic factor in Hg induced

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autoimmunity is major histocompatibility complex(MHC) linked. Both immune cell type Th1 and Th2 cytokine responses are involved in autoimmunity(425c). One genetic difference found in animals and humans is cellular retention differences for metals related to the ability to excrete mercury(426). For example it has been found that individuals with genetic blood factor type APOE-4 do not excrete mercury readily and bioaccumulate mercury, resulting in susceptability to chronic autoimmune conditions such as Alzheimer's, Parkinsons, etc. as early as age 40, whereas those with type APOE-2 readily excrete mercury and are less susceptable. Those with type APOE-3 are intermediate to the other 2 types.

11. Long term occupational exposure to low levels of mercury can induce slight cognitive deficits, lability, fatigue, decreased stress tolerance, etc. Higher levels have been found to cause more serious neurological problems (119,128,285,etc.). Occupational exposure studies have found mercury impairs the body's ability to kill Candida albicans by impairment of the lytic activity of neutrophils and myeloperoxidase in workers whose mercury excretion levels are withing current safety limits(285,404). Such levels of mercury exposure were also found to inhibit cellular respiratory burst. A population of plant workers with average mercury excretion of 20 ug/ g creatinine was found to have long lasting impairment of neutrophil function. Another study(59) found such impairment of neutraphils decreases the body's ability to combat viruses such as those that cause heart damage, resulting in more inflamatory damage. Another group of workers with average excretion rates of 24.7 ug/ g creatinine had long lasting increases in humoral immunological stimulation of IgG, IgA, and IgM levels. Another study(285b) found that workers exposed at high levels at least 20 years previous(urine peak levels above 600 ug/L demonstrated significantly decreased strength, decreased coordination, increased tremor, decreased sensation, polyneuropathy, etc. Another study found that many of the symptoms and signs of chronic candidiasis, multiple chemical sensitivity and chronic fatigue syndromes are identical to those of chronic mercurialism and remit after removal of amalgam combined with appropriate supplementation and gave evidence to
implicate amalgam as the only underlying etiologic factor that is common to all(404).

Other studies(285c) found that mercury at levels below the current occupational safety limit causes adverse effects on mood, personality, and memory- with effects on memory at very low exposure levels.
More studies found that long term exposure causes increased micronuclei in lymphocytes and significantly increased IgE levels at exposures below current safety levels(128), as well as maternal exposure being linked to mental retardation(110) and birth defects(23,35,37,38,142,241,361/241).

III. Systemic Mercury Intake Level from Amalgam Fillings

1. The tolerable daily exposure level for mercury developed in a report for Health Canada is .014 micrograms/kilogram body weight(ug/kg) or approximately 1 ug/day for average adult(217). The U.S. EPA Health Standard for elemental mercury exposure(vapor) is 0.3 micrograms per cubic meter of air(2). The U.S. ATSDR health standard(MRL) for mercury vapor is 0.2 ug/ M3 of air, and the MRL for methyl mercury is 0.3 ug/kg body weight/day(217). For the average adult breathing 20 M3 of air per day, this amounts to an exposure of 4 or 6 ug/day for the 2 elemental mercury standards. The EPA health guideline for methyl mercury is 0.1 ug/kg body weight per day or 7 ug for the average adult(2), or approx. 14 ug for the ATSDR acute oral toxicicity standard. Since mercury is methylized in the body, some of both types are present in the body. The older World Health Organization(183) mercury health guideline(PTWI) is 300 ug per week total

exposure or approx. 42 ug/day.

2. Mercury in the presence of other metals in the oral environment undergoes galvanic action, causing movement out of amalgam and into the oral mucosa and saliva(192). Mercury in solid form is not stable due to low vapor pressure and evaporates continuously from amalgam fillings in the mouth, being transferred over a period of time to the host(15-19,26,31,36,79,83,211,182,183,199,298,299,303,332,335,371). The daily total exposure of mercury from fillings is from 3 to 1000 micrograms per day, with the average exposure being above 10 micrograms per day and the average uptake over 5 ug/day (183,199,209,18,19,77,83, 85,100,335,352,371,etc.). (see further details continued)

A large study was carried out at the Univ. Of Tubingen Health Clinic in which the level of mercury in saliva of 20,000 persons with amalgam fillings was measured(199). The level of mercury in unstimulated saliva was found to average 11.6 ug Hg/L, with the average after chewing being 3 times this level. Several were found to have mercury levels over 1100 ug/L, 1 % had unstimulated levels over 200 ug/L, and 10 % had unstimulated mercury saliva levels of over 100 ug/L.. The level of mercury in saliva has been found to be proportional to the number of amalgam fillings, and generally was higher for those with more fillings. The following table gives the average daily mercury exposure from saliva alone for those tested, based on the average levels found per number of fillings and using daily saliva volumes of 890 ml for unstimulated saliva flow and 80 ml for stimulated flow (estimated from measurements made in the study and comparisons to other studies). It also gives the 84th percentile mercury exposure from saliva for the 20,000 tested by number of fillings. Note that 16% of all of those tested with 4 amalgam fillings had daily exposure from their amalgam fillings of over 17 ug per day, and even more so for those with more than 4 fillings.

Table: Average daily mercury exposure in saliva by number of amalgam fillings(199)

Number of fillings:	4	5	6	7	8	9	10	11	12	13	14	15	16
Av. Daily Hg(ug)	6.5	8	9.5	11	12.4	14	15.4	16.9	18.3	19.8	21.3	22.8	24.3
84th percentile(ug)	17	23.5	26	30.5	35	41.5	43.8	48.6	50.3	46.7	56.6	61.4	64.5

Saliva tests for mercury are commonly performed in Europe, and many other studies have been carried out with generally comparable results(292,315,79,9b,335,179,317,352). Another large German study(352) found significantly higher levels than the study summarized here, with some with exposure levels over 1000 ug/day. Three studies that looked at a population with more than 12 fillings found generally higher levels than this study, with average mercury level in unstimulated saliva of 29 ug/L(18), 32.7 ug/L (292c), and 175 ug/day(352). The average for those with 4 or less fillings was 8 ug/L(18). While it will be seen that there is a significant correlation between exposure levels and number of amalgam surfaces and exposure generally increases as number of fillings increases, there is considerable variability for a given number of fillings. Some of the factors that will be seen to influence this variability include composition of the amalgam, whether person chews gum or drinks hot liquids, bruxism, oral environmental factors, type of tooth patse used, etc.

The Tubingen study did not assess the significant exposure route of intraoral air and lungs. One study that looked at this estimated a daily average burden of 20 ug from ionized mercury from amalgam fillings absorbed through the lungs(191), while a Norwegian study found the average level in oral air to be 0.8 ug/M3(176). Another study at a Swedish University(335) measured intraoral air mercury levels from fillings of from 20 to 125 ug per day, for persons with from 18 to 82 filling surfaces. Another study found similar results(83), and some individuals have been found to have intraoral air mercury levels above 400 ug/ M3 (319). Most of those

whose intraoral air mercury levels were measured exceeded Gov't health guidelines for workplace exposure(2).

The studies also determined that the number of fillings is the most important factor related to mercury level, with age of filling being much less significant(319b). Different filling composition/manufacturer can also make a difference in exposure levels(as will be further discussed). The authors of the Tubingen study calculated that based on the test results with estimates of mercury from food and oral air included, over 40 % of those tested in the study received daily mercury exposure higher than the WHO standard(PTWI). As can be seen most people with several fillings have daily exposure exceeding the Health Canada TDE and the U.S. EPA and ATSDR health guideline for mercury(2,209,199,etc.), and many tested in past studies have exceeded the older and higher WHO guideline for mercury(183), without consideration of exposure from food, etc..

3. The main exposure paths for mercury from amalgam fillings are absorption by the lungs from intraoral air; vapor absorbed by saliva or swallowed; amalgam particles swallowed; and membrane, olfactory, venous, and neural path transfer of mercury absorbed by oral mucosa, gums, etc. (6,17,18,31,34,77,79,83,94,133,182,209,211, 216,222,319, 335,348,364) A study at Stockholm Univ.(335) made an effort to determine the respective parts in exposure made by these paths. It found that the majority of excretion is through feces, and that the majority of mercury exposure was from elemental vapor. Daily exposure from intraoral air ranged from 20 to 125 ug of mercury vapor, for subjects with number of filling surfaces ranging from 18 to 82. Daily excretion through feces amounted to from 30 to 190 ug of mercury, being more variable than other paths. Other studies had similar findings(6,15,16,18,19,25,31,36,79,80,83,115,196,386.)

The feces mercury was essentially all inorganic with particles making up at most 25%, and the majority being mercury sulfuhydryl compounds- likely originating as vapor. Their study and others reviewed found that at least 80% of mercury vapor reaching the lungs is absorbed and enters the blood from which it is taken to all other parts of the body(335,348,349,363). Elemental mercury swallowed in saliva can be absorbed in the digestive tract by the blood or bound in sulfhydryl compounds and excreted through the feces. A review determined that approx.20 % of swallowed mercury sulfhydryl compounds are absorbed in the digestive tract, but approx 60% of swallowed mercury vapor is absorbed(292,335,348). At least 80% of particle mercury is excreted. Approx. 80% of swallowed methyl mercury is absorbed(335,199,etc.)e, with most of the rest being converted to inorganic forms apparently. The primary detoxification/excretion pathway for mercury absorbed by the body is as mercury-glutathione compounds through the liver/bile loop to feces(111,252), but some mercury is also excreted though the kidneys in urine and in sweat. The range of mercury excreted in urine per day by those with amalgams is usually less than 15 ug(6,49,83,138,174,335,etc.), but some patients are much higher(93). A large NIDH study of the U.S. military population(49) with an average of 19.9 amalgam surfaces and range of 0 to 60 surfaces found the average urine level was 3.1 ug/L, with 93% being inorganic mercury. The average in those with amalgam was 4.5 times that of controls and more than the U.S. EPA maximum limit for mercury in drinking water(218). The avergage level of those with over 49 surfaces was over 8 times that of controls. The same study found that the average blood level was 2.55 ug/L, with 79 % being organic mercuy. The total mercury level had a significant correlation to the number of amalgam fillings, with fillings appearing to be reponsible for over 75% of total mercury. From the study results it was found that each 10 amalgam surfaces increased urine mercury by approx. 1 ug/L. A study of mercury species found blood mercury was 89% organic and urine mercury was 87% inorganic(349b), whicle another study(363) found on average 77% of the mercury in the occipital cortex was inorganic. In a population of women tested In the Middle East(254), the number of fillings was highly correlated with the mercury level in urine, mean= 7 ug/L. Nutrient transport and renal function were also found to be adversely affected by higher levels of mercury in the urine.

Facts about Mercury and Dental Amalgam
(with Medical Study References)

As is known from autopsy studies for those with chronic exposure such as amalgam fillings (1,14,17,20,31,34,85,94), mercury also bioaccumulates in the brain/CNS(301,274,327,329,348,18,19,85),liver, kidneys, (14,85)heart(59,205,348)), and oral mucosa(174,192) with the half life in the brain being over 20 years. Elemental mercury vapor is transmitted throughout the body via the blood and readily enters cells and crosses the blood-brain barrier, and the placenta of pregnant women(38,61,287,311,361), at much higher levels than inorganic mercury and also higher levels than organic mercury. Significant levels are able to cross the blood brain barrier, placenta, and also cellular membranes into major organs such as the heart since the oxidation rate of Hg0 though relatively fast is slower than the time required by pumped blood to reach these organs(290,370). Thus the level in the brain and heart is higher after exposure to Hg vapor than for other forms(360,370). While mercury vapor and methyl Hg readily cross cell membranes and the blood-brain barrier, once in cells they form inorganic mercury that does not readily cross cell membranes or the blood brain barrier readily and is responsible for the majority of toxicity effects. Thus inorganic mercury in the brain has a very long half life(274,etc.).

4. The average amalgam filling has approximately 0.5 grams(500,000 ug) of mercury. As much as 50% of mercury in fillings has been found to have vaporized after 5 years and 80% by 20 years(182,204). Mercury vapor from amalgam is the single largest source of systemic mercury intake for persons with amalgam fillings, ranging from 50 to 90 % of total exposure. (14,16,17,19,36,57,61,78-83,94,129,130,138,161,167,183, 191, 196,211,216,273,292,303,332,), averaging about 80% of total systemic intake. After filling replacement levels of mercury in the blood, urine, and feces typically temporarily are increased for a few days, but levels usually decline in blood and urine within 6 months to from 60 to 85% of the original levels(57,79,82,89,196,303). Mercury levels in saliva and feces usually decline between 80 to 95% (79,196,335,386)

5. Having dissimilar metals in the teeth(e.g.-gold and mercury) causes galvanic action, electrical currents, and much higher mercury vapor levels and levels in tissues. (182,192,292,348,349,390,19,25,27,29,30,47,48,100) Average mercury levels in gum tissue near amalgam fillings are about 200 ppm, and are the result of flow of mercury into the mucous membrane because of galvanic currents with the mucous membrane serving as cathode and amalgam as cathode(192). Average mercury levels are often 1000 ppm near a gold cap on an amalgam filling due to higher currents when gold is in contact with amalgam (30,25,35,48,58). These levels are among the highest levels ever measured in tissues of living organisms, exceeding the highest levels found in chronically exposed chloralkali workers, those who died in Minamata, or animals that died from mercury poisoning. Concentrations of mercury in oral mucosa for a population of patients with 6 or more amalgam fillings taken during oral surgery were 20 times the level of controls(174). These levels are much higher than the FDA/EPA action level for prohibiting use of food with over 1 ppm mercury. Likewise the level is tremendously over the U.S. Dept. Of Health/EPA drinking water limit for mercury which is 2 parts per billion(218). Studies have shown that mercury in the gums such as from root caps for root canaled teeth result in chronic inflammation, in addtion to migration to other parts of the body(200,47). Mercury and silver from fillings can be seen in the tissues as amalgam "tatoos", which have been found to accumulate in the oral mucosa as granules along collagen bundles, blood vessels, nerve sheaths, elastic fibers, membranes, striated muscle fibers, and acini of minor salivary glands. Dark granules are also present intracellularly within macrophasges, multinucleated giant cells, endothelial cells, and fibroblasts. There is in most cases chronic inflammatory response or macrophagic reaction the the metals(47), usually in the form of a foreingn body granuloma with multinucleated giant cells of the foreign body and Langhans types.

Facts about Mercury and Dental Amalgam
(with Medical Study References)

The component mix in amalgams has also been found to be an important factor in mercury vapor emissions. The level of mercury and copper released from high copper amalgam is as much as 50 times that of low copper amalgams(191). Studies have consistently found modern high copper non gamma-two amalgams have greater release of mercury vapor than conventional silver amalgams (298,299). While the non gamma-two amalgams were developed to be less corrosive and less prone to marginal fractures than conventional silver amalgams, they have been found to be instable in a different mechanism when subjected to wear/polishing/ chewing/ brushing: they form droplets of mercury on the surface of the amalgams(182,297). This has been found to be a factor in the much higher release of mercury vapor by the modern non gamma-two amalgams. Recent studies have concluded that because the high mercury release levels of modern amalgams, mercury poisoning from amalgam fillings is widespread throughout the population"(95,199,238). Numerous other studies also support this finding(Section IV).

Amalgam also releases significant amounts of silver, tin, and copper which also have toxic effects, with organic tin compounds formed in the body being even more neurotoxic than mercury(51,222,262)

7. Feces is the major path of excretion of mercury from the body, having a higher correlation to systemic body burden than urine or blood, which tend to correlate with recent exposure level (35,36,79,80,183, 278). For this reason many researchers consider feces to be the most reliable indicator of daily exposure level to mercury or other toxics. The average level of mercury in feces of those with fillings is over 1 ppm and approx. 10 times that of a similar group without fillings (79,80,83,335,386,25,), with significant numbers of those with several filings having over 10 ppm and 170 times those without fillings(80). The saliva test is another good test for daily mercury exposure, done commonly in Europe and representing one of the largest sources of mercury exposure.

There is only a weak correlation between blood or urine mercury levels and body burden or level in a target organ(36,157,183,278,11,etc.). Mercury vapor passes through the blood rapidly(half-life in blood is less than 10 seconds,370) and accumulates in other parts of the body such as the brain, kidneys, liver, thyroid gland, pituitary gland, etc. Thus blood test measures mostly recent exposure. As damage occurs to kidneys over time, mercury is less efficiently eliminated (11,36,57,183, 216,260), so urine tests are not reliable for body burden after long term exposure. Some researchers suggest hair offers a better indicator of mercury body burden than blood or urine(279), though still not totally reliable and may be a better indicator for organic mercury than inorganic. This study found a significant positive correlation between maternal hair mercury and mercury level in nursing infants. Medical labs that do a lot of testing for toxic metals consider hair to be one of the easiest and most accurate tests for body metal levels(386). The Kirkman lab for example indicated that "Hair analysis is a very accurate way to assess the concentration of toxic compounds in the body such as heavy metals. It is a very good way to give early detection for mercury etc./ When we have compared hair with highly accurate mag scans - it is close. Urine and serusm(blood) is not as accurate and only show circulating levels in the system instead of the concentration in the tissues.". Hair mercury levels did not have a significant correlation with urine mercury in one study(340) and did not have a significant correlation to number of fillings(350).

A new test approved by the FDA for diagnosing damage that has been caused by toxic metals like mercury is the fractionated porphyrin test(260), that measures amount of damage as well as likely source. Provocation challenge tests after use of chemical chelators such as DMPS or DMSA also are effective at measuring body burden(57), but can be dangerous to some people- especially those still having amalgam fillings or those allergic to sulfur drugs or sulfites. Many studies using chemical chelators such as DMPS or DMSA have found post chelation levels to be poorly correlated with prechelation blood or urine levels(57,115,303), but one study

(340) found a significant correlation between pre and post chelation values when using DMPS. Challange tests using DMPS or DMSA appear to have a better correlation with body burden and toxicity symptoms such as concentration , memory, and motor deficits(290)- with many studies finding a significant correration between post chelation mercury level and the number of amalgam surfaces(57,172,173,222,290,292,273,303). Several doctors use 16 ug/L as the upper bound for mercury after DMPS challange, and consider anyone with higher levels to have excess body burdern(222,352). However one study(290) found significant effects at lower levels. Some researchers believe DMSA has less adverse side effects than DMPS and prefer to use DMSA for chelation for this reason. Some studies have also found DMSA as more effective at removing mercury from the brain. Another chelator used for clogged arteries, EDTA, forms toxic compounds with mercury and can damage brain function(307). Use of EDTA may need to be restricted in those with high Hg levels. N-acetylcystein(NAC) has been found to be effective at increasing cellular glutathione levels and chelating mercury(54). Experienced doctors have also found additional zinc to be useful when chelating mercury(222) as well as counteracting mercury's oxidative damage(43). Zinc induces metallothionein which protects against oxidative damage and increases protective enzyme activities and glutathione which tend to inhibit lipid peroxidation and suppress mercury toxicity(430). Also lipoic acid has been found to dramatically increase excretion of inorganic mercury(over 12 fold), but to cause decreased excretion of organic mercury(54).

8. The number of amalgam surfaces has a statistically significant correlation to :

(a) blood plasma mercury level (17,49,79,89,133,211)(usually not as strong as other measures)
(b) urine mercury level (38,49,57,76,77,79,82,83,134,138,167,176,254,303,332,335)
© oral air(16,18,100,176,335)
(d) saliva and oral mucosa(18,58,77,79,117,179,174,199,211,222,292,315,317)
(e) feces mercury (25,79,80,83,115,117,182,335,386)
(f) pituitary gland (19,20,25,85,99,273/274)
(g) brain occipital cortex (14,16,19,25,34,85,211,273,348,366/274)
(h) renal(kidney) cortex(14,16,19,20,85,273,348,366)
(I) liver(14,19,85,366)
(j) motor function areas of the brain & CNS: brain stem, cerebellum, rhombencephalon, dorsal root ganglia, and anterior horn motor neurons (48,291,327,329,etc.)
(k) fetal and infant liver/brain levels(61,112,186,231) related to maternal fillings.

9. A person with amalgam fillings has daily systemic intake from mercury vapor of between 3 and 70 micrograms of mercury, with the average being at least 7 micrograms(ug) per day (18,77,83,85,93,138,183,199,211,292,315,335). In a large German study, the median daily exposure for those with fillings through saliva was approx. 10 ug/day, 4% of those with fillings had daily exposure through saliva of over 80 ug/day, and 1% had over 160 ug/day(199). The methods and results of the Tubingen study(199) were similar to those of other German studies(292,315,9, 138, 317,335). Total intake is proportional to the number and extent of amalgam surfaces, but other factors such as chewing gum, drinking hot liquids, brushing or polishing, and using fluoride toothpaste significantly increase the intake(15,18,28,31,100,134-137,182, 183,199,209,211,292,317,319,348,349,350). Vapor emissions range up to 200 ug/M3 (35) and are much higher after chewing(137,319). After chewing, those with amalgams had levels over 50 times higher than those without, and the average level of exposure was 29 ug/day for those with at least 12 occlusal surfaces(18). At

Facts about Mercury and Dental Amalgam
(with Medical Study References)

least 30% of those having amalgam fillings tested in a large German study had ingested mercury levels exceeding the WHO PTWI mercury standard of 43 ug/day (199,183), and over 50% of those with 6 or more fillings had daily exposures more than the U.S. EPA health guideline level(199) of 0.1 ug/kg body weight/day(199). The median daily exposure through saliva for those with 10 or more fillings was over 10 times that of those with no fillings(199,292,315,318). Mercury level in saliva has been found to give much better indication of body levels than blood or urine levels(36). Most people with fillings have daily exposure levels exceeding the U.S. ATSDR and EPA health guideline levels (2,36,83,89,183,199,209,217,261,292,335,93)

10. The blood and urine mercury load of a person with amalgam fillings is often 5 times that of a similar person without.(14,16,17,79,80,82,93,136,138, 303,315,317,318) The average blood level for one large population was 5 ug/l(176). Normal blood levels are less than 20 ppb, but health effects have been observed in patients in the upper part of this range. A Swedish study estimated the total amount mercury swallowed per day from intra-oral vapor was 10 micrograms per day(177),and a large German study(199) found median exposure through saliva alone for those with fillings to be about 10 ug/day, with many having several fillings with over 10 times that level. Other studies have found similar amounts(18,83,211,183,209).

11. Teeth are living tissue and have massive communication with the rest of the body via blood, lymph, and nerves. Mercury vapor (and bacteria in teeth) have paths to the rest of the body. (34,etc.) German studies of mercury loss from vapor in unstimulated saliva found the saliva of those with amalgams had at least 5 times as much mercury as for controls(138,199,292,315).

12. Mercury (especially mercury vapor) rapidly crosses the blood brain barrier and is stored preferentially in the pituitary gland, hypothalamus, and occipital cortex in direct proportion to the number and extent of amalgam surfaces.(14,19,20,25,34,38,85,99,273,274,287,348,366) Thus mercury has a greater effect on the functions of these areas. The range in one study was 2.4 to 28.7 ppb(85), and one study found on average that 77% of the mercury in the occipital cortex was inorganic(363).

13. Some mercury entering nasal passages is absorbed directly into the olfactory lobe and brain without coming from blood(34,35,182,222,348,364). Mercury also is transported along the axons of nerve fibres (5,25,34,35,327,329).

14. Mercury has a long half life in the body and over 20 years in the brain, and chronic low level intake results in a slow accumulation in body tissues. (20,34,35,38,85,etc.)

15. Methyl mercury is more toxic to some body processes than inorganic mercury. Mercury from amalgam is methylated by bacteria and candida albicans in the mouth and intestines(51,81,98,182,225). Oral bacteria streptococommus mitior,S.mutans, and S.sanguis were all found to methylate mercury(81). High levels of Vit B12 in the system also have been found to result in increased methyl mercury concentrations in the liver and brain(51). Methyl mercury is 10 times more potent in causing genetic damage than any other known chemical (Ramel, in(35)), and also crosses the blood-brain barrier readily. Once mercury vapor or methyl mercury are converted to inorganic mercury in cells or the brain, the mercury does not readily cross cell membranes or the blood-brain barrier. Thus mercury has a very long half life in the brain. N-acetylcysteine(NAC) has been found to be effective at increasing glutathione levels and chelating methyl mercury(54,126).

16. The level of mercury in the tissue of the fetus, new born, and young children is directly proportional to the number of amalgam surfaces in the mother's mouth. (20,23,61,112,210,361) The level of mercury in umbilical cord blood and placenta was higher than that in mother's blood(22,186). The saliva and feces of children with amalgams have approximately 10 times the level of mercury as children without(25,315,386), and much higher levels in saliva after chewing. A group of German children with amalgam fillings had urine mercury level 4 times that of a control group without amalgams(76), and in a Norwegian group with average age 12 there was a significant correlation between urine mercury level and number of amalgam fillings(167). The level of mercury in maternal hair was significantly correlated to level of mercury in nursing infants(279). One study found a 60% increase in average cord blood mercury level between 1980 and 1990 in Japan(186).

17. The fetal mercury content after maternal inhalation of mercury vapor was found to be higher than in the mother(4,etc.) Mercury from amalgam in the blood of pregnant women crosses the placenta and appears in amniotic fluid and fetal blood, liver, and pituitary gland soon after placement (20,22,23,31,36,61,162,186,281,348,366). Dental amalgams are the main source of mercury in breast milk(112,186,304,339,20). Milk increases the bioavailability of mercury(112,304,391) and mercury is often stored in breast milk and the fetus at much higher levels than that in the mother's tissues (19,20,22,23,61,112,186,210, 287,304). The level of mercury in breast milk was found to be significantly correlated with the number of amalgam fillings(61), with milk from mothers with 7 or more fillings having levels in milk approx. 10 times that of amalgam free mothers. The milk sampled ranged from 0.2 to 6.9 ug/L. Several authors suggest use of early mother's milk as a screen for potenital problems since it is correlated both to maternal and infant mercury levels. The highest level is in the pituitary gland of the fetus which affects development of the endocrine to be approx 0 times that for maternal exposure to an equivalent dose of inorganic mercury(281,287), and developmental behavioral effects from vapor have been found at levels considerably below that required for similar effects by methyl mercury(20,49,119c,264,287,304,338). The level of total mercury in nursing infants was significantly correlated to total mercury level in maternal hair(22,279).

18. There is a significant correlation between number of amalgam fillings of the mother and the level of the fetus and older infants(20,23,61,304), and also with the level in mother's milk (19,20,38,112, 304). Fertile women should not be exposed to vapor levels above government health guidelines(38,61,182,282) ;the U.S. ATSDR mercury health MRL of 0.2 mcg/M3 (2,217); or have amalgams placed or removed during pregnancy(20,182,231,304,etc.).

IV. Immune System Effects and Autoimmune Disease

1. Many thousands of people with symptoms of mercury toxicity have been found in tests to have high levels of mercury, and many thousands who have had amalgam fillings removed(most) have had health problems and symptoms alleviated or greatly improved(see Section VI). From clinical experience some of the symptoms of mercury sensitivity/mercury poisoning include chronic fatigue, dizziness, frequent urination, insomnia, headaches, chronic skin problems, metallic taste, gastrointestinal problems, asthma(8,97), stuffy nose, drycrusts in nose, rhinitis, plugged ears, ringing ears, chest pain, hyperventilation, diabetes, spacy feeling, chilly, chronic skin problems, immune and autoimmune diseases, cardiovascular problems and many types of neurological problems (26,34,35,36,38,45,59,60,69,70,71,75,91,109,148,165,204,212,199,246,255,268-270,290,291,294,

313,343). Amalgam results is chronic exposure rather than acute exposure and accumulation in body organs over time, so most health effects are of the chronic rather than acute in nature, but serious health problems have been documented to be related to amalgam and researchers have attributed some deaths as due to amalgam (356,32,245).

2. Mercury vapor exposure at very low levels adversely affects the immune system(17,27,31,38,45,60,84,118,129, 131,165,226,270,285,296,313,314,355368,369). From animal studies it has been determined that mercury damages T-cells by generating reactive oxygen species(ROS), depleting the thiol reserves of cells, damaging and decreasing the dimension of mitochondria, causing destruction of cytoplasmic organelles with loss of cell membrane integrity, inhibiting ability to secrete interleukin IL-1 and IL-2R, causing activation of glial cells to produce superoxide and nitric oxide, and inactivating or inhibiting enzyme systems involving the sulphydrol protein groups(226,424). Mercury caused adverse effects on both neutrophil and macrophage function and after depletion of thiol reserves, T-cells were susceptible to Hg induced cellular death (apoptosis).(226,272,355) Interferon syntheses was reduced in a concentration dependent manner with either mercury or methyl mercury as well as other immune functions(131), and low doses also induce aggregation of cell surface proteins and dramatic tyrosine phosporlation of cellular proteins related to asthma, allergic diseases such as eczema and lupus(234), and autoimmunity(181,314). One study found that insertion of amalgam fillings or nickel dental materials causes a supression of the number of T-lympocytes(270), and impairs the T-4/T-8 ratio. Low T4/T8 ratio has been found to be a factor in lupus, anemia, MS, eczema, inflamatory bowel disease, and glomerulonephritis. Mercury induced autoimmunity in animals and humans has been found to be associated with mercury's expression of major histocompatibility complex(MHC) class II genes(314,181,226,425c). Both mercuric and methyl mercury chlorides caused dose dependent reduction in immune B-cell production. (316) B-cell expression of IgE receptors were significantly reduced(316,165), with a rapid and sustained elevation in intracellular levels of calcium induced(316,333). Both forms are immontoxic and cytotoxic ant very low levels seen in individuals. Mercury also inhibited B-cell and T-cell RNA and DNA synthesis. The inhibition of these functins by 50 % occurred rapidly at very low levels, in the range of 10 to 25 ug/L. All types of cells exhibited a dose dependent reduct in cellular glutathione when exposed to mercury, inhibiting generation of GSH by lumpocutes and moncytes(252). Workers occupationally exposed to mercury at levels within guidelines have been found to have impairment of lytic activity of neutrophils and reduced abiltiy of neutraphils to kill invaders such as candida(285,404). Immune Th1 cells inhibit candida by cytokine related activation of macrophages and neutraphils. Development of Th2 type immune responses deactivate such defenses(404b). Mercury inhibits macrophage and neutraphil defense against candida by its affects on Th1 and Th2 cytokine effects(181,285). Low doses also induced autoimmuntiy in some species(181,314,404,131,129,43). Another effect found is increase in the average blood white cell count significantly (35). The increased white count usually normalizes after amalgam removal. Mercury also blocks the immune function of magnesium and zinc (198,427,43,38). Several studies found adverse health effects at mercury vapor levels of 1 to 5 mcg/M3 (35). Large numbers of people undergoing amalgam removal have clinically demonstrated significant improvements in the immune system parameters discussed here and recovery and significant improvement in immune system problems in most cases surveryed(Section VI).

3. Mercury from amalgam interferes with production of cytokines that activate macrophage and neutraphils, disabling early control of viruses and leading to enhanced infection(131,251). Animal studies have confirmed

that
mercury increases effects of the herpes simplex veris type 2 for example(131). Both mercuric and methyl mercury were equally highly toxic at the cellular level and in causing cell volume redcuctions(131). However methyl mercury inhibits macrophage functions such as migration and phagocytosis at lower levels.

4. Body mercury burden was found to play a role in resistant infections such as Chlamydia trachomatis and herpes family viral infections; it was found many cases can only be effectively treated by antibiotics after removal of body mercury burden(cilantro tablets were used with followup antibiotics)(251,131). Similar results have been found for treatment of cancer.

5. Mercury by its effect of weakening the immune system contributes to increased chronic diseases and cancer(91,180,237,239,222,234,355,38,40,etc,). Exposure to mercury vapor causes decreased zinc and methionine availability, depresses rates of methylation, and increased free radicals-all factors in increased suscepability to cancer(14,34,38,43,143,144,180,237,239,251,256,283). Amalgam fillings have also been found to be positively associated with mouth cancer(206,251,403).

6. Among a group of patients testing positive as allergic to mercury, low level mercury exposure was found to cause adverse immune system response, including reduction of in vitro production of tumor necrosis factor TNF alfa and interleukin-1. (131,152) Mercury also interrupts the cytochrome oxidase system, blocking the ATP energy function (35,232) and impairing astrocyte function(119).. These effects often result in fatigue and reduced energy levels (35,60,119,140,141,182,202,212,232,235,313).

7. Toxic/allergic reactions to metals such as mercury often result in lichen planus lesions in oral mucosa or gums and play a roll in pathogenesis of periodontal disease. A high percentage of patients with oral mucosal problems along with other autoimmune problems such as CFS have significant immune reactions to mercury, palladium, gold, and nickel(60,118,313,81,90,212,313,342,368,369,375), including to mercury preservatives such as thimersol. 94% of such patients had significant immune reactions to inorganic mercury(MELISA test) and 72% had immune reactions to low concentrations of $HgCl_2$(<0.5 ug/ml). 61% also had immune reaction to phenylHg, which has been commonly used in root canals and cosmetics(313). 10% of controls had significant immune reactions to HgCl and 8.3% to palladium. Removal of amalgam fillings usually results in cure of such lesions. (46,60,75,78,82, 86, 87,90,94,101,118,133,168,313). Other studies of patients suffering from chronic fatigue found similar results(369,375). Of 50 patients suffering from serious fatigue refered for MELISA test(369), over 70% had significant immune reaction to inorganic mercury and 50% to nickel, with most patients also reactive to one or more other metals such as palladium, cadmium, lead, and methyl mercury. Mercury has been found to impair conversion of thyroid T4 hormone to the active T3 form as well as causing autoimmune thyroiditis common to such patients(369,382). In general immune activation from toxics such as heavy metals resulting in cytokine release and abnormalities of the hypothalamus-pituitary-adrenal axis can cause changes in the brain, fatigue, and severe psycholgical symtoms(379-382,385,369,375, 118,60) such as profound fatigue, muscosketal pain, sleep disturbances, gastrointestinal and neurological problems as are seen in CFS, fibromyalgia, and autoimmune thyroiditis. Such symptoms usually improve significantly after amalgam removal. Such hypersensitivity has been found most common in those with genetic predisposition to heavy metal sensitivity(369,60), such as found more frequently in patients with HLA-

Facts about Mercury and Dental Amalgam
(with Medical Study References)

DRA antigens(383). A significant portions of the population appear to fall in this category.

8. Patients with other systemic neurological or immune symptoms such as arthritis, myalgia, eczema, CFS, MS, diabetes, etc. also often recover after amalgam replacement (60,212,313,342,368,369,section VI). Of a group of 86 patients with CFS symptoms, 78% reported significant health improvements after replacement of amalgam fillings within a relatively short period, and MELISA test found significant reduction in lymphocyte reactivity compared to pre removal tests(342,368). The improvement in symptoms and lymphocute reactivity imply that most of the Hg-induced lymphocyte reactivity is allergenic in nature. Although patch tests for mercury allergy are often given for unresolved oral symptoms, this is not generally recommended as a high percentage of such problems are resolved irrespective of the outcome of a patch test(87,86,90,101,168,etc.) Also using mercury in a patch test has resulted in some adverse health effects. A group of patients that had amalgams removed because of chronic health problems, was able to detect subjectively when a patch test used mercury salts in a double blind study(373).

Of the over 3,000 patients tested for lymphocyte reactivity to metals(342,368,375), the following were the percentages testing positive: nickel- 34%, inorganic mercury- 23%, phenol mercury- 13%, gold- 12%, cadmium- 11%, palladium- 11%, silver- 1%. Other studies have also found relatively high rates of allergic reactions to inorganic mercury and nickel(81,etc.). For groups with suspected autoimmune diseases such as neurological problems, CFS, and oral lichen planus; most of the patients tested positive to inorganic mercury and most of such patients health improved significantly and immune reactivity declined after amalgam removal. In a group of patients tested by MELISA before and after amalgam removal at a clinic in Uppsula Sweden, the patients reactivity to inorganic mercury, palladium, gold and phenyl mercury all had highly significant differences from the control group, with over 20 % being hihgly reactive to each of these metals(375). A high percentage were also reactive to nickel in both groups. After amalgam revoval the immune reactivity to all of these metals other than nickel declined significantly, and 76% reported significant long term health improvements after 2 years. Only 2% were worse. The study concluded that immune reactivity to mercury and palladium is common and appears to be allegenic/immune related in nature since immune reactivity declines when exposure levels are reduced. Such studies have also found that deficiencies in detoxification enzymes such as glutathione transfereases cause increased susceptibility to metals and other chemicals(384). Such deficiencies can be due to genetic predisposition, but are also known to be caused by acute or chronic toxic exposures.

For MS and lupus patients, a high percentage tested positive to nickel and/or inorganic mercury.

A patch test was given to a large group of medical students to assess factors that lead to sensitization to mercury(132). 13% tested positive for allergy to mercury. Eating fish was not a significant factor between sensitive and non- sensitized students, but the sensitized group had a significantly higher average number of amalgam fillings and higher hair mercury levels. In a population of dental students tested, 44% were positive for allergy to mercury(156).

9. A high correlation has been found between patients subjectively diagnosed with CNS & systemic symptoms suggestive of mercury intoxication and immune reactivity to inorganic mercury(MELISA test,118) as well as with MRI positive patients for brain damage. 81% of the group with health complaints had pathological MRI results including signs of degeneration of the basal ganglia of the brain, but none in the controls. 60% of the symptom group tested positive for immune system reaction to mercury. Controls without CNS problems did not have such positive correlations. The authors concluded that immune reactions have an important role in

development of brain lesions ,and amalgam fillings induce immune reactions in many patients (91,118)(270,286). Mercury,nickel,palladium, and gold induce autoimmunity in genetically predisposed or highly exposed individuals(314,234,130,342,). Tests have found a significant portion of people to be in this category and thus more affected by exposure to amalgam than others.

10. Low level mercury exposure(as well as other toxic metals) including exposure to amalgam fillings has been found to be associated with increased autoimmune diseases (19, 27,34,35,44,45,60,215,234,268,269,270, 313,314), including lupus(12,60,113,234),Chrons Disease,lichen planus(86,87,90,168), endometriosis (1,9,38,229). Silver also is released from amalgam fillings and stored in the body and has been shown to cause immune complex deposits, immune reactions and autoimmunity in animal studies (77,78,129,314).

11. Mercury exposure through fillings appears to be a major factor in chronic fatigue syndrome(CFS) through its effects on ATP and immune system(lymphocute reactivity, neutraphil activity, effects on T-cells and B-cells) and its promotion of growth of candida albicans in the body and the methylation of inorganic mercury by candida to the extremely toxic methyl mercury form which like mercury vapor crosses the blood-brain barrier and also damages and weakens the immune system(222,225,226,234,235,265,293,60,313,314,342,368,369, 404), and both inorganic and methyl mercury have been shown in animal studies to induce autoimmune reactions and disease in susceptible types through effects on immune system T cells (226,234,268,269,270,314,425,426/272.)

Spatial and temporal changes in intracellular calcium concentrations are critical for controlling gene expression and neurotransmitter release in neurons(432). Mercury alters calcium homeostasis and calcium levles in the brain and affects gene expression and neurotransmitter release through its effects on calcium, etc. Mercury inhibits sodium and potassium (N,K)ATPase in dose dependent manner and inhibits dopamine and noreprenephrine uptake by synaptosomes(288,50,270).

Mercury lymphocyte reactivity and effects on glutamate in the CNS induce CFS type symptoms including profound tiredness, musculoskeletal pain, sleep distubances, gastrointestinal and neurological problems along with other CFS symptoms and fibromyalgia(342,346,368,369). Mercury has been found to be a common cause of fibromyalgia(293,346,369). Glutamate is the most abundant amino acid in the body and in the CNS acts as excitory neurotransmitter(346,386), which also causes inflow of calcium. Astrocytes, a type of cell in the brain and CNS with the task of keeping clean the area around nerve cells, have a function of neutralizing excess glutamate by transforming it to glutamic acid. If astrocytes are not able to rapidly neutralize excess glutamate, then a buildup of glutamate and calcium occurs, causing swelling and neurotoxic effects(119,333). Mercury and other toxic metals inhibit astrocyte function in the brain and CNS(119), causing increased glutamate and calcium related neurotoxicity(119,333,226a) which are responsible for much of the fibromylgia symptoms. This is also a factor in conditions such as CFS, Parkinson's, and ALS(346,416). Animal studies have confirmed that increased levels of glutamate(or aspartate, another amino acid excitory neurotransmitter) cause increased sensitivity to pain , as well as higher body temperature- both found in CFS/fibromyalgia. Mercury and increased glutamate activate free radical forming processes like xanthine oxidase which produce oxygen radicals and oxidative neurological damage(346,142,13). Medical studies and doctors treating fibromylagia have found that supplements which cause a decrease in glutamate or protect against its effects have a positive effect on fibromyalgia. Some that have been found to be effective include Vit B6, methyl cobalamine(B12), L-carnitine, choline, ginseng, Ginkgo biloba,vitamins C and E, nicotine, and omega 3 fatty acids(fish and flaxseed

oil)(417).

V. Medical Studies Finding Health Problems Related to Amalgam Fillings (other than immune)

1. Neurological problems are among the most common and serious and include memory loss, moodiness, depression, anger and sudden bursts of anger/rage(434), self-effacement, suicidal thoughts, lack of strength/force to resolve doubts or resist obsessions or compulsions, etc. Many studies of patients with major neurological diseases have found evidence amalgam fillings may play a major role in development of conditions such as depression(107,109,212,222,271,294,212,229,233,285e,317,320,322), schizophrenia(34,35,295), memory problems(212,222), and other more serious neurological diseases such as MS, ALS, Parkinson's, and Alzheimer's(see # 25.).

Calcium plays a major role in the extreme neurotoxicity of mercury and methyl mercury. Both inhibit cellular calcium ATPase and calcium uptake by brain microsomes at very low levels of exposure(270,288,329,333,432,56,). Protein Kinase C (PKC) regulates intracellular and extra cellular singals across neuronal membranes, and both forms of mercury inhibit PKC at micromolar levels, as well as inhibiting phorbal ester binding(43,432). They also block or inhibit calcium L-channel currents in the brain in an irreversable and concecentration dependent manner. Mecury vapor or inorganic mercury exposure affects the posterior cingulate cortex and causes sysregulation with sufficient exposure(428). Some of the resulting conditions include stomatitis, tremor, ADD, erythism, etc. Metallic mercury is much more potent than methyl mercury in such actions, with 50 % inhibitation in animal studies at 13 ppb(333,329).

Mercury causes decreased lithium levels, which is a factor in neurological diseases such as depression and Alzheimer's. Lithium protects brain cells against excess glutamate and calcium, and low levels cause abnormal brain cell balance and neurological disturbances (280,294,333,33,56). Medical texts on neurology (27,295) point out that chronic mercurialism is often not recognized by diagnosticians and misdiagnosed as dementia or neurosis or functional psychosis or just "nerves". "Early manifestations are likely to be subtle and diagnosis difficult: Insomnia, nervousness, mild tremor, impaired judgment and coordination, decreased mental efficiency, emotional lability, headache, fatigue, loss of sexual drive, depression, etc. are often mistakenly ascribed to psychogenic causes". Very high levels of mercury are found in brain memory areas such as the cerebral cortex and hippocampus of patients with diseases with memory related symptoms (158,34,207,etc.} Mercury interacts with brain tubulin and disassembles microtubiles that maintain neurite structure(207b). Thus chronic exposure to low level mercury vapor can inhibit polymerzation of brain tubulin essential to formation of microtubles. Studeis of mercury studies on animals give results similar to that found the the Alzheimer brain.

Animal studies of developmental effects of mercury on the brain have found significant effects at extremely low exposure levels, levels commonly seen in those with amalgam fillings or in dental staff working with amalgam. One study(175) found mercury vapor decreased NGF concentration in rat's forebrain at 4 parts per billion(ppb) tissue concentration. Another study(134) found general toxicity effects at 1 micromole(uM) levels in immature cell cultures, increased immunoreactivity for glial fibrillary protein at 1 nanamole (0.2 ppb) concentration, and microglial response at even lower levels. Other animal studies on rodents and monkeys have found brain cellular migration disturbances, behavioral changes, along with reduced learning and adaption capacity after low levels of mercury vapor exposure (210,264,287,149). The exposure levels in these studies are seen in the fetus and newborn babies of mother's with amalgam fillings or who had work involving

16. The level of mercury released by amalgam fillings is often more than the levels documented in medical studies to produce adverse effects and above the U.S. government health guidelines for mercury exposure(see previous text).

17. Many studies of patients with major neurological or degenerative diseases have found evidence amalgam fillings may play a major role in development of conditions such as such as Alzheimers (66,67,158,166,204, 207,221,238,242,244,257,295,300), ALS(92,97,325,346,416,423), MS(102,163,170,183,184,212,285,291, 302, 324,326), Parkinson's(98,169,248,250,258,363,56,84),ADD(285e), etc. Mercury exposure causes high levels of oxidative stress/reactive oxygen species(ROS)(13), which has been found to be a major factor in neurological disease(56). Mercury and quinones form conjugates with thiol compounds such as glutathione and cysteine and cause depletion of glutathione, which is necessary to mitigate reactive damage. Such congugates are found to be highest in the brain substantia nigra with similar congugates formed with L-Dopa and dopamine in Parkinson's disease(56). Mercury depletion of GSH and damage to cellular mitochrondria and the increased lipid perxodation in protein and DNA oxidation in the brain appear to be a major factor in Parkinson's disease(33,346). One study found higher than average levels of mercury in the blood, urine, and hair of Parkinson's disease patients(363). Another study(169) found blood and urine mercury levels to be very strongly related to Parkinson's with odds ratios of approx. 20 at high levels of Hg exposure. Increased formation of reactive oxygen species(ROS) has also been found to increase formation of advanced glycation end products(AGEs) that have been found to cause activation of glial cells to produce superoxide and nitric oxide, they can be
considered part of a vicious cycle, which finally leads to neuronal cell death in the substantia nigra in PD(424). Another study (145) that reveiwed occupational exposure data found that occupational exposure to manganese and copper have high odds rations for relation to PD, as well as multiple exposures to these and lead, but noted that this effect was only seen for exposure of over 20 years.

Mercury has been found to accumulate preferentially in the primary motor function related areas such as the brain stem, cerebellum, rhombencephalon, dorsal root ganglia, and anterior horn motor neurons, which enervate the skeletal muscles(48,291,327,329). There is considerable indication this may be a factor in ALS development (48,325,405,416,423). Mercury penetrates and damages the blood brain barrier allowing penetration of the barrier by other substances that are neurotoxic (20,38,85,105,162,301,311/262). Such damage to the blood brain barrier's function has been found to be a major factor in chronic neurological diseases such as MS(286,289,291,302, 324,326). MS patients have been found to have much higher levels of mercury in cerebrospinal fluid compared to controls (163,35,139). Large German studies including studies at German universities have found that MS patients usually have high levels of mercury body burden, with one study finding 300% higher than controls(271). Most recovered after mercury detox, with some requiring addtional treatment for viruses and intestinal dysbiosis. Studies have found mercury related mental effects to be indistinguishable from those of MS (207,212,222,244,271,289,291,302,183,184,324,326).

Low levels of toxic metals have been found to inhibit dihydroteridine reductase, which affects the neural system function by inhibiting brain transmitters through its effect on phenylalanine, tyrosine and tryptophan transport into neurons(122,257,289,372). This was found to cause severe impaired amine synthesis and hypokinesis. Tetrahydro-biopterin, which is essential in production of nerurotransmitters, is significantly decreased in patients with Alzheimer's's, Parkinson's, and MS. Such patients have abnormal inhibition of neurotransmitter production.(supplements which inhibit breach of the blood brain barrier such as bioflavonoids

have been found to slow such neurological damage).

Clinical tests of patients with MND,ALS, Parkinson's, Alzheimer's, Lupus(SLE), and rheumatoid arthritis have found that the patients generally have elevated plasma cysteine to sulphate ratios, with the average being 500%higher than controls(330,331,56), and in general being poor sulphur oxidizers. Mercury has been shown to diminish and block sulphur oxidation and thus reducing glutathione levels which is the part of this process involved in detoxifying and excretion of toxics like mercury(33). Glutathion is produced through the sulphur oxidation side of this process. Low levels of available glutathione have been shown to increase mercury retention and increase toxic effects(111), while high levels of free cysteine have been demonstrated to make toxicity due to inorganic mercury more severe(333,194,56). Mercury has also been found to play a part in neuronal problems through blockage of the P-450 enzymatic process(84).

18. Mercury at extremely low levels also interferes with formation of tubulin producing neurofibrillary tangles in the brain similar to those observed in Alzheimers patients, with high levels of mercury in the brain (207), and low levels of zinc(363,43). Mercury and the induced neurofibrillary tangles also appear to produce a functional zinc deficiency in the of AD sufferers(242),as well as causing reduced lithium levels which is another factor in such diseases. Lithium protects brain cells against excess glutamate induced excitability and calcium influx(280,56). Also mercury binds with cell membranes interfering with sodium and potassium enzyme functions, causing excess membrane permeability, especially in terms of the blood-brain barrier (155,207,311). Less than 1ppm mercury in the blood stream can impair the blood- brain barrier. Mercury was also found to accumulate in the mitochondria and interfere with their vital functions, and to inhibit cytochrome C enzymes which affect energy supply to the brain(43). Persons with the Apo-E4 gene form of apolipoprotein E which transports cholesterol in the blood, are especially susceptible to this damage(207,221,346), while those with Apo-E2 which has extra cysteine and is a better mercury scavanger have less damage. The majority have an intermediate form Apo-E3. This appears to be a factor in susceptablity to Alzheimer's disease, Parkinson's disease and multiple schlerosis. Ones susceptability can be estimated by testing for this condition. In many cases (many thousand documented)removal of amalgam fillings and treatment for metal toxicity led to "cure' or significant improvement in health(see Section V). There is some evidence that some forms of leukemia are abnormal response to antigenic stimulation by mercury or other such toxics and removal of amalgam has led to remission in some cases(35,38,180,239).

19. Mercury and methyl mercury impair or inhibit all cell functions and deplete calcium stores(96). This can be a major factor in bone loss of calcium(osteoperosis).

VI. Results of Removal of Amalgam Fillings

1. For the week following amalgam removal, body mercury levels increase significantly, depending on protective measures taken, but within 2 weeks levels fall significantly.(82,89) Chronic conditions can worsen temporarily, but usually improve if adequate precautions are taken to reduce exposure during removal.

2. Removal of amalgam fillings resulted in a significant reduction in body burden and body waste product load of mercury(75,82,88,89,93,95,115).

Facts about Mercury and Dental Amalgam
(with Medical Study References)

3. Total reduction in mercury levels in blood and urine is often over 80% within a few months(79,82,89,93,115,57).

4. There are extensive documented cases (many thousands) where removal of amalgam fillings led to cure or significant improvement of serious health problems such as periodontal diseases(40,46,57,60,75,78,82,86,87,90, 94,95,100,101,115,133,168,212,222,233,271,313,317,320,321,322,376), oral keratosis(pre cancer)(87,251), immune system/autoimmune problems (8,222,270,271,313,323,368,91,212,229,291,35,etc.), allergies(8,26,40,46,94, 95,97,165,212,222,228,229,233,271,317,322,349,376), asthma(8,75,97,222,228,271,322), chronic headaches/ migraines(5,34,95,212 222,229,233,271,317,322,349,354,115,376), multiple chemical sensitivities (26,95,222,229,232,233, 35,115,313,320,368), epilepsy (5,309,229), blood conditions(212,222,232,233,271, 35,95), eczema (60,212,222, 271,313,317,323,94,376,341), chron's disease(222,229), stomach problems (95,212,222,228,229,233,271,317, 320, 322,35), lupus(12,113,222, 229,233), dizzyness/vertigo(40,95,212,222,271,322,376), arthritis(95,103,212, 222,271,313,322,358), MS(94,95,102,170,212,222,271,291,302,34,35,229), ALS(97,229,423,405,35), Parkinson's/ muscle tremor(222,248,229,271,212,94,98,35), Alzheimer's(204), muscular/joint pain/fibromyalgia (222,293,317,322,369, 94), infertility(9,38,229,367), depression (94,107,222,271,294,212,229,233,285e,317,320,322,376), schizohprenia (294,34,35), insomnia(94,212,222,271,317,322,376), anger(212,233, 320,102), anxiety & mental confusion (94,212,222,229,233,271,317,320,322,57), susceptability to infections (40,222,251,317,349, 350), antibiotic resistant infection(251), endometriosis(229,38), Chronic Fatigue Syndrome (8,60,212,293,229,222, 232,233,271,313,317,320, 368,369,376), tachycardia and heart problems (205,59,94,115,212,222,232,233, 271,306,310,212), memory disorders(94,222),cancer/ leukemia(35,38,94,180), neuropathy/paresthesia (94,212,222,322), vision disturbances(212,271,322), alopecia/hair loss (40,187,271,317,322,349),sinus problems (40,94,222,271,322), tinnitus(94,222,271,349,376), inflamation of eye(222,271,322), psoriasis(385,375,408), skin conditions(212,222), urinary/prostrate problems(212,222), etc., or in significant improvement in symptoms (35,38,40,57,78,86-91,93-103,115,148, 165,168,170,180,182,185,199,204, 212,222,229,233, 234, 235,246, 271,282,289,312,317,320,321,322,323,376). The above over 20,000 cases of cure or significant improvements were not isolated cases of cures; the clinical studies indicated a large majority of most such type cases treated showed significant improvement. Details available and case histories. Some of the above cases used chemical or natural chelation to reduce accumulated mercury body burden in addtion to amalgam replacement. Some clinics using DMPS for chelation reported over 80% with chronic health problems were cured or significantly improved(222,271, 359). Other clinics reported similar success.

Clinical studies have found that patch testing is not a good predictor of success of amalgam remvoal, as a high percentage of those testing negative also recovered from chronic conditions after rplacement of fillings(86,87,168,etc.).

In a large German study of MS patients after amalgam revision, extraction resulted in 85% recovery rate versis only 16% for filling replacement alone (222,302). Other cases have found that recovery from serious autoimmune diseases, dementia, or cancer may require more agressive mercury removal techniques than simple filling replacement due to body burden. This appears to be due to migration of mercury into roots & gums that is not eliminated by simple filling replacement. That such mercury(and simiarly bacteria) in the teeth and gums have direct routes to the brain and CNS has been documented by several medical studies(34,325,etc.).

Among those with chronic immune system problems with related immune antibodies, the types showing the

highest level of antibody reductions after amalgam removal include glomerular basal membrane, thyreeoglobulin, and microsomal thyroid antigens(91)

Swedish researchers have developed a sophisticated test for immune/autoimmune reactions that has proved sucessful in diagnosing and treating environmetally caused diseases such as lichen planus, MS, etc. related to mercury and other immunotoxics(60,313).

Interviews of a large population of Swedish patients that had amalgams removed due to health problems found that virtually all reported significant health improvements and that the health improvements were permanent(233). (study period 17 years) A compilation of an even larger population found similar results(212,282). For example 89% of those reporting allergies had significant improvements or total elimination; extrapolated to U.S. population this would represent over 17 million people who would benefit regarding allergies alone.

VII. Health Effects from Dental Personnel Exposure to Mercury Vapor

1. It is well documented that dentists and dental personnel who work with amalgam are chronically exposed to mercury vapor, which accumulates in their bodies to much higher levels than for most non-occupationally exposed. Adverse health effects of this exposure including subtle neurological effects have also been well documented that affect most dentists and dental assistants, with measurable effects among those in the lowest levels of exposure. Mercury levels of dental personnel average at least 2 times that of controls for hair(397-401), urine(57,64,69,99,123,124,138,171,173,222,249,290,362,397-399) and for blood (124,195,253,249,397). Sweden, which has banned use of mercury in fillings, is the country with the most exposure and health effects studies regarding amalgam, and urine levels in dental professionals from Swedish and European studies ranged from 0.8 to 30.1 ug/L with study averages from 3.7 to 6.2 ug/L (124,172,253,64,68). The Swedish safety guideline for mercury in urine is 5.6 nmol Hg/mmol(11.6 ug/L). Study averages for other countries ranged from 3.3 to 36 microgram/liter(ug/L)(69,70,171,290,397). A large survey of dentists at the Norwegian Dental Assoc. meeting(171) found that the mean mercury level in 1986 was 7.8 ug/L with approx. 16% above 13.6ug/L, and for 1987 found an average of 8.6 ug/L with approx. 15% above 15.8 ug/L, with women having higher levels than men in general. A U.S. national sample of dentists provided by the American Dental Association had an average of 5.2 ug/L (70,290). In that large sample of dentists, 10% of dentists had urine mercury levels over 10.4 ug/L and 1% had levels over 33.4ug/L(290), indicating daily exposure levels of over 100 ug/day. Mercury excretion levels were found to have a positive correlation with the number of amalgams placed or replaced per week, the number of amalgams polished each week, and with the number of fillings in the dentist(171,172,173). In one study, each filling was found to increase mercury in the urine approx. 3%, though the relationship was nonlinear and increased more with larger number of fillings(124). Much higher accumulated body burden levels in dental personnel were found based on challenge tests than for controls(303), with excretion levels after a dose of a chelator as high as 10 times the corresponding levels for controls(57,69,290,303). Autopsy studies have found similar high body accumulation in dental workers, with levels in pituitary gland and thyroid over 10 times controls and levels in renal cortex 7 times controls(99,363,38). Autopsies of former dental staff found levels of mercury in the pituitary gland averaged as high as 4,040 ppb. They also found much higher levels in the brain occipital cortex(as high as 300 ppb), renal cortex(as high as 2110 ppb) and thyroid(as high as 28,000 ppb. In general dental assistants and women dental workers showed higher levels of mercury than male dentists (171,172,173,253,303,362).

amalgam during pregnancy(61).

Epidemiological studies have found that human embryos are also highly susceptible to brain damage from prenatal exposure to mercury. Studies have confirmed that there are vulnerable periods during brain and CNS development that are expecially sensitive to neurotoxic exposures and affect development processes and results(429). The fetal period is most sensitive, but neural developement extends through adolescence. Some conditions found to be related to such toxic exposures include autism, scizophrenia, ADD, dyslexia, eczema, etc. Prenatal/early postnatal exposure to mercury affects level of nerve growth factor(NGF) in the brain and causes brain damage and imbalances in development of the brain (38,119,181, 305,259,210,149,305,24/39,175,255,149). Exposure of developing neuroblastoma cells to sub-cytotoxic doses of mercuric oxide resulted in lower levels of neurofilament proteins than unexposed cells(305). Mercury vapor exposure causes impaired cell proliferation in the brain and organs, resulting in reduced volume for cerebellum and organs and subtle deficiencies(38,305). Exposure to mercury and 4 other heavy metals tested for in a study of school children accounted for 23% of the variation in test scores for reading, spelling and visual motor skills(3). A Canadian study found that blood levels of five metals were able to predict with a 98% accuracy which children were learning disabled(3). Several studies found that mercury causes learning disabilities and impairment, and reduction in IQ(3,21,38,110,264,285c,279). Mercury has an effect on the fetal nervous system at levels far below that considered toxic in adults, and background levels of mercury in mothers correlate significantly with incidence of birth defects and still births (23,38,287,10).

2. Numerous studies have found long term chronic low doses of mercury cause neurological, memory, behavior,sleep, and mood problems(3,34,60,69,70,71,74,107, 108,109,119,140,141,199,212,222,246,255,257, 258,282,290). Neurological effects have been documented at very low levels of exposure(urine Hg< 4 ug/L), levels commonly received by those with amalgam fillings(290). One of the studies at a German University(199) assessed 20,000 people. There is also evidence that fetal or infant exposure causes delayed neurotoxicity evidenced in serious effect at middle age(255,306). Organic tin compounds formed from amalgam are even more neurotoxic than mercury(222,262). Studies of groups of patients with amalgam fillings found significantly more neurological, memory, mood, and behavioral problems than the control groups. (3,34,107,108,109,140,141,199,212,222,290).

A high correlation has been found between patients subjectively diagnosed with CNS & systemic symptoms suggestive of mercury intoxication and immune reactivity to inorganic mercury(MELISA test,118) as well as with MRI positive patients for brain damage. Controls without CNS problems did not have such positive correlations. Mercury,nickel,palladium, and gold induce autoimmunity in genetically predisposed or highly exposed individuals(314,234,130,342). Tests have found a significant portion of people to be in this category and thus more affected by exposure to amalgam than others(see section V).

3. Mercury binds to hemoglobin in the red blood cells thus reducing oxygen carrying capacity(332,35) and adversely affects the vascular response to norepinepherin and potassium. Mercury also increases cytosolic fre calcium levels in lymphocytes in a concentration-dependant manner causing influx from the extracellular medium(270c), and blocks entry of calcium ions into the cytoplasm (1,16,17,21,33,35,333), and at 100 ppb can destroy the membrane of red blood cells(35,22,17,270c) and damage blood vessels- reducing blood supply to the tissues (34,202,306). Amalgam fillings have been found to be related to higher blood pressure, hemoglobin irregularities, tachycardia, chest pains, etc.(201,202,205,212,222,306,310,35). Mercury also

interrupts the cytochrome oxidase system, blocking the ATP energy function(35,232) and impairing astrocyte function(119).. These effects often result in fatigue and reduced energy levels (35,60,119,140,141, 182,202,212,232,235,313). Mercury also accumulates in the heart and damages myocardial and heart valves (Turpayev,in (35)) & (59,201,205,306,351,370). Both mercury and methyl mercury have been shown to cause depletion of calcium from the heart muscle and to inhibit myosin ATPase activity by 50% at 30 ppb(59), as well as reducing NK-cells in the blood and spleen. The interruption of the ATP energy chemistry results in high levels of porphyrins in the urine(260). Mercury,lead, and other toxics have different patterns of high levels for the 5 types of porphyrins, with pattern indicating likely source and the level extent of damage. The average for those with amalgams is over 3 time that of those without, and is over 20 times normal for some severely poisoned people(232,260). The FDA has approved a test measuring porphyrins as a test for mercury poisoning. However some other dental problems such as nickel crowns and root canals also can cause high porphyrins.

4. Patch tests for hypersensitivity to mercury have found from 2% to 44% to test positive (87,154,156, 178, 267), much higher for groups with more amalgam fillings and length of exposure than those with less. In studies of medical and dental students, those testing positive had significantly higher average number of amalgam fillings than those not testing positive(and higher levels of mercury in urine(132,156). Of the dental students with 10 or more fillings at least 5 years old, 44% tested allergic. Based on these studies and statistics for the number with 10 or more fillings, the percent of Americans allergic to mercury just from this group would be about 17 million people especially vulnerable to increased immune system reactions to amalgam fillings. However, the total would be much larger and patch tests do not measure the total population getting toxic reactions from mercury. The most sensitive reactions are immune reactions, DNA mutations, developmental,enzyme inhibition, and systemic effects(34,38,61,149,186,226,263,264,270,272,296,305,410-412/357).

5. People with amalgam fillings have an increased number of intestinal microorganisms resistant to mercury and many standard antibiotics. (35,116,117,161,389) Recent studies have found that drug resistant strains of bacteria causing ear infections, sinuitis, and pneumonia moe than doubled since 1996, and similar for strains of bacteria in U.S. rivers(53). Studies have found a significant correlation between mercury resistance and multiple antibiotic resistance (116,117,161,369), and have found that after reducing mercury burden antibiotic resistance declines(251,389,40).

6. Mercury from amalgam binds to the -SH (sulphydryl) groups, resulting in inactivation of sulfur and blocking of enzyme function, producing sulfur metobolites with extreme toxicity that the body is unable to properly detoxify(33,114). Sulfur is essential in enzymes, hormones, nerve tissue, and red blood cells. These exist in almost every enzymatic process in the body. Blocked or inhibited sulfur oxidation at the cellular level has been found in most with many of the chronic degenertive diseases, including Parkinson's, Alzheimer's, ALS, lupus, rheumatoid arthritis, MCS, autism, etc(330,331,56). Mercury also blocks the metabolic action of manganese and the entry of calcium ions into cytoplasm(333). Mercury from amalgam thus has the potential to disturb all metabolic processes(25,21,33, 35,56,60,111,180,194,197}. Mercury is transported throughout the body in blood and can affect cells in the body and organs in different ways.

7. A large study of 20,000 subjects at a German university found a significant relation between the number of

amalgam fillings with periodontal problems, neurological problems, and gastrointestinal problems(199). Allergies and hair-loss were found to be 2-3 times as high in a group with large number of amalgam fillings compared to controls(199,9). Levels of mercury in follicular fluid was significantly higher for those with amalgam fillings (9,146). Based on this finding, a Gynecological Clinic that sees a large number of women suffering from alopecia/hair loss that was not responding to treatment had amalgams replaced in 132 women who had not responded to treatment. 68 % of the women then responded to treatment and alopecia was alleviated(187). In other studies involving amalgam removal, the majority had significant improvement (40,317). Higher levels of hormone disturbances, immune disturbances, infertility, and recurrent fungal infections were also found in the amalgam group. The results of hormone tests, cell culture studies, an intervention studies agree(9,146). Other clinics have also found alleviation of hair loss/alopechia after amalgam removal and detox(40,317). Another study in Japan found significantly higher levels of mercury in gray hair than in dark hair(402).

8. Mercury accumulates in the kidneys with increasing levels over time. One study found levels ranging from 21 to 810 ppb. Mercury exposure has been shown to adversely affect kidney function in occupational and animal studies (20,203,211,260,etc.), and also in those with more than average number of amalgam fillings(254).. Inorganic mercury exposure has been found to exert a dose-dependent cytotoxicity by generating extremely high levels of hydrogen peroxide, which is normally quenched by pyruvate and catalase(203). HgCl2 also has been found to impair function of other organelles such s lysomomes that maintain transmembrane proton gradient, and to decrease glutathione peroxidase activity in the kidneys while upregulating heme oxidase function. The Government's toxic level for mercury in urine is 30 mcg/L (189), but adverse effects have been seen at lower levels and low levels in urine often mean high mercury retention and chronic toxicity problems.

9. Amalgam fillings produce electrical currents which increase mercury vapor release and may have other harmful effects(19,27,28,29,30,35,100,192,194). These currents are measured in micro amps. The central nervous system operates on signals in the range of nano-amps, which is 1000 times less than a micro amp(28). Negatively charged fillings or crown appear to cause higher mercury vapor losses(35). Some studies have also found persons with chronic exposure to electromagnetic fields(EMF) to have higher levels of mercury excretion(28).

10. Mercury from amalgam fillings is transferred to the fetus of pregnant women and children who breast feed at levels often higher than those of the mother(18,19,20,23,31,38,61,112, 186,281). Mercury has an effect on the fetal nervous system at levels far below that considered toxic in adults, and background levels of mercury in mothers correlate significantly with incidence of birth defects and still births(10,23,38,197,210,287,361). Mercury vapor exposure causes impaired cell proliferation in the brain and organs, resulting in reduced volume for cerebellum and organs and subtle deficiencies(38,305).

11. Since mercury(all forms) is documented from studies of humans and animals to be a reproductive and developmental toxin(23,38,61,105,186,224,255,287.305,etc.), mercury can reduce reproductive function and cause birth defects and developmental problems in children(2,4,9,10,20,23,24,31,37,38,39,41,55,61,104,146,159, 162,224,255). Clinical evidence indicates that amalgam fillings lead to hormone imbalances that can reduce fertility(9,38,55,4,105,146,367). Mercury has been found to cause decreased sperm volume and motility ,increased sperm abnormalities and spontaneous

abortions, increased uterine fibroids/endometritis, and decreased fertility in animals(4,104,105,162) and in humans(9,105,146,159,395,433,27,35,38). In studies of women having miscarriages or birth defects, husbands were found to typically have low sperm counts and significantly more visually abnormal sperm(393). Subfertile males in Hong Kong were found to have 40% more mercury in their hair than fertile controls(55). Studies in monkeys have found decreased sperm motility, abnormal sperm, increased infertility and abortions at low levels of methyl mercury(162,365). Researcher's advise pregnant women should not be exposed to mercury vapor levels above government health standards (2,19,25,227, 61,100,182,282,366); currently U.S. ATSDR mercury health MRL of 0.2 mcg/M3 which is exceeded by any dental work involving amalgam(Section III). Many governments have bans or restrictions on use of amalgam by women of child-bearing age.

12. Mercury causes breaks in DNA (4,38,41,42,197,272,296). Low non-cytotoxic levels of mercury induce dose dependent binding of mercury to DNA and significantly increased cell mutations (142,4) and birth defects(197,38,105).

13. Mercury has been well documented to be an endocrine system disrupting chemical in animals and people, disrupting function of the pituitary gland, hypothallamus, thyroid gland(50,369), enzyme production processes(111,194,33,56), and many hormonal functions at very low levels of exposure (9,105,146, 210, 312,369). The pituitary gland controls many of the body's endocrine system functions and secretes hormones that control most bodily processes, including the immune system and reproductive systems(105,312). The hypothallamus regulates body temperature and many metabolic processes. Mercury damage thus commonly results in poor bodily temperature control, in addtion to many problems caused by hormonal imbalances. Such hormonal secretions are affected at levels of mercury exposure much lower than the acute toxicity effects normally tested. Mercury also damages the blood brain barrier and facilitates penetration of the brain by other toxic metals and substances (311). Low levels of mercuric chloride also inhibit ATPase activity in the thyroid, with methyl mercury inhibiting ATP function at even lower levels(50). Both types of mercury were found to cause denaturing of protein, but inorganic mercury was more potent. These effects result commonly in a reduction in thyroid production(50) and an accumulation in the thyroid of radiation. Toxic metal exposure's adverse influence on thyrocytes can play a major role in thyroid cancer etiology(144) . Among those with chronic immune system problems with related immune antibodies, the types showing the highest level of antibody reductions after amalgam removal include thyreoglobulin and microsomal thyroid antigens(91)

14. There has been no evidence found that there is any safe level of mercury in the body that does not kill cells and harm body processes(WHO,183,189, etc.). This is especially so for the pituitary gland of the developing fetus where mercury has been shown to accumulate and which is the most sensitive to mercury(2-4,19-24,30,31,36-44,61,186).

15. Low levels of mercury and toxic metals have been found to inhibit dihydroteridine reductase, which affects the neural system function by inhibiting transmitters through its effect on phenylalanine, tyrosine and tryptophan transport into neurons(27,98,122,257,289,372,342). This was found to cause severe impaired amine synthesis and hypokinesis. Tetrahydrobiopterin, which is essential in production of neurotransmitters, is significantly decreased in patients with alzheimer's, Parkinson's, and MS. Such patients have abnormal inhibition of neurotransmitter production. Such symptoms improved for some patients after administration of 5-formyltetrahydrofolate or tyrosine(257).

cleaning teeth. Face masks worn by dental workers filter out only about 40% of small dislodged amalgam particles from drilling or polishing, and very little mercury vapor(247,). Dental staff have been found to have significantly higher prevalence of eye problems, conjunctivitis, atopic dermatitis, and contact urticaria(247,156,74).

An epidemiological survey conducted in Lithuania on women working in dental offices(where Hg concentrations were < 80 ug/M3) had increased incidence of spontaneous abortions and breast pathologies that were directly related to the length of time on the job(277a). A large U.S. survey also found higher spontaneous abortion rate among dental assistants and wives of dentists(193), and another study found an increased risk of spontaneous abortions and other pregnancy complications among women working in dental surguries(277b). A study of dentist and dental assistants in the Netherlands found 50% higher rates of spontaneous abortions, stillbirths, and congenital defects than for the control group(394), with unusually high occurance of spina bifida. A study in Poland also found a significant positive association between mercury levels and occurrence of reproductive failures(401).

5. Body burden increases with time and older dentists have median mercury urine levels about 4 times those of controls, as well as higher brain and body burdens(1,34, 68-74,99), and poor performance on memory tests(68, 69,70,249,290) Some older dentists have mercury levels in some parts of the brain as much as 80 times higher than normal levels(14,34,99). Dentists and dental personnel experience significantly higher levels of neurological, memory, musculoskeletal, visiomotor, mood, and behavioral problems, which increase with years of exposure (1,34,68-73,88,123,188,246,247,248,249,290,369,395). Even dental personnel with relatively low exposure(urine Hg<4 ug/l) were found to have significant neurological effects(290) and was found to be correlated with body burden of mercury. Most studies find dentists have increased levels of irritability and tension(1), high rates of drug dependancy and disability due to psychological problems(15), and higher suicide rates than the general white population (284), but one study found rates in same range as doctors.

6. Female dental technicians who work with amalgam tend to have increased menstrual disturbances (275,401,10,38), significantly reduced fertility and lowered probability of conception (10,24,38,121), increased spontaneous abortions (10,38,277,433), and their children have significantly lower average IQ compared to the general population (1,279,38,110). Populations with only slightly increased levels of mercury in hair had decreases in academic ability(3). Effects are directly related to length of time on the job(277). The level of mercury excreted in urine is significantly higher for female dental assistants than dentists due to biological factors (171,172, 173,247). Several dental assistants have been diagnosed with mercury toxicity and some have died of related health effects(32,245,246,247,248). From the medical register of births since 1967 in Norway, it can be seen that dental nurse/assistants have a clearly increased risk of having a deformed child or spontaneous abortion(433). Female dentists have increased rates of spontaneous abortion and perinatal mortality(193,38,10,433)),compared to controls. A study in Poland found a much higher incidence of birth defects among female dentist and dental assistants than normal(10). A chronically ill dental nurse diagnosed with mercury sensitivity recovered after replacement of fillings and changing jobs(60), and a female dentist recovered from Parkinson's after mercury detox(248). Some studies have found increased risk of lung, kidney, brain, and CNS system cancers among dental workers(14,34,99,143,283).

7. Many homes of dentists have been found to have high levels of mercury contamination used by dentists bringing mercury home on shoes and clothes(188).

Facts about Mercury and Dental Amalgam
(with Medical Study References)

VIII. Scientists and Government Panels or Bodies That Have Found Amalgam Fillings to be Unsafe.

1. A World Health Organization Scientific Panel concluded that there is no safe level of mercury exposure(183,189,208). The Chairman of the panel, Lars Friberg stated that "dental amalgam is not safe for everyone to use(208,238). A study of dental personnel having very low levels of mercury excretion found measurable neurological effects including memory, mood, and motor function related to mercury exposure level as measured by excretion levels(290). and found no threshhold level below which effects were not measurable.. Other studies have found measurable effects to the immune, cardiovascular, hormonal, and reproductive systems from common levels of exposure(Section IV). Studies have found significant measurable adverse health effects at levels far below current government regulatory levels for mercury(290).

2. In 1987 the Federal Dept. of Health in Germany issued an advisory warning against use of dental amalgam in pregnant women(61). Most major countries other than the U.S. have similar or more extensive bans or health warnings regarding the use of amalgam, including Canada, Great Britain, France, Austria, Norway, Sweden, Japan, Australia, New Zealand, etc. A Swedish National Mercury Amalgam Review Panel found that "from a toxicological point of view, mercury is too toxic to use as a filling material"(164). A major amalgam manufacturer, Caulk Inc., advises that amalgam should not be used as a base for crowns or for retrograde root fillings as is commonly done in some coutries(387). A Swedish medical panel unanimously recommended to the government "discontinuing the use of amalgam as a dental material"(282). The U.S. EPA found that removed amalgam fillings are hazardous and must be sealed airtight and exposed of as hazardous waste(214). Most European countries require controls on dental waste amalgam emissions to sewers or air. A Canadian Government study for Health Canada concluded that any person with any number of amalgam fillings receives exposure beyond that recommended by the USPHS Standard(209). Many of those researching amalgam related health effects including several very prominent scientists have concluded that the health effects are widespread and serious so that mercury should not be used as a filling material (1,18,19,20, 36,38,57,60,61,88,94,99,125,148, 153,164,170,183,208, 209,210,212,222, 227,236, 238,282).

3. The use of mercury amalgams has been banned for children and women of child-bearing age or put on a schedule for phase out by several European countries. The use of amalgam is declining in Europe and Germany's largest producer of amalgam has ceased production, The director of the U.S. Federal program overseeing dental safety advises against using mercury amalgam for new fillings.

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Facts about Mercury and Dental Amalgam
(with Medical Study References)

Mercury levels in blood of dental professionals ranged from 0.6 to 57 ug/L, with study averages ranging from 1.34 to 9.8 ug/L (124,195,253,249). A review of several studies of mercury level in hair or nails of dentists and dental workers found median levels were 50 to 300% more than those of controls(38, p287-288,& 10,16,178). A group of dental students taking a course involving work with amalgam had their urine tested before and after the course was over. The average urine level increased by 500% during the course(63). Allergy tests given to another group of dental students found 44% of them were allergic to mercury(156). Studies have found that the longer time exposed, the more likely to be allergic. Another group of dental students had similar results(362), while another group of dental student showed comprimized immune systems compared to medical students. The total lympocyte count, total T cell numbers(CD3), T helper/ inducer(CD4+CD8-), and T suppressor/cytotoxic(CD4-CD8+) numbers were singinficantly elevated in the dental students compared to the matched control group(407).

Urinary porphyrin profiles were found to be an excellent biomarker of level of body mercury level and mercury damage neurological effects, with coprorphyrin significantly higher in those with higher mercury exposure and urine levels(70,260). Coproporphyrin levels have a higher correlation with symptoms and body mercury levels as tested by challenge test(69,303), but care should be taken regarding challenge tests as the high levels of mercury released can cause serious health effects in some, especially those who still have amalgam fillings or high accumulations of mercury. Screening test that are less burdensome and less expensive are now available as first morning void urine samples have been found to be highly correlations to 24 hour urine test for mercury level or porphyrins(73).

2. The average dental office exposure affects the body mercury level at least as much as the workers on fillings(57,64,69,123,138,171,173,303), with several studies finding levels approximately the same as having 19 amalgam fillings(123,124,173). Many surveys have been made of office exposure levels(1,6,7,10, etc.) The level of mercury at breathing point in offices measured ranged form 0.7 to over 300 micrograms per cubic meter(ug/M3) (120,172,253,249). The average levels in offices with reasonable controls ranged from 1.5 to 3.6 ug/M3, but even in Sweden which has had more office environmental controls than others spot levels of over 150 ug/M3 were found in 8 offices(172). Another study found spot readings as high as 200 ug/M3 in offices with few controls that only used saliva extractor(120). OSHA surveys find 6-16% of U.S. dental offices exceed the OSHA dental office standard of 50 ug/M3. The U.S. ATSDR mercury vapor exposure MRL for chronic exposure is much lower, 0.2 ug/M3 (217) (giving approx. 4 ug/day exposure), similar to U.S. EPA and Health Canada guidelines(2,209). Thus most office mercury levels were found to far exceed the U.S. guidelines for chronic mercury exposure.

Use of high speed drill in removal or replacement has been found to create high volume of mercury vapor and respirable particles, and dental masks to only filter out about 40 % of such particles(219,247). This produces high levels of exposure to patient and dental staff. Use of water spray, high velocity evacuation and rubber dam reduce exposure to patient and dental staff significantly, as seen in previous discussion. In addition to these measures researchers also advise all dental staff should wear face masks and patients be supplied with outside air(120,153). Some studies note that carpeting in dental offices should be avoided as it is a major repository of mercury(188,7)

Use of such measures along with a Clean-Up™ aspirator tip was found to reduce exposure to patient and staff approximately 90%(397).

3. Dentists were found to score significantly worse than a comparable control group on neurobehavioral tests

of motor speed, visual scanning,and visuomotor coordination(69,70,123,249,290,395), concentration , verbal memory, visual memory(68,69,70,249,290,395), and emotional/mood tests(70,249,290,395). Test performance was found to be proportional to exposure/body levels of mercury(68,70,249,290,395). Significant adverse neurobehavioral effects were found even for dental personnel receiving low exposure levels(less than 4 ug/l Hg in urine)(290). This study was for dental personnel having mercury excretion levels below the 10th percentile of the overall dental population. Such levels are also common among the general population of non- dental personnel with several fillings. This study used a new methodology which used standard urine mercury levels as a measure of recent exposure, and urine levels after chelation with a chemical, DMPS, to measure body burden mercury levels. Chelators like DMPS have been found after a fast to release mercury from cells in tissue to be available for excretion. This method was found to give enhanced precision and power to the results of the tests and correlations. Even at the low levels of exposure of the subjects of this study, there were clear demonstrated differences in test scores involving memory, mood, and motor skills related to the level of exposure pre and post chelation(290). Those with higher levels of mercury had deficits in both memory, mood, and motor function compared to those with lower exposure levels. And the plotted test results gave no indication of there existing a theshhold below effects were not measurable. Mood scores including anger were found to correlate more strongly with pre chelation urine mercury levels; while toxicity symptoms, concentration, memory(vocabulary,word), and motor function correlated more strongly with post-chelation mercury levels.

Several dentists have been documented to suffer from mercury poisoning(72,74,193,246,247,248,369), other than the documented neurological effects. One of the common effects of chronic mercury exposure is chronic fatigue due to immune system overload and activation. Many studies have found this occurs frequently in dentists and dental staff along with other related symtoms- lack of ability to concentrate, chronic muscular pain, burnout, etc.(249,369.377.378). In a group of dentists and dental workers suffering from extreme fatigue and tested by the immune test MELISA, 50% had autoimmune reaction to inorganic mercury and immune reactions to other metals used in dentistry were also common(369). Tests of controls did not find such immune reactions common.

One dentist with severe symptoms similar to ALS improved after treatment for mercury poisoning(246), and another with Parkinson's disease recovered after reduction of exposure and chelation(248). Similar cases among those with other occupational exposure have been seen. A survey of over 60,000 U.S. dentists and dental assistants with chronic exposure to mercury vapor and anesthetics found increased health problems compared to controls, including significantly higher liver, kidney, and neurological diseases(99,193). Other studies reviewed found increased rates of brain cancer and allergies(99,193). Swedish male dentists were found to have an elevated standardized mortality ratio compared to other male academic groups(284). Dental workers and other workers exposed to mercury vapor were found to have a shortening of visual evoked potential latency and a decrease in amplitude, with magnitudes correlated with urine excretion levels(190). Dentists were also found to have a high incidence of radicular muscular neuralgia and peripheral sensory degradation(190,395).

4. Both dental hygienists and patients get high doses of mercury vapor when dental hygienists polish or use ultrasonic scalers on amalgam surfaces(240,400). Pregnant women or pregnant hygienist especially should avoid these practices during pregnancy or while nursing since maternal mercury exposure has been shown to affect the fetus and to be related to birth defects, SIDS, etc.(23,37,38,110,142,146,19,31). Amalgam has been shown to be the main source of mercury in most infants and breast milk, which often contain higher mercury levels than in the mother's blood (20,61,112,186,287). Because of high documented exposure levels when amalgam fillings are brushed(182,222,348) dental hygienist are advised not to polish dental amalgams when

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Dr. Vasken Aposhian, Dept. Head, Molecular and Cellular Biology, Univ. Of Arizona; Dr. David Eggleston, Univ. Of Califoria, researcher on mercury in the brain; Dr. Boyd Haley, Univ. Of Kentucky reasearcher on mercury in the brain and Alzheimer's Disease (http://www.altcorp.com/); Dr. Gustav Drasch, Univ. Of Munich, reaearcher on mercury in brains of dead infants and fetuses; Dr. D. Echeverria, Neuro-Toxicologist, researcher on reproductive problems and birth defects in dental workers; BBC Panorama Program on Dental Amalgam:"The Poison in Your Mouth", June 1994.

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PERSONAL ACCOUNTS OF DENTAL AMALGAM MERCURY ILLNESS

Submitted to Committee on Government Reform

July 18, 2000

Mercury In Medicine
Are We Taking Unnecessary Risks?

Compiled by: Freya B. Koss
For Consumers for Dental Choice

The stories contained herein were submitted via the Internet for this hearing , a previous National Academy of Sciences workshop on *The Toxcicological Effects of Mercury* and to the organization DAMS, (Dental Amalgam Mercury Syndrome).
These are just a few of 1,000's of stories of victims of mercury toxicity from dental amalgams.

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Call: (610) 649-2606

Date: July 18, 2000

Fax: 202 265-6564

From: Dr. Hal Huggins
Phone: 719 593-9616
Fax: 719 548-8220

Subject: **Congressional Hearing on Dental Mercury/Personal Story**

To whom may be concerned:

Regarding mercury in dental fillings

Since my introduction to mercury toxicity from silver-mercury amalgam dental fillings in 1973, I have treated over two thousand patients who had adverse reactions to that material. I have many more thousands of blood tests indicating changes in these patients.

I have treated over 1000 patients with Multiple Sclerosis with about an 85% success rate. Spinal taps have confirmed the dramatic changes in proteins in the spinal fluid. Videos have showed stunning improvements, yet it seems that the American Dental Association values its patent rights for amalgam more than the health of millions of people in our nation.

Ten years ago I returned to the University to obtain a post doctoral masters in science. I concentrated on immunology and toxicology. This information has been very helpful in learning to treat Lou Gehrig's disease, arthritis, chronic fatigue, diabetes, Alzheimer's, Parkinson's and a variety of other autoimmune type diseases.

Most recently, we applied our protocol to Gulf War Disease, and obtained a 6 out of 6 case total improvement. This was one of our biggest challenges, and we were delighted to see the response, for there are many people who could benefit from help.

Mercury from fillings is similar to handcuffing a person. They can still walk, climb stairs, perhaps feed themselves, but should something knock them down, it is very difficult to get up.

The elimination of mercury from fillings (proved to be the largest single exposure to mankind) would eliminate many autoimmune diseases and render the current ones more treatable. It is appalling that so many people are effected, and so few people are willing to help them. Are you willing to help people with these controllable diseases?

We have about 900 hours of patient videos before and after dental revision should anyone be interested in seeing what can happen. We also have a few books on the topics and a few thousand blood chemistry reports that indicate what has happened to these patients.

Sincerely,

Hal A. Huggins DDS, MS

Environmental Dental Association
PO Box 2184
Rancho Santa Fe, CA 92067
(619) 586-7626
Fax (619) 756-7843
eda1@ix.netcom.com

Gloria Markus, Esq.
2185 Rayburn House Office Building
Washington, DC 20515

Dear Gloria Marcus,

It is my understanding that Congressman Dan Burton is interested in looking into the issue of dental amalgam. Amalgam contains about 50% mercury (an element more poisonous that lead or arsenic). This mercury gasses off of the surface and is quickly taken into the body. The Environmental Dental Association encourages Congressman Burton in his efforts because he will receive pressure against him from the ADA etc.

Sincerely,

Grant H. Layton, D.D.S.

Sent 5-5-00

Grant Layton

To: ADA

From: Dr. Stuart Scheckner, DMD – A Disabled Dentist

June 13, 2000

Gentlemen:

I am a disabled dentist. Please take what I have to say extremely seriously.

In 1978, my office receptionist was assisting me in preparing amalgam since my dental assistant was sick. She inadvertently spilled 800 grams (3/4 lb.) of mercury from a Caulk dispensing bottle into deep shag carpeting adjacent to my dental operating chair in 1978. I never heard of a dentist being poisoned with mercury so I did not take the spill seriously. Several months later, I had varied symptoms of tremors, nausea, diarrhea, and occasional anxiety. My pulse was higher than normal. I went to my physician, and he thought it was stress related and had me work out with him at the local YMCA. I mentioned the mercury spill, and his exact words which I shall never forget were: "Forget about it, just stay away from it." He never performed a urine mercury test, and years later in a letter to a friend physician of mine stated he was told about the mercury spill but no urine mercury level was available. This type of ignorance regarding the effects of mercury, diagnosis, and treatment are typical in my experience. I had no one to help me.

It was not until 1984 when I was completely disabled and had read something about the symptoms of mercury poisoning from a translation of the head German chemist in 1927, Dr. Alfred Stock, that I related my symptoms to mercury poisoning. I called the American Dental Association for help. I told them that my hair analysis showed 15 parts per million by one lab. This was confirmed by another lab several months later with a new hair sample. This amount was 18 parts per million. My urine mercury level was .1 parts per million. Since my urine mercury level was so low, the ADA told me that I could not possibly be mercury poisoned. I could site peer review research that a low mercury urine level does not necessarily disclude mercury toxicity, but that is not my intent in this letter. Albeit to say just that a low urine mercury level in 1984 when the mercury exposure occurred from 1978 to 1980 does not disclude damage from mercury exposure.

I have studied thousands of pages of documentation. I would like to request your assistance. I am asking you not to have a defensive position of amalgams but a scientific position. The statement that dental amalgam has been used for over 150 years without incident is not scientific but defensive and anecdotal. The statement that once mercury is combined with dental silver, it's toxic properties are made inert is not a scientific statements. Mercury does escape from an amalgam. The ADA's position is that this amount is too minute to make a difference. I want you to have an open mind so you can assist me in the scientific research for the truth.

Urine mercury levels from very low mercury vapor exposure is not a key criteria for a diagnostic test. There may be people with low urine mercury levels with more symptoms than those with higher levels. The effect of mercury on RNA sequencing has never been pursued. I am asking for your assistance to help me with this research project. I have personal results that show damage to my RNA.

Sincerely,

Stuart Scheckner, DMD

Battle with Mercury Poisoning - one-hundred million amalgams are placed per year

Doctors Don't Believe In Mercury Poisoning!

Date: 1/16/00 10:24:42 AM Eastern Standard Time
From: Beansalot
To: lhollida@nas.edu
CC: Fre Koss

MISDIAGNOSED: MULTIPLE SCLEROSIS OR A BRAIN TUMOR

To: Committee - Toxicological Effects of Mercury

Dear Ms. Holliday,

I am writing to you in hopes that the story of my battle with mercury poisoning will help put a stop to this toxic substance being used as a dental filling material in the United States. As I understand it, one-hundred million amalgams are placed per year (statement made by ADA a couple of years ago).

Approximately four years ago, my left big toe went numb. Over the course of a week, the numbness moved up my leg, into my arm and into my face prompting me to seek medical attention. I had a CAT scan and a blood test which revealed nothing. My M.D. referred me to a neurologist who told me that I most likely had MS or a brain tumor and needed an MRI. I had to wait an agonizing two weeks until I could get in for the MRI.

Subsequent tests (blood, urine, MRI) showed nothing abnormal. Eventually, I had a spinal tap, spent ten days at the Mayo Clinic in Minnesota and came home with a clean bill of health. The only problem was the persistent pain and numbness in my left side. The symptoms would come and go at first, then fatigue set in and all of the symptoms became constant. Over a period of two years my health deteriorated gradually until it became quite difficult to take care of my two children or even to drag myself out of bed.

All the while I continued to see doctor after doctor, most of whom prescribed anti-depressants because there was no physical manifestation of illness, so they decided it must be psychological. I never got any relief from these drugs, as a matter of fact, they seemed to make me feel worse. I was beginning to experience more and more strange symptoms; ringing in the ears (used to come and go, now constant), fluid leaking from the ears while sleeping, neck pain and headaches, heart palpitations, a feeling of falling backwards while drifting off to sleep, dizziness, night sweats, memory loss, confusion, always feeling cold (especially hands and feet), loss of balance, quick to anger, intolerant of loud noises, chronic yeast and probably some symptoms that I am forgetting right now.

(2) From: Kim Horton, 1/16/2000
To: Committee- Toxicological Effects of Mercury

Upon doing some research into these symptoms on the Internet, my husband came across some information on mercury poisoning. He suggested that I look into it, and I thought it was crazy. It wasn't until he prompted me to check it out again about three months later that I decided it was worth a shot. What I read chilled me to the bone. Every symptom that I had experienced was listed and more. I had a mouthful of amalgam (fourteen teeth in all) and realized that it had been poisoning me gradually for years.

I went back to my doctor and told him that I had found the answer, that I was poisoned by mercury. He refused to believe that it was true and even showed me a reference in his medical journal that stated that mercury, when used in dental restorations is not harmful. I have not found a doctor yet (other than holistic healers) who will admit that mercury in dental work can poison you.

I still suffer from most of the symptoms listed above and have four old crowns to replace before I have all the mercury out of my teeth. Getting it out of my body will be a life-long endeavor, but one I am totally committed to, as I to regain as much of a normal life as possible. I will do all I can to see that the use of amalgam as a suitable material for dental work is stopped. After all, mercury is toxic before they put it in your mouth and treated as toxic waste after it is removed from your mouth, yet many claim it is 100% safe while it's IN your mouth. This makes absolutely NO sense to me.

Thank you for taking an interest in this topic and helping us convince others that there is no place for mercury in the human body.

Sincerely,
Kim Horton

(2) Christy's Story

represented himself to be the epitome of what I was looking for. Why he even was just getting his degree as a naturopath! I paid him...lots of money to replace my amalgam fillings with composite and to replace my caps with porcelain. And his secretary was none too nice about collecting it either. During the series of appointments, I remember thinking I was coming down with something. On several occasions I attempted to reschedule but his secretary threatened me with a hefty no show fee if I changed my appointment. So I went - sick and all.

I couldn't figure it out. Here I had all the metal out of my mouth and I felt horrible. I could hardly function! The doctors insinuated it was stress and I may have emotional problems...Huh? Well I was certainly emotional. Who wouldn't be feeling the way I did? So maybe I did have emotional problems. But...I was sooo tired. I didn't have enough energy to have emotional problems. By now my marriage had failed and I was raising two small children alone. I was self-employed and did everything in my power to operate from my bed because I didn't have the strength to get up. I had to rest and sleep all the time. My children became so accustomed to it they just thought this was normal. I became so apathetic that I just wished I would die. If it were not for my drive to be there for my children, I might have. I honestly don't know how I survived. I had no one to help me really. My mother was beside herself doing what she could. I had batteries of tests done. Nothing.

Somehow time marched on. I kept reading everything I could lay my hands on that might give me a clue as to what my problems were. I devised ways around my maladies, one day at a time. I investigated every avenue of possibilities assuming my dental work was fixed. After doing everything else I finally came to the conclusion after another degree's worth of study that my dental metal was not..."fixed."

As you might imagine, by now I could ill afford any dental work to be done. I tried three dentists in my area. All of which, promised to one thing and began to change their tune when I got into the chair to the tune of $250 worth, you know cleaning, x-rays, etc. Oh and by the way, I wasn't feeling any better either.

Finally I was referred to a mercury free dentist who practiced to remove mercury, root canals, and cavitations. Even with him, it took an entire year to find all the mercury that had been insidiously hidden by my former dentist in the hopes of precipitating new business for himself. I had new developed arthritis, chronic fatigue, (obviously), I had difficulty working and thinking, I couldn't remember how to spell, I had short term memory loss severely, I could not remember how to pronounce certain words nor could I retain them after correcting it, I sometimes I could not read my own handwriting or remember where I put things, I had to write everything down or I would forget it and I sometimes would forget where I put my notes that I wrote down so I wouldn't forget things... I had a plethora of chronic nagging symptoms that could not be explained. Last but not least, I began to develop liquid filled cysts in my breasts. During my new dental revision, there was so much electricity being generated by the nickel/porcelain crowns on my lower molars that my dentist was forced to remove them at the same time as my tongue had developed burn cankers adjoining each cap.

That was approximately two years ago. I am going to be 48 years old in August. I am finally feeling more "normal". I still have bad days but more good ones than bad. It used to be the opposite. I recently discovered that both my children, now 18 and 21, are metal poisoned from my dental work in vitro. They have no dental work of their own but they have exactly the same nine metals that showed up on my tests. I have the tests to prove it.

How do I feel? I am ready. I am ready to do whatever it takes. I am cool at a deep passionate level. I will not apathetically pass by a system that let me grow up believing that I was protected against such atrocities to find out I was on my own. I have lost an incredible amount of quality of life during the prime of my life...with my children. I will not leave this legacy to my children or anyone else's children either. I am the epiphany of the saying that there is no fury like a mother's wrath. This will change and it will be now. I will fight to save the thousands and thousands of my brothers, sisters and children on this globe who are imprisoned and kept ill by diseases that are claimed to be incurable. I have religion of a different type. I know I will and others who walk beside me will succeed. I believe the truth will prevail. You know, good guys, white hats and all... it's happening as we speak. I will not let our sufferings go unnoticed!

Submitted by Christy Diemond, Founder, www.universityofhealth.net for the education of how to get well.

July 10, 2000

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Building
Washington, DC 20514

RE: **Dental Amalgam Mercury – Sleep Apnea**

Dear Congressman Burton:

There was a survey taken of something like 1500 people that had their amalgams removed, which is noted in the book "Dental Mercury Detox" by Michael Ziff, DDS. Ziff. In this survey, the vast majority of people showed improvements or cure from insomnia and fatigue

My personal experience:
I was suffering from insomnia. Within ONE DAY of removing my first quadrant, my insomnia condition improved and still slowly continues to get better. (7 1/2 months post-amalgam).

Sincerely,
Don
condit@jps.net (DPCondit)

Now that some patients are learning which tests to demand there are even papers in the medical literature stating, e. g. that an abnormal result on tests like fractionated urine porphyrins doesn't actually mean that the patient has abnormal porphyrins if they claim they have something like multiple chemical sensitivity or amalgam illness that EVERYONE KNOWS is psychosomatic. I gather that medical education has declined to the point where MD's don't read their own textbooks - when I checked that one in standard medical school texts they all agreed that the porphyrins are made by the LIVER, not the BRAIN, and that elevated porphyrins CAUSE emotional problems rather than being due to them.

You can certainly see why the present state of affairs has many physicians confused - if they search medline they find abstracts saying that amalgam illness is psychosomatic and the abnormal results from the test the patient insisted on don't mean anything. Few practicing physicians have the time or inclination to get the actual papers and check to see if the abstracts accurately portray the results.

I will leave it to you to speculate on the politics that led to the current state of affairs. All I can say about it is that there is a need for clear regulatory action to ban amalgam, and for a public pronouncement on the part of appropriate government agencies that many people really do have chronic mercury poisoning from their amalgam fillings.

Please do let me know if you would like any further detail on the above, or if you need this letter in hard copy rather than electronic form.

Sincerely yours,

Andrew Cutler

Christy's Story

I was 8 years old when I had my first visit to the dentist. Before it was over, I had 4 gold crowns and several amalgam fillings placed. Oh of course, a stern lecture on drinking too much pop and brushing my teeth properly. I remember that during one appointment in particular, the dentist was using a hammer to place my cap, pop it out, exclaim exclamatories laced with profanity, put the cap back in, pop it out, exclaim again and so on. I used to have special permission arranged to leave my grade school and walk to the dentist's office during the school year. This walk usually entailed a great deal of thought anticipating the dentist's next behaviors during our next visit.

Within a few short months my eyes began to inexplicitly water as if I were crying. I remember asking my mother why I was crying because I wasn't sad. Within 6 months, I began to have my first hay fever symptoms. Soon, in order to function, I was completely dependent on Dimatapp, an antihistamine, prescribed by my medical doctor. The side affects from this caused me at the age of 8 on to have to sleep for about 3 days straight for my body to acclimate at the beginning of each hay fever season.

During 7th through 9th grade, I began to think I was stupid because all of a sudden, I could not retain my studies. I could not fully comprehend math. I had gone from an average "A" student to barely passing in all my classes. I was lucky I made it into high school.

When I arrived in high school, I arrived just wishing I could be as smart as other kids. I managed to get ok grades so I didn't try very hard thus I had an excuse for getting ok grades.

By the time I hit college, community college then a 4 year, I spend the entire time fighting off "viruses" every 4 weeks. Inevitability the "bug" would hit me at finals. I honestly don't know how I made through getting my degree. It must have been sheer will.

During the first year of my marriage I had restorative dentistry done and I had my two wisdom teeth removed. My big toes on each foot became numb for two months after the wisdom teeth removal. My doctor, who I quickly deducted to be a complete idiot, walked into my appointment so convinced that I had ingrown toenails, he sported the tools to fix it in his hand before he even examined me. He couldn't figure it out and within a short month I became so ill, I could not find the strength to go to the bathroom without someone helping me. I suddenly developed endometriosis and an ovarian cyst which I prompted was placed in the hospital for surgery. Supposedly all my problems were a result of the endometriosis. No one ever questioned my dental work.

After the surgery, the doctor recommended that I become pregnant because if I didn't now, he feared I would never be able to conceive. And besides, this would give the surgery time to heal with no cycles thus the endometriosis would dry up. So I became pregnant. I even nursed for nine months for good measure thinking I was doing my baby such a good service. I was very tired. I swore I would die before I allowed anyone near me with a scalpel again. It took a very long two years to regain my life.

When I weaned my baby, after nine months of nursing, within a short period of time, I began to experience the same symptoms as before. I began to think that I believed this doctor and paid him all this money to get well, and I wasn't well and I wasn't getting what I paid for either. I was desperate. So I did something REALLY crazy. I didn't tell anyone, I went to a local naturopathic college, paid them $10 for a health screen special and walked away with a year's worth of life style changes to get well.

Over the next year of following their advice and many mega supplements, I began to feel better. That is until I had some repair work done on my teeth. Then I decided to have my second child. Funny, I conceived right away.

It was two and a half years since my first pregnancy and although I felt stronger than during the first pregnancy, I developed walking pneumonia during nursing and could not shake it. I was forced to wean the baby, who was not ready to be weaned.

I still could not shake the pneumonia after 3 months. I began to have trouble breathing and asthma. There was not any food I could safely eat without rotating it. I went from a normal weight of 120 lbs to a gaunt 98 lbs in about three weeks. I was...dying. So I returned to the naturopathic college to find that I now had developed food allergies. Amazingly a homeopathic remedy was prescribed for me and in three weeks I was recovered! My reproductive symptoms began to clear up as well. I thought this homeopathy to be pretty amazing stuff so I began to learn about it and study it. I was about 30 years old then.

Keeping my health was certainly a struggle all the time, but if I was careful during the next few years, the homeopathic medicine seemed to keep me and the children in the saddle for the most part. We survived.

In my quest for health I came across a book about mercury in fillings. I decided that it really fit and I called around to find a dentist who knew about these kinds of things. When I was about 32, I found one who

Virginia Cuny
5200 Arden Way, Apt 161B
Carmichael, CA 95608

July 13, 2000

Committee on Government Reform

RE: Urging you to Ban Mercury in Medicine

Dear Chairman Burton:

I understand there will be Congressional Hearing on "Mercury in Medicine" by the Committee on Government Reform in the House of Representatives. I am very concerned about the practice of using mercury in dentistry and urge you start the process that would eliminate it totally from medicine.

For years I have studied about the dangers of this element. The EPA has classified amalgams as a hazardous waste. If so how can the dentists continue to use it? Mercury is a highly toxic metal... dentists are given very strict regulations about handling and disposing of it. That in it's self should be a red flag. Why are they permitted to put poison in our teeth?

Many research studies indicate that when we chew our food, mercury vapors are released from the fillings into our mouths and absorbed into our bodies. For years dentists themselves have disputed the dangers of mercury.

It also poses an environmental problem. When the mercury is removed in the dental office, few clinics have the proper equipment to contain it from being pasted in the waste. Also, when a person dies if the mercury isn't removed from the teeth it goes back into the earth when the person is buried or cremated.

Once I heard on TV a new process that would eliminate the need of putting mercury in vaccinations. Who ever knew they put mercury in vaccinations. To think we have been having our children injected with it!

AGAIN I URGE YOU TO PUT A STOP TO USING MERCURY IN MEDICINE.

Thanking you in advance for your time.

Sincerely,

Virginia Cuny
doug.ose@mail.house.gov

Dohenwend, BZ. (1)

bj: "Mercury in Medicine" Hearings - U.S. House of Representatives
Date: 7/12/00 12:04:30 AM Eastern Daylight Time
From: cdohrenwend@email.msn.com (Carolyn Dohrenwend)
To: freedom1@extremezone.com (James V. Durlacher), frekoss@aol.com

To: The Honorable J.D. Hayworth, AZ

Sent: Email Over house.gov web site July 11, 2000

Re: "Mercury in Medicine" Hearings

CC:

Fax to Representative Henry Waxman, CA 202-225-3976
Fax to Representative Dan Burton, IN 202-225-0016
Fax to Representative Christopher Shays, CT 202-225-5541
Fax to Representative Jim Turner, TX 202-225-2401

It is my understanding that hearings are going to be held on July 18, by the Committee on Government Reform of the U.S. House of Representatives on "Mercury in Medicine".

1. I am writing first on the topic of "Mercury in Dentistry".

I have never been advised by the dentists in any of the following states that when they were putting silver colored fillings called amalgams that they were putting mercury in my mouth. I have lived in the following states as an adult and have had amalgams put in: IN, CT, TX, AL, and AZ.

Additionally, I have never been advised about the potential dangers of the mercury in amalgams by the dentist in any of these states. Nor have any of these dentists ever asked if I had kidney problems prior to placing amalgam fillings.

It is my understanding that under AZ law, a dentist could loose their license if they advise me of the dangers of the mercury in amalgams.

About 1 year ago, I was diagnosed with mercury toxicity. The source of the mercury toxicity was dental fillings. The symptoms I had included extreme dizziness, fatigue, and impaired thinking.

I had the visible dental fillings removed. The levels of mercury in my blood stream were elevated by 50% following the removal of these fillings and confirmed by a test called a DMPS challenge. All my symptoms worsened substantially after the removal of the fillings.

About 9 months later, I also had nickel crowns removed and there was more mercury fillings underneath. During this removal, I had blood in my urine for a number of weeks following the additional removal of the fillings because of the stress that the mercury puts on the kidneys.

Dohrenwend #2 (2)

I have been told that leaving the amalgams in place when putting on a crown is a very common dental practice. I was never advised in either CT or AZ that the mercury fillings were being left under the crowns or any potential dangers.

I am still detoxifying from the mercury and probably will be for another year. Chronic mercury poisoning can occur simply from the action of chewing. I am concerned about the long term impact on my kidneys and my health.

It is hard to summarize the impact the mercury toxicity has had my health, my career, or my family. I am a full-time working single parent and I have been through the hardest year of my life physically, emotionally, and mentally. It has also cost thousands of dollars in both medical and dental bills.

I urge you to support the elimination of the use of amalgam fillings.

2. I am writing on the subject of "Mercury in Medicine". It is my understanding that congressional hearings have been held by Dan Burton, IN on the use of mercury and aluminum in children's vaccines and flu shots.

Both my adopted daughters, ages 12 and 11 show accumulation of mercury and aluminum. They do not have any amalgam fillings. The suspected source of the metal toxicities is their childhood vaccines. Mercury without some proactive detoxification will remain for decades. There are studies that show the toxicity of these metals to the brain as well as the kidneys.

I was never advised about the mercury or aluminum content in these vaccines or their potential dangers. I was also never asked in either of my children had kidney problems.

I also urge you to support the elimination of the use of mercury and aluminum in vaccines.

3. Let me close by relaying a story. A mercury thermometer was broken at a school in Flagstaff, AZ a number of months ago. The school was evacuated and a hazardous clean up crew was sent in complete with the hazardous substance suits.

I am appalled that a substance that is considered an environmental toxin is still being used in both dentistry and medicine in this country. How could a substance that is hazardous to the environment not also be hazardous to humans?

I urge you to support the elimination of toxic metals in both dentistry and medicine.

Thank you for your time and your attention to this matter.

Best regards, Carolyn Dohrenwend, Gilbert, AZ

Earl

July'2000

Congressman Dan Burton
Committee on Government Reform

SHORT TERM MEMORY LOSS, DEPRESSION, FATIGUE, ALLERGIES

Dear Congressman Burton:

Consider having mercury removed from the teeth. I did, and got rid of considerable depression and memory problems. It also eliminated many illnesses and fatigue, as well as allergy symptoms.

I had amalgam removed, and had immediate relief from many distressing problems, including very expensive allergies. In fact, my antihistamine budget of one thousand dollars per year and increasing yearly, has more than paid for the cost of amalgam removal since 1990. My antihistamine budget dropped to nearly nothing almost immediately, huge stress levels were reduced, short-term memory problems were drastically reduced, and I could eat all the citrus wanted without lichen outbreaks.

Long term memory was not affected. Short-term memory had become so poor that I had to often look at a phone number seven times while dialing. I also often went back into the house for something I had forgotten, only to realize that I had forgotten what I went back in there for, sometimes requiring three trips back in before I got the forgotten item!

The problem disappeared with amalgam removal.

Earl

Ebert

January'2000

Personal Account of Melody Ebert's Experiences with Mercury Amalgams

Multiple Sclerosis and Endometriosis

Multiple Sclerosis and Endometriosis became a thing of the past for me after I had nine mercury amalgams removed at age 30. At age 25, unexplained fatigue began to plague me, followed by an endless array of symptoms that would come and go. At first some of the symptoms were just nuisances and I wondered if it was my imagination.

Some areas affected were balance, thinking, memory, concentration, and bladder (frequency and urgency). My hands were clumsy and several times I fell down for no apparent reason. Sometimes my arms were weak or sore, other times it was my legs, wrists or ankles. Also, tingling, numbness and brief sharp pains would come and go in different directions. I was often irritated and had serious mood swings. Menstrual cramps brought on excruciating pain. Prescription painkillers were useless. Diarrhea and severe cramps would strike without warning. For the past ten years, I had an unquenchable thirst and drank water constantly. I also had extremely thick calluses covering the bottoms of both feet.

The fatigue gradually worsened until it was controlling my life. I was not looking for a cure, but after researching the mercury issue, I realized it would be crazy not to have the amalgams removed. After the first four of nine amalgams were removed and I stepped out of the dentist's chair, I immediately noticed two changes. For the first time since I could remember, I was not thirsty. Also, I felt very calm and relaxed. Two weeks later, the last five amalgams were removed and replaced with composites. The fatigue started to lift immediately. One year after having the mercury amalgams removed, almost all of my energy has returned. The thick calluses on my feet are slowly being replaced with new skin. All other symptoms were mostly gone immediately. My immune system is much stronger now and my muscles rarely get stiff and sore from hard work, as they often did before.

I praise God for leading me to the answer to my health problems and whenever possible, I will help spread the truth about the dangers of mercury.

Melody Ebert
1505 8th St.
Keosauqua, Iowa 52565
319-293-2571

Fechner

Date: 1/12/00 6:01:39 PM Eastern Daylight Time

To: FreKoss@aol.com
To: lhollida@nas.edu (Laura Holliday)

Re: Manic Depression and amalgams

To: Commission for Toxicological Effects of Mercury

Dear Ms. Holliday:

I had nine amalgams by the time I was 27, and I suffered from manic depression.

I worked as a pipe fitter at a refinery in South Texas in extreme heat for up to 16 hours a day. I got to where the only thing I could hold on my stomach was beer. Can you imagine, manic depression, those working conditions and surviving on beer? I crashed and burned my house down. After the fire, I contacted my mother for help.

Since my life had totally fallen apart and I was suicidal, she put me in a psychiatric hospital for 3 days. Then she took me to a dentist and had him remove my amalgams, and to a doctor for a candida/mercury detoxification program.

I'm 39 years old now and I have not had another manic depressive episode. My health has been good and I've been a productive member of society. I'm also a father of seven healthy children who do not have amalgams.

Layne Fechner
4026 Cork Dr.
Corpus Christi TX 78413

Fellon (11

July 11, 2000

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Building
Washington, DC 20514

RE: **Dental Amalgam Mercury**

Dear Congressman Burton:
MY NAME IS GINA, I am 30 yrs. of age, and was perfectly normal and healthy or so I thought. I was running the Lancome counter for cosmetics (managing) and was doing great! Then... I went to the dentist to take care of my teeth back in June. My teeth had lots of cavities. Neglect to take care of them along with sugar and coffee as my daily meals.

I went to a dentist after he told me I had 10 cavities in my mouth. The first one he did was a bad cavitiy. It took the dentist 3 1/2 hours to do this. He seemed to be having trouble with this tooth, as it was way in the back and hard to reach he said. Well, I was concerned. I never heard of a dentist taking this long for anything not even my wisdom teeth that were pulled took 1/2 hour. I still went to the same dentist and he moved to the tooth next to this one, and he said he was going to do three cavities in this visit in an hour and half. He did two ... and then the next visit I went back and told him of this pain I was having in the teeth he just filled. He spent the visit filing the first tooth I was still having pain.

To make a long story short .. he only worked on 5 teeth and I started a month after that having pain in my mouth and a white coating on my tongue. Months this went on. My dentist would not agree that my tongue was coated, and he just asked me to scrape my tongue and that is when I noticed how bad it was. Scraping my tongue would not make it go away. Then I had this metal chemical, bleach taste in my mouth. It would not go away. The dentist said it was normal and probably would go away in time. Then my tongue was burning and it felt like acid was burning away at my tongue and it hurt. My saliva glands had changed and now my saliva was turning into foam ... my tongue was dry no matter how much I drank water, (3 gallons a day). It would not penetrate my tongue.... it was so dry. I went to my family doctor and he put my on Nystatin because I had thrush. I was on that for 10 days and went back to the dentist ,and he ordered more Nystain for me and still I had thrush . He then put me on a foot fungus for 10 days, and it still did not go away. Every time I went to the dentist my foam got e

I heard about amalgam fillings and told the dentist maybe I was allergic to them. He said no, and said that my tongue was normal and I didn't have thrush. I asked him if he would remove one of my fillings. He did and I swallowed half of it. He didn't protect me with a rubber dam. He didn't believe me. After that about an hour later I had hives all over my face and heat down my throat on my neck and on my jaw foaming was

worse and my tongue felt like acid was burning holes in. I called for an emergency but they never called back .. so I asked my husband to call ..he said to go to drug store and get benedryl allergy. I was upset crying thinking I was dying and no one could help but My health and energy was gone .. my face breaking out .. hives on my neck.

Thinking I had a very serious disease, I took an HIV test and was fine and thyroid AND OTHER BLOOD TEST IT WAS FINE ... all were negative. I went back to the dentist he sent me to a root canal specialist , who said he would not do it till they found out why my tongue was coated. I told him to tell my dentist that because he said it was normal. Ii was distressed. I told the root canal dentist that it started the dentist who filled my teeth. He sent me to an allergist who said I had glausitis (he didn't even test me) he said i didn't have symptoms of allergy. He said I had a vitamin b vitamin deficiency .
I took lots of vitamin B and it didn't go away. I went to another dentist who said my tongue was fine . I was crying in his chair. He said I had a hole in my root canal tooth and scraped it out and asked if that was the taste I was having. He took out the old temporary and put in a new temporary in my root canal, and I started feeling better and my tongue was getting pinker. well that took a week and the foaming was back and then the white coating and burning.

Finally, I read your letter someone gave to me. It was from Jean Griffin. She is a DAMS coordinator in the Boston area. I didn't know her but she had problems from amalgam. Your letter sounded like me. I went to a DENTIST who specializes in amalgam removal, and uses nothing but white special fillings. He tests my teeth and said there was a lot of electrical currant coming from one tooth the highest he has ever seen. Amalgam filling that could fill five teeth! That was the first filling the first dentist put in and it took him 3 hours to fill (not exaggerating). Well, the dentist took out all my Amalgam fillings and the root canals are next. I am feeling better. My tongue is bright red, however, I still have yeast candida, and am on a special diet. I take vitamin C intravenous to help build my immune system and strength.

I had to writ e to you because I felt like was alone and dying . The doctors think I'm nuts. The DDS (dentist) I go to now, Dr. Ganong, is a member of DAMS and understands how to take out fillings safely.

IT'S GOING TO TAKE AWHILE FOR ME TO FEEL LIKE MYSELF.

I NEED SOMEONE TO TALK TO THAT KNOWS ABOUT THE SYMPOTMS AND RECOVERY, AND DAMS (DENTAL AMALGAM MERCURY SYNDROME SUPPORT GROUP) HAS HELPED ME SO MUCH. IM AM 31 YEARS OF AGE.

Sincerely,
GINA FELLER
GMARIE85@AOL.COM
(508)833-4945

Ferreira (1)

Anne Ferreira
22 Neff Drive
Hampton, VA 23669-1153

March 8, 2000

Congressman Dan Burton
2157 Rayburn House Office Building
Washington DC 20515

Dear Congressman:

I am writing to you in regard to dental amalgam fillings, commonly called "silver fillings", which are literally so close to the brain of millions of Americans. The public is health conscious, but unaware of what is being placed on their teeth when they have a cavity filled. Silver fillings or amalgams have never been approved by the Federal Drug Administration (FDA) although they have been used for over 160 years. There have been thousands of scientific research papers written and published worldwide on the toxicity of amalgams. The contents of amalgams is approximately 50% mercury, 35% silver and the remaining 15% consisting of copper, tin, and zinc. The mercury is used because of its binding properties. However, mercury is one of the most toxic substances known to man, more toxic than lead, arsenic and cadmium. There is no safe level of mercury. It is not a question of being allergic. It is extremely poisonous. This is even more crucial with children. How can we tolerate the poisoning of our children – the future of our country?

I would like to share my personal experience and how mercury/silver fillings have affected my health and how difficult it was to have it diagnosed. I experienced long and intense sensations of tingling and numbing on top of my head, eyes, face, and a sharp shooting pain in my head. A neurologist ordered a MRI of the brain. It revealed brain lesions. The doctor told me that it was normal and that he saw it in lots of patients. According to him, it was due to the aging process (I was then 48 years old). He could not explain what was causing the problem. I was left untreated and forced to go to another doctor who gave me beta blockers after reviewing the MRI. I was given high blood pressure medicine to carry oxygen to the brain. I actually had low blood pressure. Nothing helped! I felt weak, sick and unable to function. Doctors were unable to diagnose the problem. I had several other symptoms: heart palpitations, fibromyalgia, cold extremities, high sensitivity to noise, sudden episodes of nervousness and anxiety, candidas, severe digestive problems, low immune function, food and chemical allergies, very low energy level, and extreme fatigue. Lying in bed, many times, I wished I could stop breathing because it was exhausting.

Doctors ordered lab work and the results were within normal range. They could not help me. I had a doctor, at Walter Reed Army Medical Center, tell me that "It is all in your head; you are making up the symptoms". What a way to add insult to injury! Doctors are not trained to diagnose mercury toxicity. They are ignorant of its symptoms. I had faith in

Ferreira (e)...

God and prayed every day that I would get relief and be able to find a doctor who could help me.

In November 1996, I went to see a Doctor in Maryland. He ordered a hair analysis for toxic metals. When I went back one month later for a follow-up visit, I found out I had aluminum, nickel and a very high level of mercury – 11.7 parts per million (ppm). The "normal" level considered tolerable is 1.1 ppm. I had another hair analysis done two months later and the mercury level had gone up to 12.6 ppm. My Doctor recommended I have all the amalgam fillings and all other metals removed from my teeth.

I had a difficult time finding a toxic-free dentist. I was told to get educated on the issue by a dentist in Richmond and when I was ready, to tell the dentist exactly what to do. I was in tears, sick, very weak and frightened, and now I was to get educated? I learned quickly that it is "unethical" for a dentist to talk about the mercury in amalgams and that if he does, he is at great risk of losing his license. I went to a dentist in North Carolina who refused to talk to me about the dangers of amalgams, but measured the electrical charges in my teeth. I had high negative charges (-22) on the top right molar and I had positive charges. I understand, from my research, that dissimilar metals and water (saliva) have a battery effect and create electricity. One amalgam generates one thousand times more electricity than what the nerve ending needs to function. Once I had the metals removed, the tingling, numbing sensation disappeared. The electrical charges were eliminated.

My health is improving, but I still have to deal with the mercury poisoning. I still have a long way to go. One must wonder how many millions of dollars are spent and the diagnoses are missed due to mercury toxicity and high electrical current in the mouth due to dissimilar metals. I know I am one of thousands and maybe millions of people that have come to recognize that mercury amalgams have been a major contributor to health problems. Yet, the public is not aware of the magnitude of this problem and that the FDA has a medwatch to report adverse reactions to dental materials.

I ask that you do not delay, but give priority to investigate as soon as possible this major health issue.

According to the EPA, dental amalgams are a highly toxic waste before placing it in the teeth and after removal from the teeth. What is it, when in the person's mouth? I would appreciate your help as a public servant to protect the public. I have done a lot of research on this issue, which I can provide you. My home phone is 757 – 851-4805. My e-mail is virginia@portone.com . Please advise if I can be of further assistance. Anything you can do to achieve any or all of the above objectives would be deeply appreciated.

Sincerely,

Anne Ferreira

Ferreira (3)

HAIR MULTIELEMENT ANALYSIS REPORT

DOCTOR'S DATA
P.O. Box 111
170 W. Roosevelt Rd.
West Chicago, IL 60185 U.S.A.
630/231-3649

LAB. NO.: 97021-0741 ACCT.: 4494
PATIENT: Anne Ferreira AGE: 43 SEX: F
DOCTOR: Ahmad Shamim MD
OFFICE:

SAMPLE SIZE: 0.19 g
SAMPLE TYPE: head hair
DATE SAMPLED: 01/16/1997
DATE IN: 01/21/97
DATE OUT: 01/24/97
OFFICE CODE: 2-2
ICP-MS analyzed
RACE: caucasian
HAIR COLOR: brown
HAIR PREPS:
SHAMPOO:

Elements Regarded As Toxic

TOXIC ELEMENTS	PATIENT LEVEL (parts per million)	ONE STANDARD DEVIATION ABOVE MEAN	TWO STANDARD DEVIATIONS ABOVE MEAN → HIGH	MORE THAN TWO STANDARD DEVIATIONS ABOVE MEAN
Aluminum	5	9		
Antimony	0.056	.15		
Arsenic	0.029	.15		
Beryllium	<dl .002	.03		
Bismuth	0.048	.3		
Cadmium	0.027	.25		
Lead	0.6	4.0		
Mercury	12.67	1.5		
Nickel	0.46	0.7		
Platinum	<dl .001	.02		
Silver	0.03	0.4		
Thallium	<dl .001	.05		
Thorium	<dl .001	.01		
Tin	<dl .016	0.8		
Uranium	0.040	.2		
TOTAL TOXIC REPRESENTATION				

Ratios

	PATIENT RATIO	EXPECTED RANGE
CA/MG	53.5	5- 15
CA/P	20.3	2.5- 6.5
MG/K	23.7	1.5- 6.0
NA/K	0.7	1.5- 4.0
ZN/CU	9.2	5- 11
ZN/CD	>999	>800

Elements Regarded As Nutrients

NUTRIENT ELEMENT	PATIENT LEVEL (parts per million)	LOW ◆ REFERENCE RANGE ● HIGH	NUMERICAL VALUE OF REFERENCE ◆ RANGE ●
Calcium	3810		350- 860
Magnesium	71		40- 110
Sodium	2		18- 87
Potassium	3		8- 38
Copper	42		13- 35
Zinc	382		125- 155
Iron	5		6- 15
Manganese	0.37		0.30- 0.75
Chromium	0.63		0.80- 1.25
Cobalt	0.042		0.020- 0.045
Vanadium	0.030		0.009- 0.080
Molybdenum	0.040		0.030- 0.080
Boron	<dl .008		0.80- 2.80
Iodine	0.4		0.3- 1.2
Lithium	<dl .007		0.050- 0.120
Phosphorus	188		144- 216
Selenium	1.518		0.950- 1.700
Strontium	11.03		1.00- 7.60
Sulfur	44981		48000- 52500

Other Elements

ELEMENT	PATIENT LEVELS	EXPECTED RANGE	ONE STANDARD DEVIATION HIGH →	TWO STANDARD DEVIATIONS HIGH →
Barium	4.23	0.40- 2.50		
Germanium	0.049	0.003- 0.028		
Gold	<dl .001	0.020- 0.150		
Titanium	0.078	0.100- 0.700		
Zirconium	0.132	0.020- 0.500		

COMMENTS:
After
Detoxification

Laboratory Work Performed By Doctor's Data Laboratories, Inc. CLIA ID #14D0646470 COPYRIGHT 1995 Doctor's Data Inc.
James T. Hicks, MD, PhD, FCAP - Laboratory Director

dl=detection limit, n/a=currently not available, qns=quantity not sufficient

Finland

INFERTILITY FROM DENTAL AMALGAMS
FROM: FINLAND

My family has a long history of amalgam, starting from my grandparents. Both my parents had amalgam fillings as well. My older sister was born over 2 months premature and the doctors said she was lucky to survive. My parents wanted to have another baby soon after my sister was 1 yr, but it took 5,5 years before I was born. I had several allergies and an infantile atopic dermatitis. Most of my amalgam fillings were made when I was 5-15 years old. Now I'm 36 years, still allergic to fish, animal epitel and some pollen and my complexion is dry, atopic.

When I was in my late twenties, I noticed I was loosing a lot of hair. I had plenty of it, so I didn't really worry. I was around 30 years when my tummy troubles started. We were having a Christmas dinner when a terrible diarrhea struck me and it has been my loyal companion ever since.

A long jorney from one doctor to another followed. They took blood and stool tests, lactose intolerance and celiac disease tested negative, nothing was found in ultrasound, colonoscopy and gastroscopy. The doctors gave up, said it's probably colon irritabile and that I would just have to learn to live with it.

I got married in 1993 and in 1995 we had a house, a car and steady jobs and decided it was time to have a baby. We tried for 8 months before the pregnancy test was positive. On week 8 I saw the tiny little creature with a heartbeat. We were in seventh heaven, our life seemed absolutely perfect. On week 13 I had a miscarriage, for unknown reasons. The doctors kept telling us that 40% of all pregnancies end up in a miscarriage, often in such an early stage that the mother-to-be doesn't even know she has been pregnant. We were told to try again.

We tried for a year and then went to an infertility clinic. After thorough examinations we were assured that as they could find no reason for our infertility and as we had succeeded already once, our chances of having a baby with infertily treatment was good. After 4 failed intrauterine inseminations and 4 unsuccesful in vitro fertilisations they told us to give up and consider adoption. It goes without saying that we were heartbroken, not that adoption was a bad alternative, but we ached for a biological child.

The doctors did not know why the treatments did not work for us. They still had not found any clear medical reasons for our infertility. However, time after time we got less egg cells, the quality of the embryos got worse and my endometrial lining refused to thicken. The lining should ideally be at least 10 mm at the time of the embryo transfer, mine was never more than 7 mm even though I was on heavy estrogen medication.

We insisted on having some more blood tests to see if our problems were autoimmune related. My rheumatoid factor test came back positive and a few months later I was diagnosed a very rare autoimmune disease (systemic connective tissue disease) called CREST which, by the way, is quite common among a native North American tribe, the choctows. CREST is short for Calcinosis, Raynauds, Esophageal Dysfunction, Sclerodactyly,Telangiectasia. (More info http://hometown.aol.com/REDAPRIL4/index.html).

Finland

I started diligently to dig up information on CREST as even the doctors did not know much about it. I found an enourmous amount of information from the Net and even some personal experience stories which were very helpful when negotiating with my doctors. We started our 5th IVF and demanded to use mini heparin shots, baby aspirin and Prednison which in the States have proven to be useful in similar cases. Unfortunately we failed once again and were emotionally so exhausted that we decided to give it a rest.

My diarrhea was still going strong, I was tired and had no energy. My hair loss got worse, I had strange red, couperosa like rash on my cheeks & nose and my eye sight was "funny". A friend of mine had been on an antioxidant diet & had her amalgam fillings removed a few years back and suggested the same to me. I went to see her doctor who took one look in my mouth and stated that the root of my problems was there.

I started the antioxidant diet, including A, B, C, E vitamins, Se, Cu, Mg, Mn, Zn, fish oil etc. among others. My tummy troubles got better, but cyclically, there were better days and worse. I felt that I was on the right path but then I got a stomach flu virus and was back in square one again with the diarrhea.

(By the way, I had been on antioxidants for little more than a month when I went to rheumatoid factor tests again. The results were negative! The doctor was dumbfounded.)

I continued taking the antioxidants, and had my amalgams (16) removed all at once by a dentist specialized in amalgam removals. It was surprisingly easy and I got no symptoms after the removal, but the diarrhea was the same as before.

I went to see the antioxidant doctor again and got some new medicines that seem to have helped. My removal was a month ago and I'm anxiously waiting to see some improvement, I'm confident there is going to be some!

I am certain that amalgam has had at least some affect on our infertility problems. Maybe it has caused the diarrhea, which has kept me painfully slender (BMI around 17) and that has affected the reproductive system somehow. I do not know enough about amalgam to make more elaborate conclusions, but I KNOW there is a connection.

Godsey(1)

MY DENTAL FILLINGS WERE POISONING ME

by Linda R. Godsey
maggierac@earthlink.net

The lab results were in; after four years of declining health and the futility of seeing six doctors and three dentists I finally had a diagnosis. I was suffering from **mercury poisoning!** By the time I saw Dr. Arlette Pharo D.O. I was terribly ill; just being on my feet long enough to brush my teeth was a real effort. According to the lab report my mercury level at 16 ppb was equivalent to heavy industrial exposure. How could this be, I had never worked in any industry let alone one where I might be exposed to this heavy metal.

Although it was a relief to finally have a diagnosis, I was also somewhat skeptical about the accuracy of the lab test. Where and how could I have been exposed to mercury? As part of discussing my health history I casually mentioned that in the past 8 years I had almost continuously been undergoing various dental work, much of it filling replacement resulting from previous inferior dentistry; whereupon the doctor asked to look in my mouth. While noting the number of fillings and crowns Dr. Pharo informed me that silver amalgam dental fillings contained mercury. She then suggested that I see a dentist for an oral mercury vapor test. The dentist used a metered device, much like the one the Occupational Safety and Health Agency (OSHA) uses to measure for mercury in the work environment. This instrument measured the mercury vapor in my mouth to be approximately 18 milligrams per cubic meter of air. My breath was way above the legal safe limits for air in the work place and I should have been fined and shut down if my mouth were a place of employment.

I was shocked and surprised to learn that silver amalgam fillings are 50% mercury; it seems to me they should more accurately be called mercury fillings as they contain only about 33% silver. Hadn't I learned in my eighth grade science class that mercury was even more toxic to the human body than lead. Could you imagine anyone knowingly allowing a dentist to fill his or her teeth with lead! Yet most of us **unknowingly** allow mercury to be placed in our teeth every day. The American Dental Association (ADA) would like you to believe that the mercury is locked into the filling once it hardens, but there are many scientific tests that disprove this theory. In fact when tested for mercury content a 10 year old filling no longer contains any mercury, as it has leached into the body. Mercury can cross the blood-brain barrier and even the placenta; test on the brains of fetuses show the amount of mercury in the fetal brain corresponds to the amount of mercury in the mother's teeth.

Some people have a sudden reaction to their mercury fillings but mine was a slow cumulative reaction as the mercury level in my body increased. My earliest symptoms were digestive problems and fatigue and I wasn't overly concerned when the doctor said they were probably stress induced. When I began having bouts of irregular heartbeat I visited a cardiologist. He ordered a echo-cardiogram which showed my heart to be

perfectly normal but as a precaution he had me wear a Holter monitor for 24 hours which did show I was experiencing spells of arrhythmia, for which the doctor could offer no explanation except possibly stress. Managing a family business it was easy for me to except this diagnoses. But the fatigue was steadily increasing and no amount of sleep ever left me feeling rested.

Soon I was affected by a loss of my short-term memory. I was experiencing difficulty remembering events from the previous day and ultimately I could not keep a simple seven digit phone number in my head long enough to dial it. I also began to have trouble performing my job. Tasks I had been performing for over 25 years became a struggle as I stared at them not knowing what to do, it was as though my IQ had decreased to a much lower level. I became overwhelmed by things like balancing a checkbook unable to remember how to do it. Even following a simple conversation became impossible for me; it seemed everyone was talking faster than I could comprehend. I also suffered from tremendous anxiety and whether this was a result of the mercury damage to my nervous system or my fear of being unable to cope with ordinary daily life experiences, I'm not sure. Most likely it was a combination of both.

Added to the steadily increasing fatigue and cognitive difficulties I began to experience bouts of emotional instability, insomnia, and hot flashes coupled with severe night sweats. Although I was only in my early forties I visited my gynecologist thinking perhaps menopause might be the source of the many health problems I was experiencing. Lab tests and a thorough physical revealed that I was not experiencing menopause; and once again the diagnosis of stress was tossed at me. Certainly I was feeling stressed, but what was stressing me was the myriad of health problems I was experiencing along with the omnipresent ever increasing fatigue.

I was also plagued with repeated sinus infections and had developed a strong metallic taste that was constantly present in my mouth along with oral thrush and patches of leukoplakia (pre-cancerous). I saw three different dentists for this condition, a dental pathologist was able to clear up the thrush only to have it repeatedly reappear; none of them could offer any insight on the metallic taste. I was becoming obsessed with finding a solution to all these health problems and meeting with little or no success I was also becoming very depressed. It was my experience that some doctors cannot admit it when they don't know what is wrong with you and stress becomes the catchall diagnoses thereby dumping the problem back in the patient's lap. My oral health problems certainly could not be blamed on stress.

I had developed a loud bellows-like noise in my left ear that seemed to correspond with the rhythm of my heartbeat and Dr. Pharo sent me to see another cardiologist, who upon placing his stethoscope on my carotid artery announced that he could hear a blockage in my carotid artery. However the results of several test he ordered did not bear this out much to the doctors surprise, but in the interval since my last echo-cardiogram I had now developed a prolapsed mitral valve. Eventually when I researched mercury poisoning I

Godsey 3 -

would discover that prolapsed mitral valve is common among victims of mercury poisoning.

Space does not permit me to list all of the symptoms I was plagued with but the following were some of the most troubling and frightening to me: excessive salivating, causing me to drool uncontrollably; adrenal failure, B-cell defect, impaired immune system, depression, numbness in my fingers and toes, tremors in my hands. hearing loss and bouts of vertigo. Most of these symptoms have cleared up with the removal of my amalgam fillings except for the fatigue and it continues to improve with time. This is a very preventable illness and more importantly I think it is inexcusable and unconscionable to place a known poison in the teeth of unsuspecting patients without so much as a warning about the possible health risk. In researching mercury and its affect on the human body, I've read numerous stories of people who experienced a reaction to *mercury fillings* similar to my own. We've been using mercury in amalgam fillings in this country for over 160 years, yet it has never been tested by the Food and Drug Administration (FDA) for safety.

Some day future generations will look back and think we were incredibly stupid for allowing a known toxic heavy metal like mercury to be used as dental filling material.

Gorsuch

July'2000

Committee on Government Reform

Please add mine to the pile of opponents to punishment for the removal of amalgum fillings. The following reasons solidify my argument and appeal;

1. Consumers are never told "silver" fillings are really mercury - and consumers don't know dentists are putting a gram of mercury in their mouths for each fillings.

2. The government of Canada says children and pregnant women and those with kidney problems should not get amalgam fillings. So do the manufacturer warnings. Even the ADA says it's not for everyone. Yet consumers are not given warnings about having Hg in their mouths.

3. Studies increasingly show the dangers of mercury fillings. And mercury is being eliminated in all other health care uses.

4. Environmental danger: Hg is a hazardous substance coming out. Hg is a problem all over

Sincerely, Dr. Rich Gorsuch
PO box 574
Haines, Alaska
99827

Gould

Subj: Mercury fillings

To: Committee on Government Reform

Dear Sir:

WHILE MY HUSBAND WAS ACTIVE DUTY AIR FORCE AND WE WERE STATIONED IN GERMANY DENTAL WAS PART OF OUR FEW BENEFITS I HAD MANY TEETH FILLED AND UNKNOWN TO ME WITH MERCURY. I HAD NO IDEA OF THE LIFETIME OF TROUBLES I WOULD ENCOUNTER. AND FINALLY MY DENTIST TOLD ME IT WAS RELATED TO MY TEETH..HE ESTIMATED THAT I HAVE $8000.OO WORTH OF WORK TO BE REDONE AND WITHOUT DENTAL BENEFITS. THATS INCREDIBLE. PLUS MY IMMUNE SYSTEM WAS WORN DOWN FROM EACH BITE WOULD RELEASE TOXINS INTO MY SYSTEM

I HAVE BEEN CHRONICALLY ILL AND HAD TO BECOME A VEGETARIAN TO TRY AND COMBAT THE EFFECTS AND ALLERGIES THAT HAS BEEN A RESULT AGAIN OF MERCURY.

IT LEADS ME TO BELIEVE THERE IS NO ONE WATCHING FOR THE CARE OF INDIVIDUALS AND THAT WE SHOULD NOT TRUST DOCTORS AS THEY LISTEN TO THE DRUG COMPANYS NOT ALWAYS ON RESEARCH OVER A LENGTH OF TIME PLEASE DO WHAT YOU CAN I WILL BE GREATFUL IF THE PUBLIC IS NOTIFIED OF ANOTHER BLOOPER..

SINCERELY
KAY L GOULD

Griffin

January 14, 2000

To: National Institute of Science Academy

Dear Scientist:

Enclosed is a copy of a letter recently sent to DAMS organization.

I am voicing my concerns and outrage as I am a victim of mercury poisoning from mercury based dental fillings, known as amalgams or silver amalgams. Mercury is highly toxic and although amalgams contain 50% mercury, conventional dentistry misleads patients by calling them silver fillings rather mercury fillings. On at least twenty occasions through the years, dentist used this poison to fill my teeth and never explained its potential harm. AS a result, I have suffered greatly, and still suffer illness that I may not have if I had been "informed" and given a choice of having different filling materials.

As stated in my letter to DAMS, most of my life I have suffered symptoms of mercury poison. These include autoimmune illnesses involving my thryoid gland, and more recently my eyes and also a recently positive test for lupus. I have also had cancer and chronic pains and fatigue. I am having ear and head noises from probable galvanism caused by the mixed metals in my mouth since the dentist started placing gold material for crowns. It is taking away all quality of life, as the noise worsens when I am around TV,s, radios and fans, including heating and AC. There have been times I have cut off or turned back the heat in my house in order to get relief from the noises in my ear. The ear specialists can find no problem with my ears. The tinnitus experts have not heard of this. In addition to the ear problems in the past two years, I have had eye problems. This involves severe vitreous detachments in both eyes and my vision has deteriorated and the Doctors have no explanation or hope for treating me. I have been told the flashes of light I have continued to see in my eyes at night for two years is abnormal. Mercury is known to affect the optic nerve. I have already lost some of my independence because of the visual problems and live in anxiety and fear of facing possible blindness. Dim or low vision is a symptom of mercury poisoning. Although I have problems that do not fit the conventional medical "cookbooks" for diagnosis or treatment, the conventional Doctors ridicule me when I bring up the issue of mercury poisoning. Although it is common knowledge that amalgams contain mercury, my family MD told me I don't have any mercury in my mouth. Either he is ignorant or trying to be sarcastic. Another MD told me the stories of people picking up radio signals from their metal fillings is "crazy." When one may be going blind, one must then begin to

consider environmental factors, such as mercury exposure and poisoning as it is highly toxic to the nervous system. There needs to be more education before it is too late for me, and others in my situation.

I have also recently developed some unexplained pain in my finger joints, burning sensation in my head, eyelid and other muscle twitches and sensations of electric shocks in my head. I am also under treatment for GI problems, I have severe problems digesting food and I am concerned about esophogeal cancer. I also have arthritis, foot, heart, severe insomnia - poor constitution My current conventional dentist says there is no possibility I have galvanism problems from my teeth. However, this is not what I have read in the books. He also left amalgam under my gold crowns as he said this is the best core foundation for a crown. I was not informed or given a choice at the time. The dentists have not, and still do not obey the amalgam manufacturers warnings. ONe manufacturer says amalgam is contraindicated in proximal or occlusal contact when other metal restorations are present, for retrograde or endodontic restorations, as a material for core buildups under crowns and the number of amalgams should be limited. All of these would apply in my situation but the dentists have ignored the warnings and my current dentist has washed his hands of trying to help me. The warnings also state that mercury expressed during condensation and unset amalgam may cause amalgamation or galvanic effect if in contact with other metal restorations. If symptoms persist, the amalgam should be replaced by a different material. I had to ask my dentist three times for copies of my dental records, and was only successful in obtaining them by quoting to him the dental laws of my state.

Mercury leaches out faster when a gold crown is placed over it. My dentist justifies his work by saying the cement separates the gold from the amalgam. (I have seven crowns and seven amalgam fillings) I have had a root canal tooth that has hurt for twenty years. The dentist have brushed me off as to my complaints. The tooth is restored with a gold crown and is in occlusion contact with a tooth with amalgam fillings. I wrote the dentist who did the root canal filling as to information about the materials used and as to any number of reasons the tooth may be hurting, such as infection. He did not respond to my letter or suggest I come into the office. He has shown no interest. I have spent a good deal of money to have all this toxic junk put into my mouth.

There is also a possiblity I need cavitation treatment. INsurance does not pay for this, or for any of the other treatment I need at this time. I am not able to pay for amalgam replacement and detox treatment. Not only is it not affordable, the hand full of practitioners that may know something about treating it is located great distances from

me. I am unable to make these long trips. The alternative MD's are doing the best they can, but they need help. There is an urgent need for the government to fund more research and education in this area. The Dental Profession, especially the ADA, needs to be accountable. The insurance companies, such as Medicare and private ones such as Blue Cross should be required to cover treatment for amalgam illness. Without fianancial help, myself and others in my situation, will go without adequate treatment and only become more ill. Chronic illnesses are costly, especially if inadequate treatment is given. There is also the reality of people like me having to enter institutional care at a premature age, and this could also be more costly to the government in the long term. Someone in my situation sees no light at the end of the tunnel. If things turn out too late for me, I hope this letter will help someone else. I plead that you will do what you can, as soon as you can to bring the amalgam issues out in the open so the truth will be known. There is a lot of confusion now among both patients and practicioners attempting to treat it. Practicioners need to be trained and able to practice mercury free dentistry or treat amalgam illness without fear. This treatment needs to become more affordable and accessible for the average person. More educated and skilled practicioners are needed, and soon. This is the only hope and answer that I see for myself, and perhaps others. (amalgam illness needs to be recognized.)

Thank you for your attention to this matter and your interest is greatly appreciated.

Sincerely,
Mary Jo Griffin

Mary Jo Griffin
113-C N. Edgemont Ave.
Gastonia, NC 28054

Also, I had the heavy metal test done out of Canada (I retained Lake assoc.) The toxicologist told me no mercury was spilling out of my liver, as it is not detoxing - Mercury is being passed into my tissues - I am toxic and she recommended amalgam removal as soon as possible - Lab report is admissible in court - This test was done several months ago.

Guillet

July'2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Bldg.
Washington, DC 20515

ALZHEIMER'S DISEASE AT AGE 49
CURED WITH AMALGAM REMOVAL

Dear Congressman Burton:

The Alzheimer Disease symptoms experienced at age 49 (loss of sentence thread, failure to remember names of family members and friends, inability to remember why I was doing things, etc.) Miraculously it disappeared overnight when a recent Amalgam filling was removed from above an old Amalgam filling (actually All Amalgam was removed at one sitting).

Galvanism between new #2 (-11mv) and old #31 (+2mv) not only increased the Hg vaporization, but it also overloaded the thought process / body electric.

Michael Guillet

DIAGNOSED WITH MULTIPLE SCLEROSIS

July 10, 2000

Dan Burton, Chairman
Committee on Government Reform
102 Cannon House Office Building
Washington DC 20515

Dear Congressman Burton:

I am writing this letter to tell you my experiences with mercury poisoning and to suggest that mercury be removed from dental, pharmaceutical and consumer products.

As a child I was acutely poisoned with mercury and admitted to Children's Hospital in Denver, Colorado with inflamed joints and inability to walk due to a lack of balance. At age 11, I had my first amalgam filling. My parents were not informed that amalgam fillings were 50% mercury: they were not questioned about my medical history regarding mercury exposure. Because of my history, I should never-ever have had mercury fillings placed in my mouth. Later on, I was diagnosed with Multiple Sclerosis. I have never had
a symptom of "MS" without first having had an exposure to mercury, be it in fish, thimerosal (the mercury preservative in vaccinations such as tetanus and flu shots), or paint.

I have the same symptoms with "MS" that I had when I was poisoned as a child. When my fillings were removed, I was free of all "MS" symptoms. I remain free of all symptoms as long as I am not exposed to any form of mercury.

It is ironic that millions of dollars are spent each year to remove mercury from the environment, yet each year Americans spend millions of dollars to have mercury placed in their mouth, a known poison and neurotoxin which has never been tested for safety. (A safe poison?)

Thank you very much for considering this explosive issue.

Sincerely,

Kathleen Harner
7305 Turkey Point Drive
Titusville, FL 32780
407 / 268 - 8099
e-mail: PKRTJB
cc/ : Waxman, Burton (in Jan), Mica, Scarborough, Ross-Lehtinen, Miller, Brown, Swankin & Turner

July 10, 2000

Dan Burton, Chairman
Committee on Government Reform
102 Cannon House Office Building
Washington DC 20515

Dear Congressman Burton:

RE: VISION PROBLEMS

I get some blurry vision and my vision went black once, it would get real blurry sometimes, and I could not focus when I looked at different things. It took an abnormally long time to focus.

Since I had my amalgam fillings removed I do not get these symptoms anyone. I do still have sensitivity to light though but not as severe as before.

Laura
Lilwhits@aol.com

Heidelberger-(1)

May 7, 2000

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Building
Washington, DC 20514

Re: IF I GIVE UP OR DIE THEY WILL HAVE WON
I CANNOT ALLOW THAT.

Dear Congressman Burton:

I'm losing not only my eyelashes, but my hair is falling out at an alarming rate. I guess the body is so beaten down that it cannot support even the basics. The depression I have been battling for over two years now, some days have felt very suicidal also. Am having a terrible time dealing with the fatigue and inability to work to support my self on the level that I use to. I find it very difficult to even interact with my seven grandchildren, which is the hardest thing of all, since I raised my three daughter alone without the benefit of support. I worked two jobs all the time and missed a lot of precious moments with them.....Now to make matters worse the candida has moved into my gut from my mouth. Seems there is not a space in my body that this metal is not taking it toll. Will be testing for porphria next. Seems that may be what is going on with my skin.

I am determined to not let this get the best of me. I have my faith to sustain me and will not allow the criminal acts of this dentist to take me down. When I am faced with the depression, the hopelessness and the pain I pick myself up by the bootstraps and force myself to go to work, I also find ways to try and make a difference to make changes in this issue of poisonous heavy metal toxicity. This is what drives me on and lifts the depression and pity party I find myself in so many days. If I give up or die they will have won. I cannot allow that.

I certainly hope that you will take a hard and serious look at this issue.

Sincerely,
Joyce Heidelberger

E-Mail: bizzyblonde1@prodigy.net

Heidelberger (2)

Was There Justice?

It's a cold wintry day in December and there are not too many days left before the millennium is too arrive. I have just had my last glimmer of hope taken away from me. An accumulation of eleven years of pain and suffering and ten years fighting a long grueling legal battle, which would take me to the belly of both the legal and medical professions. I would find corruption, lies, and unethical practices and down right immoral actions taken by two professions supposedly held high in eyes of the community.

I would have said all those years ago that I might have agreed that by rights of education, knowledge and their oath "TO DO NO HARM" they might have belonged on a thrown of trust. I would not have believed that physicians could be bought and sold to tell a lie or the truth depending on the motivation. That doctors of all degrees would stand by and watch injustice being performed on a regular basis would be passed over due to fear of involvement. I find now that there are a few really bad ones, a few more who are mediocre and a lot who put their heads in the sand and allow the lousy few (who they figure do no harm) to continue to operate business as usual. But what I also found on the top of the pile, was even fewer who not only believe that there is a "standard of care", but believe in true justice and fairness, not just winning. The ones, who put, at times, their reputations and even friendships on the line by taking up a cause, righting the injustices done by someone in their own profession. These blessed ones are few and far between. Yet somehow with God's blessing I found one of each. First a lawyer who took pity on me and my long struggle to get to the court house. Another in the medical community that came forward against all odds, jeopardizing his career, to speak the truth against a colleague. But lastly a practitioner who treated my condition for years, with reluctance and a court ordered paper came forward and tried to tell the truth as he straddled the fence. Trying to save face and his license, he skirted the truth, but at least he came forward, when so many would not. From these three and their staff I would learn that not all is lost. That from the many who don't care, the few that do no harm and go out their way to find justice for you, I have found the strength to fight on. Through loss of reputation, years of fighting the legal system and a dentist and his cohorts who believe that the end justifies the means, I will prevail hold my head high for even trying to make changes.

We the public deserve the assurance from their licensing boards and associations that they are capable of policing their own. Rather than putting on a pony show that gives the delusion of fair action. Yet protection for the general public appears to take second place to protecting their good olde boy system, this truth would be a shocking revelation to all consumers.

When this story began I lived in the world of ignorance obviously, or surely none of this would have happened. I would have known that just because a dentist has a license, takes $13,000 of your money, tells you that he is qualified, capable to perform the task at hand that it might not be so. That his skills may be less than that promised and I might find myself paying $100,000 to repair the damage to my teeth and TMJ joints, must less spending years ridding my body of the toxic materials he placed their. Would I have known that his ethics and standard of care would be so low that he would not only destroy my teeth but also put my very life in jeopardy because of his greed and carelessness?

I would find myself being found responsible by a jury of my piers who were to listen to all the facts, then judge me. Before the end of the trial I would witness the defense lawyers bringing forth court ordered restricted information before these 12 people who were to judge me. Facts that did not relate to the issue at hand, then at the end would bring forth a dentist who would once again speak of that restricted information one more time, to make sure that the jury received full benefit of their plan to cause a mistrial if they could not contaminate the jury against my case. A mistrial would be ordered by the judge, but rejected by me, as I felt innocently enough that these few people could look beyond the carefully planned plan by the defense attorneys to destroy my case. Without a chance to speak and explain the events they divulged, the jury would leave to seal my fait. Nine would vote against me, three would see beyond the carefully laid plans of the defense team and lean toward my case. But three was not enough. The Forman of the jury would bounce her self out that door, with a smile on her face that would rival any cat that ate the mouse scenario. Proud of herself, she was that day, you would have thought that she was the one that I was suing.

To add insult to injury once the defense team received the ruling that they gave up their ethics for they would come back and try blackmailing me into giving up my rights of appeal. They would charge me with all of the defendant's trial cost if I would not agree to give up my rights. Blackmail, what else was I to expect. They win by default and I

Heidelberg (3)

am supposed to tuck my tail between my legs and be happy that they could not do more to me. At first in shock I thought why not, then as daylight struck my heart I thought why would I. I have lost everything to fight this battle, my very life depended upon it. Now I'm left with mounting legal debts and judgements from the defendant's lawyers. Needing thousands of dollars to save my life and no where to turn. But I do have the pride in that I fought the battle; I went to make changes, which one-day will help others. Today I go to desolve the remainder of my sixteen-year marriage to a warm and loving man. The events of the previous years and the events to come have washed away all thoughts of joy and any hope of a bright future is gone. The events to come are mind boggling, the healing if it is to come will be hard, and I cannot share this burden one more time. And yet the experience of injustice to painful to just walk away from after all I have lost in pursuing her

Next week I will again go before the judge who heard my trial, this time to hear his decisions on the many motions that my team of lawyers and the dentist I sued have put before him. The judge will place a judgement against me for the cost of the dentist side of the trial, thousands of dollars will levy against me as a punishment for losing and not remaining quiet. All my motions for a new trial, jury decision reversal and request that due to unethical tactics by the defense team that they pay my trial cost. Again this one man will impact my life, not caring what he is doing to me, only caring about his pride and reputation, which if the truth were to be told was damaged due to his incompetence long before I came into the picture. Not caring about the true consequences of his legal action against me, only the win, he went on to throw the biggest celebration he could to celebrate his win. Bringing in ten top pornographic stars from the West Coast to perform sexual acts on each other and his guest, while keeping open a nightclub after hours to house this extravaganza. Illegal open gambling tables, free booze, wild women were the fare of the night, all to celebrate the win against the enemy, me. I might add, all of which are against the law in the state of Oklahoma. Amazing what you can accomplish when you have the right contacts and excessive money. How is it that a man who has serious addictions such as Gambling, alcoholism, cocaine and other recreational drug abuse problems, a well-known womanizer, can be so well liked and protected by his piers in the community?

When I approached the Dental Licensing Board they seemed so sincerely concerned about the problem of control over their profession, just not concerned enough to do a thorough investigation. A few years later during a visit with the director, I would hear come out of her mouth what a wonderful person he seemed to be. The truth of the above mentioned faults seems to hold no weight with the dental board or the dental community. Having held office in the dental pier review board as well as the Okla. Dental Association, this man has clout, finding justice will not be an easy task, looking impossible at the moment.

Again I will walk on, again I will prevail for to survive all this I must move along with my quest. To make changes in laws that will help the many against the unethical practices of the few. This I cannot do alone, this will require the masses, but they cannot help if they do not know that their own plight is so closely interlocked with mine.

The issues that I have for so long fought against are not just about standard of care; they are also about the unethical practices of using a dangerous combination if heavy metals in dental work that are deemed toxic to the human body. They are placed in the mouths of unknowing, unsuspecting patient's everyday in many forms, from root canals, fillings, braces, denture and crowns. This is done without so much as a consented choice, which is our right to judge for ourselves the dangers of these materials. We are as usual kept in the dark, as we have been for generations, while these professionals are reaping the benefits of this dangerous material, on the concept that it easier for the dentist to use and less expensive for the patient. Heavy metal poisoning from dentistry is now at epidemic proportion. The use has gone on for so long and accepted due to the approval of the American Dental Association, regardless of the facts that the health of the general population of the world has been adversely affected. Yet due to heavy lobbying from the dental community, trying to save their backsides from enormous litigation, has allowed this situation to continue. The role the medical community holds in this conspiracy is confusing, as until you look at all the revenue that these diseases bring forth for the doctors, hospitals and pharmaceutical companies. If we were to eliminate all the diseases with such an easy cure as removal of these toxic elements through extraction of these toxic materials. Then clean the system through a cost-effective form of cleansing such as Chelation therapy and vitamin therapy to repair the immune systems, where would these people make their fortunes? Some patients will not be able to find relief from even this therapy, as the window of opportunity is limited to the amount of damage the metals have taken on the human system. Some will be too far advanced to be helped, some will be lucky enough to have caught this situation in time to reverse the damage done. As much as the body is a remarkable organisms it can only tolerate so much abuse before it can not heal itself.

Heidelberger (4)

Since the late 1800's ethical, concerned practitioners from all fields have tried many a time to bring this problem to a stop. But due to the enormous profit and loss in this issue for the American Dental Association and the dental practitioners, their lawyers have managed to hold the possibility of change at bay for almost a hundred years. Even with all the information that is made available by these experts that heavy metal toxicity is the destroyer of the human autoimmune system, leaving the body defenseless against major diseases. Lupus, Heart Attacks, Alzheimer's, Cancer of all kinds, Multiple Sclerosis, Lou Gehrigs Disease, Renal Failure, Rheumatoid Arthritis, Leukemia (heaviest hit by children) and countless other diseases. These were non existent until the introduction of these materials into the human system through the so-called innocent acts of dentistry. Many doctors will come to see the dental community as the one medical field most responsible for the failing health of the human race. We have for generations held these people in high regard, believing that the interaction they hold in our health is minimal at best, not realizing the enormous affect they have on our overall health. Through the years European and Canadian countries have concluded that the Heavy Metal Materials used in dentistry was and is a hazard to the human population. They have taken measures to stop the practice and yet due to heavy lobbying and an enormous amount of clout from the American Dental Association these practices are alive and well in the United States. Several states are trying to address this issue, as their efforts are being stopped time and time again by special interest groups. We as a concerned community literally stopped the use of lead in paint to protect our children from being poisoned. Yet everyday unknowingly and with trust we set our children and ourselves into the chair of a dentist and allow this poison to be placed into our systems and that of our loved ones without question. Enough investigation and research has been done to prove these issues, now it's time for the American public to put their foot down, yell out in harmony, "NO MORE" "WE WILL NOT TAKE THIS ANYMORE". We, the American people, have rights of protection from these practices, now is the time to exercise those rights, before it is too late for all of us.

I speak as one of the fortunate people who have learned of this problem. Since having been diagnosed with Atypical Rheumatory Arthritis and showing now the signs of Multiple Sclerosis, if I had insurance (which I do not) or the money to rid myself of these materials (which I do not) I could find health again. Many do not know, which means there is no hope for them. They will continue to follow the traditional treatments, which are costly and debilitating. The cures will elude them because the real cause will never be brought forward in order to protect the few and feed the lavish lifestyles of the few. For most part these people will die of these diseases and they will die of painful agonizing senseless deaths. And we the general public will accept it as just part of life, never knowing the truth.

If I could have only one wish it would be that this life threatening issue be brought forward, that the lawmakers would forever ban the use of the toxic materials from ever being used again. I would wish for only this for Christmas. Not for myself but for the countless innocent children who will be crippled and who will die needlessly so that this group of professionals can continue on with business as usual to feed off our misery and protect themselves.

May God help us all,

Joyce Heidelberger,

Oklahoma City, Okla.

Hope 1

Date: 1/19/00 4:42:08 AM Eastern Daylight Time
From: mritch@erols.com
To Dan Burton, Committee on Government Reform

[redacted]

nausea	concentration problems
shyness	bleeding gums
throbbing nerve pain	chest pain
memory problem	depression
irritability	bladder infections
depression	arthritis
muscle weakness	Irregular heart beat

To The Committee:

Along with many others, I was poisoned by mercury from dental amalgams. You could say I was fortunate in a way because I found out I had been amalgam poisoned while countless numbers of people don't know they are amalgam poisoned and are suffering badly. Fortunate because I, at least found the cause of my painful symptoms and had a fighting chance to get better.

Meanwhile, many people's illnesses are given labels without a cause. Their symptoms are treated with drugs which are harmful; often drugs' side effects cause other symptoms which cause more drugs to be taken. It does not make sense to just treat symptoms rather than to look for what might be causing the illness. This is what often occurs when people who are mercury poisoned are misdiagnosed, and treated for symptoms thought to be other diseases.

Mercury amalgam poisoning causes very serious physical and mental damage, often irreparable. How in this world can people attempt to live peacefully amongst each other when there are so many minds and bodies malfunctioning from being poisoned? Many of us who understand the unlimited symptoms that mercury amalgam poisoning can cause, are terrified and sad for the future of our children. Violence is a major public concern, and mercury amalgam can easily be one of the main contributing factors . Mercury amalgam also causes alcohol and drug abuse as well as learning disabilities just to name a few. A medical doctor has stated that "Mercury amalgams are as close as you can get to the illness universe; their use in dentistry has set us up for most of the health problems we see today." Many would add "root canals" to that also, as per the scientific research done by Dr. Boyd Haley.

There are thousands of people who have been mercury amalgam poisoned most of their lives, and really don't know what feeling good is, and if they're knew what was wrong with them they would have a fighting chance to get better and start a new life. Not only does mercury amalgam poisoning harm the people who are walking around with it in their mouths, it can harm the unborn child and wreck havoc in family relationships.
More than a dozen of my teeth were filled with mercury, and than later redone with more mercury amalgam. My symptoms started with just not feeling right, nausea, shyness, throbbing nerve pain at tailbone area, memory problem, irritable, depression, concentration problems and bleeding gums. As the old amalgam was replaced, symptoms worsened with new symptoms and pain: I woke up once and couldn't breathing. At times couldn't yawn all the way, and many times didn't inhale all the way because it caused sharp chest pain. I experienced throbbing nerve pain in the pelvic floor areas and tailbone (similar to lingering pain of a smashed finger), burning in legs that would go from one leg to the other. Reoccurring bladder infections, constipation, low back pain, arthritis were other reoccurring symptoms, as well as debilitating fatigue that was so bad that I had to hold rails to pull myself up the stairs.

The doctors I saw didn't have answers and some would take guesses as to what might be wrong with me, and I wasn't interested in taking drugs to appease the symptoms. The mercury amalgam poisoning had settled in my tissues, and over the next decade and in mid thirties, the mercury amalgam had entered my blood stream, nerves, and vaporized continuously causing new symptoms. I started having bad attacks of irregular heartbeats along with spasms everywhere and head pain. Those bad irregular heartbeats felt the way a cartoon looked with the heart pouncing out.

That did it. I remembered hearing about mercury in silver fillings, and researched, diligently..... discovering that I had been systemically poisoned. I found a doctor who listened to me and helped me when others wouldn't, mainly because of ignorance. An EMG showed I had nerve damage in my legs. An MRI was done to see if I had multiple sclerosis and I didn't; mercury amalgam poisoning mimics MS.

People are taught that "our whole notion of the self is shaped by the culture in which we have been reared." So there's no doubt in my mind that the self and our society has been shaped by the poison of mercury in dental amalgams. Our government must ban mercury amalgams and follow other countries who have done their scientific homework and recognized the extreme health hazards of this toxic material.

Thank you for listening.

Sincerely,

Deborah Hope

Clark (1)

July'2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Bldg.
Washington DC 20515

Better After Amalgam Replacement

Dear Congressman Burton:

Recently I had all (8) amalgams removed completely along with six extractions under general anaesthetic last week - took nearly four hours, and I sure didn't feel too good last week ...

But now, WHAT A DIFFERENCE already. My vision is improving, morning, migraines have vanished, much less muscular pain, clarity of thought is returning. I have a long way to go and I did promise myself to be patient and cautious, but I really can tell a big difference already (less than ten days!).

The whole thing was done under Hal Huggin's "protocol". I was very impressed with the equipment (very high tech stuff), knowledge and care, EVEN MORE impressed with the sudden relief of some symptoms. I have even noticed my left nostril is easing (after nearly five years of being blocked) and my sense of smell is also returning. Generally feeling stronger and "sharper".

Thank you. I hope that you will seriously investigate the amalgam mercury problem.

jumar@CLARA.net

Criswell

July 13, 2000

Members of the Committee on Government Reform
Congressman Dan Burton
US House of Representatives
Washington, DC 20510

Re: Multiple Sclerosis for Sixteen Years

Dear Congressman Burton,

By 1989 I had MS for over 16 years. I had tried just about everything by then. I was starting to accept the fact that it would not get any better, instead it would continue to worsen. Then in December of 1989, I saw on 60 minutes about amalgam fillings and their link with MS.

Back into the 70's I told my wife, Gayle that I consistently tasted metal (now I learn it is a symptom of mercury toxicity). When I think back in Jr. High I had 3 fillings, summer of 68 I got 8 fillings in the summer of 73 I got 1 filling, in 78 got 1, and in 85 got 1 more, for a total of 12. Mercury fillings release microscopic particles and vapors of mercury every time a person chews. Vapors are inhaled while particles are absorbed by tooth roots, mucous membranes of the mouth and gums, and the stomach lining, it then absorbed by the nerves, muscles and every organ inn the body. It settles in fatty tissue (brain, spinal column).

I had a hair mineral analysis done in 1985. It showed that the mercury in my system was at a suspicious level. The Doctor who did the analysis said that the mercury was nothing to worry about. Ignoring his unconcern, I had all fillings removed in February and March of 1990. After the fact, I found that there is a procedure to take the fillings out without disturbing the mercury. Unfortunately, this was not the procedure followed in removing my fillings. In February of 1991, I was tested for mercury, and found that I was saturated with it. My condition worsened with the mercury now flowing freely through my system. (I later found out that having the fillings out is great but does nothing for what has accumulated in the body, over the last 28 years.).

In the early 70's it was announced that mercury from amalgams was linked to MS, I did not know this. I was not told by anyone in the medical field or at the time of any of my dental procedures. In '85 the American Dental Association had to admit that mercury vapors leaked from amalgams. The size of the filling does not matter. It is the amount of the poisonous mercury that is in the fillings. It was not until August 1999 that I learned this:

Mercury sensitivity is different for everyone. Those with a high sensitivity to this metal are more susceptible to diseases such as MS and other diseases that can be linked to mercury. My qualification in writing this is that of my 26 years of experience and research done on my own.

It is imperative that people be told about this travesty. The Dental Community must be held accountable for this mal practice. It is truly a matter of life and death that all the implications of mercury and amalgam fillings be researched and something be done for the future of mankind.

Sincerely,
John F. Criswell
E-Mail: JOHN 1833@aol.com

Cronin (1)

January 19, 2000

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Building
Washington, D.C. 20515

Re: Mercury Toxin from Amalgams

Dear Mr. Burton,

I am writing this letter with hopes that you will help increase public awareness to the topic mercury poisoning from amalgam fillings. Hearings and other public awareness initiatives are needed to expose the truth about mercury poisoning and your leadership on this issue can make a difference.

Ever since I was a young child my mouth has been full of amalgams. Through the years fillings and teeth have broken and been replaced with other amalgams. Neither my parents nor myself were aware of the health damage caused by amalgam fillings. Growing up I had intestinal problems and various symptoms typical of mercury poisoning. While in my 30's intestinal problems became more frequent. My stomach would be very tender and swollen and I would run a fever. For eight years I went to my doctor who would send me to various specialists who could never come up with a specific diagnosis. I was put on anti-biotics continuously. I just learned to fight the symptoms with frequent working out and supplements from the health food store. In August of 1998 my husband's company moved us out to San Jose, California. In the short amount of time here I ended up in the emergency room at a hospital with of fever and abdominal swelling. As usual I was given anti-biotics and the names of a physician and gyn. The gyn gave me an open prescription for anti-biotics. Frustrated and worn out I went to a doctor who practices alternative medicine. Finally someone had tested me for metal toxins which is something your conventional doctors rarely do. I was diagnosed with a high level of mercury poisoning. This past summer I was also tested by a doctor associated with Tufts University in Arlington Massachusetts. He also diagnosed me with a high

Chronic (2)

level of mercury toxin. I was put on a mercury detox and the swelling and fevers subsided. This past October I had all the amalgams taken out. Once completed, the imbalance I experienced in my head has gone and I no longer have the swollen abdomen or fevers. How many other people are out there with chronic conditions which may in fact be contributed to the amalgams in their mouth? I am not saying that mercury poisoning is the root of all evil but it is something that needs to be investigated. There are a host of proven symptoms and diseases which can be attributed to amalgam fillings.

I've been doing a lot of research on this topic and feel quite frustrated at the lack of attention and action in the United States. Action is being taking in other countries already banning the use of amalgams. Back in 1845 the American Society of Dental Surgeons was in existence. Dentists were concerned back then about mercury poisoning and the many side effects including dementia and loss of motor coordination. The association and affiliated regional dental societies adopted a resolution that members sign a pledge not to use amalgam fillings. During the next decade some members were suspended for the malpractice of using amalgam. Advocates of amalgam prevailed due to the inexpensive cost of mercury fillings and the membership in the American Society of Dental Surgeons declined forcing it to disband in 1856. In its place arose the American Dental Association founded in 1859 based on the advocacy of amalgam as a safe and desirable tooth filling material.

I have enclosed just a few pieces of material which reinforce this reality. The public needs to be educated. People should be given a choice of the type of fillings in their mouth. Young children are innocently having this metal put in their mouth which causes anxiety, irritability, fatigue, outbursts of temper, stress intolerance, decreased simultaneous capacity, loss of self confidence, indecision, headache, depression, learning disabilities, etc. This is all confirmed by the Agency for Toxic Substances and Disease Registry. The cost to have non-metal fillings should not be more than amalgams. I had my fillings replaced at the same cost of amalgam. Testing for metal toxins and parasites should be done on a routine basis as regular blood work and urine testing for physicals. Mercury poisoning is real and is happening. Action is currently being taken in other countries and ours should not

Cronin CS1

DMPS 5CC

DOCTOR'S DATA, INC.
Doctor's Data, Inc. Chicago, Illinois 60186-0111
CALL TOLL FREE (800) 323-2784
Fax: (630) 587-7860
E-mail: inquiries@doctorsdata.com
Web site: www.doctorsdata.com
James T. Hicks, M.D., Ph.D., FCAP
Medical Director
CLIA ID # 14D0646470, Medicare Provider # 140453

RECEIVED OCT 2

Patient: Rosanne Cronin
Doctor: D. Graeme [redacted], MD
c/o:
Collection Date: 13 Oct 1999
Date In: 15 Oct 1999

Lab #: 99288-0224 ET
Age: 46 Sex: Female
Acct #: 21662
Collection Type: Timed
hrs: 2000
Date Out: 16 Oct 1999

Per gram Creatinine

Elements	Result (µg/g creatinine)	Reference Range* (µg/g creatinine)	Within Ref. Range	Elevated	Very Elevated
Aluminum	9.6	0 - 35	••••		
Antimony	.1	0 - 5	•		
Arsenic	54	0 - 100	••••••••		
Beryllium	< dl.	0 - .5			
Bismuth	.2	0 - 30	•		
Cadmium	1.3	0 - 2	•••••••••		
Lead	3.1	0 - 15	•••		
Mercury	100	0 - 3	••••••••

Crowther

July 1, 2000

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Building
Washington DC 20515

Dental Amalgam
The Source of Mercury Poisoning American Population

Dear Congressman Burton:

I am writing because of my serious adverse health experience with the dental amalgam. It is a long sad story. After hearing several personal reports such as mine a group of conscientious dentists and scientists started to explore the safety of the dental amalgam in 1984. They have inspired the initiation of explorative studies pertaining to the amalgam at universities around the world. Consequently there now are a growing number of scientific documents that indicate mercury leaking from the dental amalgam is insidiously dangerous to a person's health. Some Documentation pertaining to the mercury amalgam is presented on the web page ww.amalgam.org.

Dental amalgam restorations consist of 50% mercury, 35% silver, 13% tin 2% copper, and a race amount of zinc. After an amalgam is installed in a tooth it slowly releases mercury and the other metals into the body. Every amalgam daily releases on the order of 10 micrograms of mercury into the body. Scientific studies have concluded that the amalgam is the source for more than two thirds of the mercury in our human population. Mercury is the single most toxic non radioactive metal; the most minute amount damages human cells. This challenges of every individual and of developing fetuses and can lead to health problems and fetal malformations.

Reports prepared by the United States Public Health Service (USPHS) dated 1993 and September 1997 discuss the safety of the dental amalgam. The USPHS has concluded that scientific literature has not revealed evidence of adverse health effects from exposure to the dental amalgam for the vast majority of people. After reviewing these reports I have concluded that the USPHS is not working with current scientific documentation.

I encourage congress to explore this very serious issue. I thank you for receiving this request.

Yours truly,

G. Scott Crowther, P.E.
1994 Alfred Noble Prize recipient
Reply-to: crowther@alaska.net

cc Congressman Don Young, Representative of Alaska

Cronin (3)

be the last to recognize this major health risk. Finally the stage has been set with the tobacco companies and now its time with the ADA on the issue of amalgam fillings. Its disgusting that the American Dental Association supports the use of amalgam fillings. I've been talking with other people who have been afflicted with this toxin and it is devistating to see how many people are out there with it and how it has impacted their health, savings and life style.

Please give this matter special and immediate attention as it is much needed. It could save a lot of people the frustration and expense that I have been through for so many years of not knowing what is wrong with their health and would also answer a lot of questions for so many physicians. I will be more than happy to supply you with more information that is needed. I've also enclosed a copy of my lab report to show the high level of mercury and also the other metals that are used in conjunction with the mercury also at high levels. My e-mail is fourpawsca@aol.com. I look forward to hearing from you.

Sincerely,

Rosanne Cronin
3013 Magnum Drive
San Jose, California 95135

408 270-3922

enclosures

LABORATORY CORPORATION OF AMERICA

Labcorp
Laboratory Corporation of America

Cronin(Y)

SPECIMEN	TYPE	PRIMARY LAB	REPORT STATUS	PAGE
201-942-1348-0	S	RN	COMPLETE	1

ADDITIONAL INFORMATION

SS#022440455 POST 6 HOURS
HEAVY METALS GR

DOB: 11/28/1952

PATIENT NAME	SEX	AGE(YR./MOS.)
CRONIN,ROSANNE	F	46/ 7

PT. ADD.: 3013 MAGNUM DR.
SAN JOSE CA 95135-0000

DATE OF SPECIMEN	TIME	DATE RECEIVED	DATE REPORTED	TIME	
7/20/1999	7:56	7/21/1999	7/23/1999	7:40	1787

CLINICAL INFORMATION
CD- 92486016933

PHYSICIAN ID.	PATIENT ID.
	022440455

ACCOUNT:AMERICAN WHOLEHEALTH/ARLINGTON

180 MASS AVENUE, SUIT 303
ARLINGTON MA 02174-0000
ACCOUNT NUMBER = 20330145

TEST	RESULT		LIMITS	LAB
HEAVY METALS PROFILE II, URINE				
Creatinine(Crt),U	.36L	g/L	.50 - 3.00	BN RN

The excretion mechanism of chemicals and metals can be altered when the urine specimen is very concentrated (creatinine >3.00 g/L) or dilute (creatinine <0.50 g/L). In such cases, urinary measurements are not reliable and should be repeated on a freshly collected specimen.

Arsenic (Total),U	None Detected		0 - 50 Detection Limit = 10 mcg/L	BN
Arsenic(Inorganic),U	None Detected		0 - 19 Detection Limit = 10 mcg/L	BN
Lead, Urine	2	mcg/L	0 - 49 Detection Limit = 1 mcg/L	BN
Lead/Creat. Ratio	5	mcg/g Crt	0 - 49 Environmental Exposure: <50 mcg/g crt Occupational Exposure: BEI(Sampling time is not critical) 150 mcg/g crt (1994-95 ACGIH Recommend.)	
Mercury, Urine	5	mcg/L	0 - 19 Detection Limit = 1 mcg/L	BN
Mercury/Creat. Ratio	13 H	mcg/g Crt	0 - 5 Environmental Exposure: <5 mcg/g Crt Occupational Exposure: BEI(Sampling time is pre-shift) 35 mcg/g Crt WHO 50 mcg/g Crt (treshold level)	

Results are Flagged in Accordance with Age Dependent Reference Ranges

July'2000

To: Committee on Government Reform

I WAS NEVER INFORMED THAT MY AMALGAM FILLINGS CONTAINED MERCURY

Dear Chairman Burton:

I was never imformed by either a dentist or a doctor that amalgam fillings and other dental materials could contain mercury or other toxic metals. That included all my regular dentists and my family doctors. My symptoms, which include numerous allergies, asthmatic conditions and depression, seem to correspond to others who declare that they suffer from amalgam poisoning. I now believe that my health conditions were strongly affected by the mercury in the dental amalgams placed in my teeth as a child and from what probably crossed the placenta boundary between my mother and the fetus. I will bless the day when mercury materials are no longer placed in human beings. I find the medical and dental community have for too long covered up the health problems that dentistry have caused by placing these harmful substances, without our informed consent, in me and my relatives including my children and grandchildren. Most of the costs of amalgam replacement ($3650) has not been covered by my health or dental insurance.

During 1995, 1996 and much of 1997, my energy level seem to shrink to a low level where I could still work and carry on but I was more and more criticized and called lazy by my spouse. Even today I don't have the energy I had in the late 80's. I continue to wonder whether my energy level will Return to my pre-root canal days. The root canal in 1995 which combined a Mercury filling with a metal crown, I feel was the straw that broke my health down. I became very fatigued and eventually, I retired early, age 59, in 1997 to try to discover what was wrong.

I also feel that the heavy load of mercury placed in my wife's teeth and therefore her body, resulted in the mercury causing her immune system to break down and allow a terminal cancer situation to develop.

In my profession as a librarian, I once worked on a bibliography on bioceramics with a Professor of Ceramic Science who was also a practicing dentist and a dental researcher. In the 4-5 years that I worked with him, not one mention of amalgam came up. I once felt rather betrayed since he was also my family's dentist. He put several amalgams in my five kids and wife and one in me. However, my realization that most practicing dentists work under a loaded gun and any mention that the mercury in amalgams may be harmful can lead to their license to practice being suspended and/or research grants being rejected if one doesn't follow the official ADA code of ethics.

Around 1990, I remember asking a new dentist in town about amalgam fillings and he had his assistant dentist, who was England-born, tell me that they were perfectly safe. No mention was ever said as to what metals were contained in amalgams. In fact, most persons including engineering professors are unaware that amalgams are mercury alloys. Only the metallugical

professor at the college where I work part-time knew that amalgam was mercury alloyed with other metals.

I had 3 amalgam fillings, a root canal filled with amalgam and porcelain base metal crown with amalgam as filling in 11 years while my wife had 16 amalgam fillings, 2 root canals, and 6 porcelain base metal crowns in the same period up to 1998. She also had her last amalgam on June 16, 1998 along with her 6th Porcelain base metal crown by a dentist the day before a blood test that prepared her to receive chemotherapy. The blood test was okay, but every blood test at 3 week intervals after that failed to have good blood results and she had to take special medicines to improve her blood markers before chemo could be performed. I have long felt that the amalgam placement (#29 tooth) next to the porcelain base metal crown (# 30 tooth) disrupted her blood chemistry by being placed during chemotherapy. My youngest son had 7 fillings in 31 day period in 1994 and I can now see the relationship between alcoholism and amalgams (mercury) after reading that there is a tendency for many amalgam poisoned persons to drink alcohol to cover the effects of the mercury leaching out.

In Augt. 1998, I read books on amalgams and root canals and got a biocompatibility test for dental materials. I found a mercury free dentist who looked at old my xrays and did a new xray on my root canal site, which showed an infected root even though, it did not hurt. He also measured my voltage and my #18 and #19 made up over half of the electrical charges going on in my mouth. I chose to get #18 extracted. He also replaced the metal crown on #19 with a resin crown. Then he said that he would not replace my 13 amalgam fillings unless I was saw a medical practitioner who would help me deal with what he thought was an autoimmune disease in me.

In April 1999, I went to a medical practitioner and his diagnosis was that my asthma was caused by a heart condition which was caused by mercury amalgams over two months in 1999. Since the last removal of fillings I have followed a regimen of supplements and diet control. I am the lightest I have cardiologists now recommend as a healthy weight range. My tendency toward depression seems to have been lifted. Now I am mostly angry about the false science that our dentists preach to the public and being frustrated at our American medical system for hiding the effects that toxic chemicals have on the health of our citizens.

Paul T. Culley
60 Pine Hill Drive
Alfred, NY 14802
607-587-8114
culleypt@infoblvd.net

Cutler

Ferreira

From: <AndyCutler@aol.com>
To: <undisclosed-recipients:;>
Sent: Tuesday, March 28, 2000 9:57 PM
Subject: Dental amalgam - my personal, professional and politicalexperience.

Dear Ms. Markus:

I understand you are investigating the issue of mercury poisoning from dental amalgam on behalf of Congressman Burton. Please allow me to share my story with you briefly - if you would like more details on any point I will be glad to provide them.

I am a PhD chemist and registered chemical engineer. Thus it is quite ironic that I got poisoned in the dentists' chair, but I knew better than to be sloppy with toxics in the lab. I made several past employers perform occupational health surveys so I could be absolutely certain where my mercury came from, even though comparison of my dental and medical history was compellingly diagnostic.

Before I became convinced that I indeed had mercury poisoning I had a large number of laboratory tests that do conclusively document it. These were mostly tests that I found discussed in the medical literature and had to browbeat, wheedle and cajole some MD into ordering - I ended up seeing about 25 doctors in 1998 to get a few tests ordered and prescriptions written so I could start to get well.

By the time I finally figured out what the problem was, I had developed disabling chronic fatigue, allergies and asthma beyond belief, food sensitivities that restricted my diet to about 8 ingredients, and partial pituitary failure. I was also beginning to experience serious emotional and intellectual disturbances.

I had my mercury fillings removed in March of 1998, used appropriate medicines and nutritional supplements to detox, and am dramatically improved. Since I didn't do anything to treat any other condition, and my laboratory tests improved as well as my symptoms, this does make it rather clear the mercury fillings were the problem. I am willing to make my medical records available if you need a well documented case of amalgam illness.

Doctors and dentists are routinely persecuted by state licensing boards for daring to diagnose "amalgam illness." In fact, the doctor who diagnosed me and thus saved my life (Dr. Ronald Wempen) was persecuted by the California Board of Medical Examiners shortly thereafter for diagnosing mercury poisoning in another patient of his. The complaint was trumped up - the patient never filed one but her insurance company chose to file a complaint on her behalf and the board refused to dismiss the case when the patient wrote to them stating she hadn't filed a complaint and didn't want the case

pursued. The board pursued it anyway. This became well known among California physicians. I actually had a couple of doctors refuse to treat me out of fear that the board might find out and discipline them.

As I mentioned I am a PhD chemist and registered chemical engineer. I also have substantial nonmedical research experience and have published many journal papers. Thus when the diagnosis of "amalgam illness" was first suggested I went to the nearest academic library to check things out since it was hard for me to believe (at first) that the FDA, ADA, etc. were in effect committing negligent genocide by filling millions of people up poison.

What I found was that the FACTS in the medical literature strongly support the existence of amalgam illness. There is no legitimate scientific basis for proclaiming its nonexistence. However, the interpretations in many papers did not follow from the data presented.

In one of the most interesting cases (J. Dent. Rsch. vol 73 pp 620-8, 1994), a journal paper states in the abstract that they proved amalgam illness is entirely psychosomatic. The conclusions state that they proved DMSA is not an effective treatment for amalgam illness prior to filling replacement. The conclusion is what actually followed from the data presented in the paper, not the abstract (but the abstract is what anyone with internet access can easily find on Grateful Med - it takes a trip to a dental school library to get the journal article and read the conclusions).

I contacted the lead author on this J. Dent. Rsch. paper and asked her about the discrepancy. She said that they were "supposed" to prove that amalgam illness wasn't real so they put that in the abstract at the insistence of others - presumably funding agency contract monitors or journal editors. This problem where the conclusions drawn in a paper are completely unrelated to the data presented is really disturbingly common in papers critical of "amalgam illness." Having read any number of real scientific papers in my career, I can say that this kind of thing does happen from time to time in all fields, but I have never seen anything like the frequency or uniformity with which it happens in the medical literature.

Having gotten deathly ill, found that the medical literature was very difficult to interpret due to the intention of many authors to draw misleading conclusions, and that physicians were seldom aware of appropriate treatment for amalgam illness I wrote a book so that other sufferers would have a place to start. If you would like a complimentary copy of <A HREF="http://hometown.aol.com/andycutler">Amalgam Illness: Diagnosis and Treatment</A> you are welcome to it. It provides some background discussion of how the medical community works from the patient's perspective, explains why it is reasonable to expect a large number of people to be mercury poisoned and not know it, provides lists of tests that often come up abnormal for mercury poisoned people (which are as a rule very difficult to get physicians to order since they are sure "it will just come back normal"), and discusses treatments to remove the mercury and suppress symptoms while it is being gotten out of the body.

Linda B (1)

STORY - MS/MERCURY

July 10, 2000

Dan Burton, Chairman
Committee on Government Reform
102 Cannon House Office Building
Washington DC 20515

Dear Congressman Burton:

I am a victim of mercury amalgam poisoning. I have written numerous letters to the media over the years regarding the silver "mercury" amalgam issue but either no answers or no acknowledgement to touch this issue. February 2000 will mark 20 years I have been suffering from amalgam mercury poisoning. Today is a day I'd like to share my story with you because I know you would listen.

I am now confined to a wheelchair as a result of the silver fillings.
Please share this with others to prevent needless years of suffering.

Sincerely,

Linda Brocato

Linda's Experience - MS/MERCURY

February 1980 after awaking and looking into the mirror the right side of my face showed signs of paralysis. The doctor said it was similar to Bells Palsey and should be better within time. Six months later I lost the vision in my left eye followed within time by numbness and tingling of the hands and feet, weakness of one leg and then the other, incoordination, imbalance, etc.

In 1981 the diagnosis of Multiple Sclerosis was established and the search for a remedy or cure began. I spent years of countless visits to neurologists (5 of the best-known hospitals in the Chicago area), nutritionists, kinesiologists, chiropractors , conventional and non-conventional practices, theories regarding Candida Albicans, reading book after book on MS and any closely related topic.

Linda B. (2)

In 1987 was the first time I ever entered a hospital. The massive doses of various medications were now ineffective and the only option offered was chemotherapy in conjunction with other therapies. I was released confined to using a walker and wheelchair.

In 1989 another exacerbation left me in the hospital for 1 1/2 months with overall generalized weakness and at times slurred speech. I was released confined totally to a wheelchair and a hospital bed...a paraplegic.

In 1990 after ten years of continuous exacerbations two to three times each year, ten years of massive doses of medication and three hospitalizations my search for an answer ended. I had contacted a speaker who sent me information on MS and silver amalgam "mercury" fillings. I discovered that the silver fillings are made up of 50% mercury along with copper, tin, zinc, and small amounts of silver, etc. My symptoms of "MS" and mercury poisoning were similar.

A dentist performed a test measuring the amount of mercury vapor being emitted from the silver fillings. The levels of the test results were high and removal was recommended. A blood test also confirmed I was "reactive" to the heavy metals in the fillings.

Even though I had much opposition from the medical and dental community the fillings (16) were completely removed by September 1990. Two weeks after the fillings were removed, improvement began. My slurred speech began to disappear and this was the last symptom to occur. April 25, 1994 test results confirmed "a degenerative disease and toxicity".

I'm out of the hospital bed now and in a regular bed and have experienced considerable improvements. I' m still in a wheelchair but have been doing some form of physical therapy. I have been at the Rehabitation Institute of Chicago, a spinal cord injury program and a continuous exercise program at the health club with limited home physical therapy. This has brought me continuing improvement with a long way to go. As of December 1989 I have NOT had any exacerbations for Multiple Sclerosis symptoms for 10 years and have NOT had any medication for 9 years.

Please understand, I'm not saying that all MS is caused by silver amalgum fillings nor am I saying that silver amalgum fillings cause all MS. What I am saying is there are people out there who may have a sensitivity to MERCURY like me and may exhibit MS symptoms.... MERCURY IS A POISON. Public awareness could prevent years of suffering. Thank you for taking the time to read my letter.

Sincerely,

Linda M. Brocato

To: Dan Burton, Chairman
Committee on Government Reform

AUSTISM – MERCURY FROM AMALGAMS

MJs Story (short version)
Date: 2/11/00 5:19:10 AM Eastern Daylight Time
From: wbwandabrown@netscape.net (Wanda Brown)
To: MFPstories@aol.com

I am a 43 y/o mother of 4. Three prior girls had timely vaccines and are all normal and healthy. When I was 35 I became pregnant with our son, MJ who's 7 1/2. During my second trimester I developed acute teeth pain. I was told to have a root canal and several amalgam fillings refilled and filled. We were reassured this was safe. I also breast fed our son exclusively until he was 15 months. At two months he had DPT and Polio and at 4 months another DPT; at 5 mths another DPT. After the 3rd DPT my husband bought to my attention MJ failed to maintain eye contact with him. He did though with me. MJ's pediatrician dismissed this concern. MJ continued to receive timely vaccines. MJ seemed to develop normally, sitting, crawling, standing, climbing stairs, even playing toddler basketball, riding motorized bike -- although he didn't walk until 16 mths. After his MMR (15 mths) he developed diarrhea and once he started to walk, he failed to develop more speech. Still, he was a very happy baby, connected with us. At 2 1/2 he began to slowly lose baby speech, lose skills and began a regression period to about age 4. MJ was diagnosed with ASD at five. I am convinced my amalgam dental work; breastmilk and vaccines caused MJ's autism. Next week we will see DAN! practitioner who's an allergist. I'd like MJ to be tested for mercury levels. I'd be happy to share more information should you need it. Thanks. Wanda Brown

Brunes (1)

BRITTA BRUNES, MD., SWEDEN
PHYSICIAN TREATING MULTIPLE SCLEROSIS AND
MERCURY AMALGAM ILLNESS

June'2000

from: brunes@swipnet.se (BRUNES PHARM AB)
Dr. Britta Brunes, M.D.
Sweden

Committee on Government Reform

Dear Sirs,

Being an M.D. I have been treating hundreds of patients who have been ill because of their amalgam fillings. Mercury vapor, released from the fillings goes to all parts of the body, passes the blood-brain-barrier and gets involved in the brain chemistry. The patients have many symptoms all over the body, but mercury, being a nerve poison can of course cause neurological symptoms.

In the book "Toxicology of Metals",edited by Louis W.Chang, there is a chapter /number 37/ called "Effects of Toxic Metals on Neurotransmitters" showing that a toxic metal (mercury) can alter almost everything in neurotransmission, that is the way the brain directs the bodily functions and thus cause damage. The researchers are Richard Mailman, Michelle Mayleben and Cindy Lawler, all connected to University of North Carolina and Medical School. There is another chapter, number 53 titled "Autoimmunity Induced by Metals", by Pierluigi E Bigazzi, M.D. Department of Pathology, University of Connecticut. Here it is shown that mercury can have the potential to provoke auto- immune responses in humans.

As an M.D. in general practice since 30 years I have seen many, many patients here in Sweden, whose disease to a great extent has been caused by mercury intoxication. Mercury has many ways of affecting the body´s chemistry. One way is to be toxic to different compounds in the cells and enzymes, one is to generate free radicals, which increase oxidation in the body and another one disturbs the immune system, causing autoimmunity. I and several of my patients have the diagnose multiple sclerosis (M.S.) and many of us have improved dramatically in health and symptoms after having had our amalgam fillings taken out with extreme precautions, pre-medications, antioxidants and in some cases C-vitamin infusions and cortisone for a period of 1 -3 weeks. I have also seen patients with psoriasis (another auto immune disease) improve and in some cases get completely well after removal of fillings, the same with eczema.

The American Dental Association reports less than 100 people with adverse effects from mercury amalgams. There must be something wrong... doctors and dentists aren't aware of the mercury connection to compromised health, something is wrong with the way they are educated or there is too much fear to acknowledge the truth.

I would be happy to here from you. I can give you Luther information and also my case report, living as a symptom-free "M.S.-patient" for the last 12 years. My amalgams were removed from 1990 to 1991, one of the best things I have done to improve on my health.

Yours Sincerely

Birgitta Brunes, M.D

STATEMENTS FROM THOSE WHO HAVE BEEN POISONING BY THE MERCURY IN THEIR MOUTH

I will do all I can to see that the use of amalgam as a suitable material for dental work is stopped. After all, mercury is toxic before they put it in your mouth and treated as toxic waste after it is removed from your mouth, yet many claim it is 100% safe while it's IN your mouth. This makes absolutely NO sense to me.....there is no place for mercury in the human body.

Kim Horter

I believe people need to know there is a potential risk to amalgam fillings..... My main concern is the incomplete information given to patients. They do not have a chance to make up their own minds about what is done to their bodies..... I hope that your organization can help to bring this critically important information to the fore where it can be appropriately studied and the people protected from mercury.

Ralph Wood Wilson, N.D., MS

hemorrhoid free after amalgam removal. Anecdotal, I know, but I don't argue with success

Pete Brake

My story began at age 9 when my parents got dental insurance and the dentist filled 6 teeth. . By the time I was 20, I had received 12 amalgams..... diagnosed as Chron's Disease, Multiple Sclerosis... suffered from allergies, chronic fatigue, respiratory infections, bouts of colds and flu and kidney and bladder infections. I hoped to die quickly ....I was tired of suffering. I had consulted lots of doctors and everything they did made me worse. After amalgam removal, I improved every single day and the symptoms of Chron's, Multiple Sclerosis and allergies stopped.
At age 46, after amalgam removal, I felt better than I could ever remember. I'm now 59 and I'm still symptom free. Life is a joy!

Murlene Brake

The results were dramatic, just from removing the bridge and visible mercury. My depression lifted, the rashes on my hands cleared (havoc for a registered nurse) and most notably my stuttering wasn't as troublesome. It was like witnessing my own little miracle.

Marilyn Kiefer,RN

I
am quite sure that the "liver spots" that started to develop on my body, the Fibromyalgia, depression and fatigue, started about the same time I had my old amalgams out and new ones put in...I now have developed a lipoma at the base of my skull..... but I personally can't help but think that there

is a connection, and do not want to run the risk of developing cancer..... I have run out of ideas and have no clue as to what kind of Dr. or tests I should even have done. I am looking at $5,500.00 just to get the amalgams outta my mouth

Linda Daughetee

I had nine amalgams by the time I was 27, and I suffered from manic depression. Since my life had totally fallen apart and I was suicidal, she put me in a psychiatric hospital for 3 days. Then she took me to a dentist and had him remove my amalgams..... I'm 39 years old now and I have not had another manic depressive episode. My health has been good and I've been a productive member of society. I'm also a father of seven healthy children who do not have amalgams.

Layne Fechner

ALL SYMPTOMS SEEM SIMILAR TO MERCURY POISONING
20 YEARS OF CHRONIC FATIGUE, MULTIPLE CHEMICAL SENSITIVITIES
NO RELIEF FROM DOCTORS!
(seeing flashes of colors, blurred vision, pain in ear, hair falling out, weak legs, jumping muscles, yeast, allergies and sinus infection)
What A Mess I Am!

Kathy B.

People are taught that "our whole notion of the self is shaped by the culture in which we have been reared." So there's no doubt in my mind that the self and our society has been shaped by the poison of mercury in dental amalgams. Our government must ban mercury amalgams and follow other countries who have done their scientific homework and recognized the extreme health hazards of this toxic material.

Deb Hope

July'2000

To: Committee on Government Reform

Dental Toxins: Your Teeth May Be Making You Sick
(From Alternative Health Digest, with permission from Burton Goldberg)

Out of the Wheelchair, Running 25 Amalgam Fillings Removed

MERCURY TOXICITY is increasingly correlated with the onset, either sudden or gradual, of numerous health conditions, such as allergies, anxiety, depression, fatigue, headaches, high blood pressure, intestinal problems, and irregular heartbeat, among others.

One study, involving 1,569 patients from four countries revealed an impressively high cure or remission rate (54%-97%) for 21 health conditions following MERCURY amalgam filling removal. A poll of 1,320 of my own dental patients proved a high degree of correlation between heavy metal TOXICITY (as demonstrated in blood tests) and up to 30 symptoms. For example, 73% of these patients had unexplained irritability, 72% frequent depression, 67% numbness or tingling in the extremities, 63% unexplained chronic fatigue, and 60% constant bloating.

MERCURY TOXICITY is also associated with the sudden onset of multiple sclerosis, as Gonzalo's case illustrates. Gonzalo, 32, was a highly athletic former Marine who ended up in a wheelchair, almost immobilized by multiple sclerosis. He had 25 MERCURY fillings in his mouth. Gonzalo's problems began when he pushed himself a little too hard with his triathlon training. He became paralyzed from the waist down and ended up in the hospital for ten days under examination by three neurologists.

Gonzalo's immune resistance lowered to 1% less than the toxic challenge—remember the concept of MERCURY retention TOXICITY—and he came down with an illness. His conventional doctors informed Gonzalo, a former Green Beret in the Army, a man believing himself capable of "handling anything," that he was facing a life of chronic, debilitating illness. "I had been around bombshells before," Gonzalo said, "but none quite as devastating as this one."

Instead of languishing into the kind of mental and physical "rot" his doctors insinuated was his future, Gonzalo researched the medical literature. He read about the toxic effects of MERCURY fillings and remembered that he had gotten sick following the placement of his last three fillings, and that two months after his latest filling and a record-breaking run "I lost strength and feeling in my legs." The combination of cumulative MERCURY TOXICITY and physical overexertion collapsed Gonzalo's immune system.

His doctors' predictions failed to materialize. After we carefully removed all of Gonzalo's MERCURY amalgams, he began to feel better. Within less than three years, he was in the triathlon again. Gonzalo commented: "Am I still in a wheelchair? Hardly. On a cane? No, I gave that up, too. My life is now renewed."

Blood: Classified into 4 blood types or groups according to the presence of type A and type B antigens on the surface of red blood cells. These antigens are also called agglutinogens and pertain to the blood cells' ability to agglutinate, or clump together. Type O blood (containing neither type) is found in 47% of the Caucasian population; type A, 41%; type B, 9%; type AB, 3%. Another form of blood grouping is according to Rh-positive and Rh-negative types, based on the distribution of 6 different Rh antigens.

Anonymous

NEED HELP FROM CALIFORNIA

I need help really bad because I'm starting to lose hope.

This is a story which was sent to one of the Metals discussion lists begging for help. This is typical of the posts received.

About three years ago ('97) I became vegetarian and shortly after this drastic change in my diet, I came down with a number of different health issues. To start, the most noticeable onset of health problems was one night I was working at my computer and I experienced a mild episode of vertigo. I thought maybe this could be attributed to long hours in front of the computer screen(it still could have been, but it goes deeper than that so please read on) I stood up and had to grab my desk to keep from falling over. So I went on for about one year as a vegetarian, and these episodes kept reoccurring, becoming progressively more frequent. I felt that it had something to do with my diet, so I switched back to eating meat.

My problems did not go away, instead I began to experience these bouts of fatigue that were getting noticeably worse. I couldn't understand what could be wrong. This fatigue meant that every day I would wake up and feel tired, nothing could remedy this problem. I tried everything from changing my sleeping pattern to taking supplements and so on. Nothing helped. So I struggled to cope with the fact that my problem could be alot more serious that I thought. I rushed over to my doctor and I had him run every blood test known to man, for STD's and everything else you name it. All tests came back negative. Except he noticed one thing, my thyroid was very low. He went on to tell me that this was my problem, low thyroid. So I go on synthriod. I kept telling him that I was getting really tired and it was affecting my thought process and I was becoming very negative as a result of my health problems. He said my dosage of synthroid needed to be adjusted. He went on and on and he asked me if I was depressed. I told him no, but my health issue was really getting to me, 2 years prior to all this I was highly energetic and extremely positive. I am now the opposite, and with every waking moment I begin to think that I am just one of those people that cannot be helped and I have to accept it.

I took my health matters into my own hands. I started to talk to a lot of people on the Internet about thyroid trouble and I did alot of reading and research about this topic. I came across an interesting subject: Candida. I researched this topic alot more, and as it turns out, I used alot of antibiotics for acne control and just recently had surgery on my right shoulder and was prescribed antibiotics. So I thought that maybe the antibiotics played a part in all this.

I seeked out a holistic doctor to do further research on this subject. I found a doctor and had a saliva test and bingo, she found it! Candida Albicans. She prescribed me a handful of herbs and sent me on my merry way (after I spent about 300 dollars on the pills that you can only buy at her store. So I'm on this diet and I have to consume over 60 pills a day which were supposed to clean out my system and rid me of Candida. Well I lasted about 2 months until these pills started to make me sick to my stomach. I had to discontinue their use. But there was a reason for that. Besides the fact that they were making me sick to my stomach, I WASN'T FEELING ANY BETTER!.
On top of that this holistic doctor was draining all my cash. I had to find some answers because I was getting pissed and was tired of all the BS.

Anonymous 2

(2) Need Help

My best friends mother was an ear nose and throat doctor years ago, but now specializes in mercury detoxification amongst other things. My friend insisted I go to see his mom, so I did

and she basically did alot for me free of charge. Except for one thing, I had to get this specialized blood test which tested for toxins in the blood. It had to be sent to New York and I would get the results in 3 weeks. This test also cost me 375 dollars... Sigh.

So I'm desperate for some answers and I'm starting to get pissed, I took the test and that was that. The test came back and I got the results. It turns out I have high traces of arsenic in my blood, high traces of mercury, and high traces of lead. Holy crap what do I do and how did this happen? It's not like I've been living next to a nuclear reactor or anything. So she goes on to ask me what kind of fillings I have and how many. I tell her I have 9 fillings, an exposed root canal that has yet to be finished, and my fillings are silver amalgams. She says holy those fillings have to come out! She gave me a DMPS iv and began detoxifying me of mercury and the ultimate plan was to go to Tijuana, Mexico to the Biological Dentistry Center and have the fillings removed, as this was the only place which was qualified to remove them.

My Grandmother and Mother caught wind of the Tijuana thing and told me this whole filling thing sounded cockamamie. My grandmother insisted that I go to see her doctor. So I did, meanwhile I'm taking Glutothionine and all the other necessary supplements needed for mercury detoxification.

I go to see her doctor and I turns out that my grandmother has a bad thyroid and my thyroid trouble could possibly be hereditary. He took some blood and sent it out and referred me to an endocrinologist in Beverly Hills. So I see this guy and he runs a bunch of test and sends them over to the other doctor, 1300 dollars later, the endocrinologist comes up with hypothyroid. Well duh. So I go back on Synthriod again. He insists I take a glucose tolerance test. But there's no way I could afford to do this with the Beverly Hills guy. Screw that! This guy just sucked me dry of 1,300 dollars to tell me something I already knew. I had my Grandmother's doctor obtain all the equipment he would need to do the test at his office. So we go for it and it takes me six hours. I had to fast the night before at 12 midnight, and have my ass in his office at 8:30 am. I drink some orange stuff and they take the first two vials of blood. I wait 30 minutes and they take another two vials. I wait another hour and

they take another two vials. I wait two more hours and they take another two vials. And I almost pass out from all this, it's like 2:30 pm. Now and I haven't eaten anything. So the test is done and I go get something to eat, needless to say. I wait three days for the results. He says he finds something that suggests hypoglysemia. And now I have to start taking one and a half synthriod pills as opposed to the usual one, and start eating more small meals throughout the day rather than less large meals.

Anonymous 3

(3) Need Help

I failed to mention that a couple months ago, my girlfriend met someone at her college that had amalgam fillings and a whole handful of health problems but that is all gone now thanks to her husband. He removed her fillings and this happens to be his specialty. His name is Jaime Azdair. I went to see him speak at some hippy bookstore and he went on and on about negative currents in the mouth and gold is the only thing you should put in your mouth but it has to be the right kind of gold and he just so happens to make this gold. He also goes on to telling the audience that he charges anywhere from 1,000 dollars to 7,000 dollars per tooth for reconstruction. He works on rock stars and movie stars teeth and so on. Well I guess you have to be a rock star or movie star to be able to afford his work and the last time I checked I was neither of these. If this guy was really into helping people and not into material possessions,

he wouldn't have been wearing a crocodile belt, a pair of Italian loafers, and had an Armani bag in which to carry his equipment. This struck me as a little odd... I do make good money right now working as a graphic designer, but if I was to go to this guy for help, I would end up homeless with a mouthful of nice teeth and he would end up with a new car. I don't choose to use his services, and I'm not going down to Tijuana.

Now here's the deal: Of all the reading I've done, I have a strong faith that many if not all of my health problems are related to my fillings. I have had them since I was 8 and I am beginning to get really sick. I am dizzy all day long, I still suffer from mild bouts of acne, my joints click and get hot, I have to force myself to exercize, I never feel rested, it's nearly impossible for me to wake up in the mornings, I get dizzy walking up stairs, I get double vision, I have extreme fatigue, I have a metallic taste in my mouth (I always have and it feels like I'm chewing on a piece of aluminum foil all day long)
I need help really bad because I'm starting to lose hope.

I live in the Los Angeles area, but I am willing to fly anywhere in the continental United States to see a professional in this field. I refuse to go to Mexico for any health care. There MUST be someone somewhere who knows what to do about my situation, but isn't going to rob me out of house and home.

Anonymous

Anonymous (1)

My Story

I had suffered from a number of types of heavy metal poisoning from my dental amalgams, namely mercury, tin and nickel.

My Symptoms

I suffered since 1991 from numerous symptoms.

- My chief complaint was numerous painful lesions on my scalp, arms and legs. These raised red lesions were full of blood in the beginning but as time passed they became filled with a collection of white blood cells, attempting to fight off the contagion. The dermatologist referred to these oily, red, itchy lesions as "seborrheic dermatitis". He prescribed, as medical doctors often do, an entire list of antibiotics to treat "the infection". Little did the dermatologist realize, nor did he suspect that my dental amalgams had been leaking for seven years.

- I also suffered from hair loss. The roots of the hair shafts were covered with a white follicle. Sometimes, the white discolorations would begin to climb up the follicle. What was so unusual was that I just recently turned 30, and I had white hairs in many areas.

- My digestive system was completely in a state of "malabsorbtion" of proteins, carbohydrates and sugars. It had been diagnosed as "toxic bowel syndrome". As a result, I had persistent abdominal discomfort and pain. The application of any pressure on my lower abdomen would be uncomfortable as my lower colon was sensitive to the touch.

- Another strange symptom was that both of my kidneys and my lower large intestine would feel cold quite often. I would describe it best as a dull aching coldness and tightness. I required the application of hot water on some occasions because of the coldness.

- On several occasions my muscles were beginning to "twitch" involuntarily. This symptom appeared to mimick symptoms similar to seizures or epilepsy. I couldn't stop the twitching, and I often wondered what was happening.

- I also must admit that there were some psychological and emotional aberrations which had been present as well. Most notably, there appeared to be a state of persistent and irrational anger. I had no explanation for it, but perhaps it was because of these toxins which had been impairing my vital organs.

Methods of Diagnosis

Mercury poisoning as well as contamination from other methods may be determined through an analysis of the minerals in hair follicles, a blood analysis, and a urine test. My results indicated that I possessed a high level of aluminum in my body (as a result from eating out of aluminum

pots and pans, and drinking from aluminum soda cans), but I have no doubt that it was the mercury which had caused my symptoms. Also present was a low level exposure to mercury, tin and nickel.

The Good Dentist

I went searching for a bio-compatible dentist with the intent in mind to have my amalgam fillings removed. I located a bio-compatible dentist by approaching a local health food store owner from a health food store which I had patronized for a long time.

The dentist was very skilled in recognizing what the symptoms were for mercury leakage from amalgams. The silvery mercury/silver amalgams were black underneath. Furthermore, another symptom of mercury leakage is that my gums were starting to become black in a few areas. Underneath many of my fillings, there were several cavities which were continuing to form. I am convinced that the cavities were somehow connected to the leakage because most of the fillings which were leaking had cavities underneath. The mercury was leaking directly into the cavities providing a direct path into my bloodstream.

The Procedure

My dentist followed the protocols for amalgam removal. The protocol requires the application of a rubber dam placed around the tooth with a clamp thereby isolating it from the body. When the fillings are drilled, any debris which falls away falls into the rubber dam and is immediately removed with a vacuum suction apparatus. Of course, the saliva suction apparatus is utilized as well to prevent the patient from drowning on his/her own saliva. I should mention that any mercury tatoos which have accumulated must be removed as well and any bacteria which is located under the filling must be removed with a scraping tool or even with "food grade" hydrogen peroxide.A material which is commonly used to replace the dental fillings is a plastic type of composite, which is squirted out from a tube directly into the tooth cavity. There is no trituration of metals, as the composite is dried with a heat lamp. After the heat lamp is applied several times, the jaw is closed and moved back and forth so that proper jaw use may be achieved. Any excess, dried composite material is sanded away with another tool. Finally, a sealing chemical named "Seal-It" is applied to the repaired tooth and allowed to dry.

Because these protocols were followed, I was not exposed to any mercury vapors or particles during the removal process. Overall, I had ten mercury-amalgam fillings. More than half of them were severely leaking. My symptoms persisted until the final two fillings were removed.

My Recovery

Just a few days after all of my fillings had been completely removed, my symptoms began to disappear. The first symptom to disappear were the scalp and arm lesions. They have almost completely disappeared. I have not even begun to take any form of "chelation therapy" yet. Some chelators for mercury and other heavy metals include garlic and the amino acid cysteine. The garlic, because it is a sulfur bearing food, chelates with the heavy metals thus helping to remove them from the body. My digestive distress has begun to repair because I have not felt any more gas bloating or pain. My kidneys have not felt cold since the amalgam removal either. My recovery is far from complete. I am certain that it will take more time to completely recover, and so I must persist at removing the heavy metals which had accumulated up until this time.

My Mission

I believe that it is my **mission**, now that I have experienced this problem first-first hand, to make certain that other people do not become effected with the same medical afflictions and others.

For this reason, I have called for a letter writing campaign to the politicians in the White House, the House of Representatives, and the Senate, to bring the issue into the public arena. If enough people make their voices heard by bombarding these elected officials with public appeals for an investigation and for action, then maybe action will be taken and the ADA could no longer bury the truth from public scrutiny. Speak Up on the Issue

Return to Main Page

July'2000

Congressman Dan Burton
Committee for Government Reorm
Cannon House Office Bldg.
Washignton, DC 20515

Dear Congressman Burton:

I am definitely convinced there is a connection between mercury and MS.

Diagnosed with MS in Jan 1985, I have had five different neurologists and four different urologists. I have had about 9 treatments of steroids (methylprednisolone) and chemotherapy (cytoxan) from Feb 1987 to May 1993 and countless prescription meds including antidepressants, antibiotics for bladder infections, muscle relaxants for spasms and tremors, and I can't remember what all else. At one point I was partially, temporarily paralyzed.

The steroids helped me walk again. The cytoxan, according to my neurologist, was supposed to suppress my immune system and make my exacerbations fewer, farther between and less severe. It did suppress my immune system, but my exacerbations got closer together and more severe. I had one bladder infection after another.

I didn't know any better at the time. But now I do. Suppressing the immune system is NOT the way to go. You should remove toxins from your body and not put any more in. You should put in healthy nutrients from whole foods, not foods processed with additives and preservatives. Help your body heal itself. It has that ability if you don't abuse it.

Anonomous

H Imay_

February 8, 2000

TO : CONGRESSMAN DAN BURTON
Committee on Government Reform

Starting in high school in 1962, I noticed a diminished mental capacity and lack of concentration. a dentist, My cousin's husband, had begun the favor of filling my decayed teeth with amalgam fillings. My quality of life continued to decline as I struggled the next few years to finish a college degree. This task was not easy. Read sentences refused to go into memory, and required re-reading. Blackout spells were becoming a new and baffling symptom. I sometimes wondered if I was losing my mind. Chronic fatigue had changed my life from a celebration to a chore. As I worked, my health continued to decline. My low point in the 80's brought me night sweats and elevated liver enzymes. Then life changed. I read of Nancy cost in an Oklahoma newspaper. Then I saw the 60 minutes show on amalgam. I found a saintly dentist who would remove my fillings on my state -employee insurance plan .my symptoms disappeared almost immediately. I soon felt 20 years younger- better than I had since high school. Truly a miracle, and without question caused from the fillings .I now feel that dentists who place amalgam should be horsewhipped as enemies of the people .all but my friend, the saintly one.

Sincerely,
Brian Altman

Letter to Freya via Internet Discussion Support Group

Date: 2/12/00 2:50:30 AM Eastern Daylight Time
From: UKLDJFK (Brian)
To: MFPStories (Freya)

Dear free, just to talk to someone who understands my suffering and frustration makes me feel good. But my symptoms were so minor compared to yours and those of so many others on the newsletter. That a group of dental "quacks" [from the German for quicksilver or mercury, I just read] could remain so uninvolved from the swirling controversy of suffering patients is beyond my understanding. This country has burned witches on less anecdotal evidence .the devastation caused to your life reminds me of that of rosemary Carter. She went from marathon runner to bedfast and back over a six-year period. I hope you have her account. she is at rcarter@netidea.com also, if you haven't already done so, please read the letter of warning sent by the Australian dental society to all Australian dentists. This is at http\\vest.ga.se/homepages/old_house/mercury/mouth/mail/mail072.html .I can't provide corroboration of mercury poisoning. Though both blood and urine were tested, nothing was remarkable. I truly feel that most of the problems caused by amalgams comes from continuous voltage they produce. This activates the immune system to fight it forever. This is called chronic fatigue. The voltage also interferes with the central envois system, being many times stronger than we can produce. This is why patients lift out of wheelchairs when their amalgams are removed. I did have allergies and rashes that disappeared along with the amalgam. Nancy cost was a lady featured in the 60 minutes episode. She had brain changes of ms, slurred her speech, and walked with a cane because of muscle weakness. She had instant recovery when the metal was removed. I live in Springfield, Illinois. The saintly dentist is Dr. George Connor. I can't say he is a practicing mercury free dentist. Dr. journal was my doctor when I had elevated liver enzymes and night swears. He can document a significant drop in enzymes shortly after some amalgam removal and a

more enthusiastic and optimistic patient .he may not believe amalgams are the problem, though. as he said at the time," I am a scientist, and besides, my brother-in-law is a dentist "
regards, Brian

Budd

To Honorable Thomas Allen

Re: Dangers of Mercury

Dear Mr. Allen,

. I understand there is to be a hearing on mercury toxicity.

I am opposed to the element Mercury being used in the human body . I have suffered from Mercury containing dental fillings for years. I just learned about the dangers of mercury from dental amalgams in November'1998.

I had Computerized Regulation Thermography which showed results consistent with mercury toxicity. I had the mercury filled teeth filled with composite filling material and I am feeling better each day. I plan to have further testing within the next week for confirmation of my progress.

Please make it unlawful to use mercury in any form for dentistry.

Sincerely,

William L. Budd, M.D.
15 Bunganuc Road
Brunswick, Maine 04011

March 19, 2000

To: Dan Burton, Chairman
Committee for Government Reform

Dear Chairman Burton and Committee:

Re: MY MERCURY ILLNESS

My health problems began Aug 31 1997 when I fragmented a disc in my lower back. I was immediately put on anti-inflammatory drugs, muscle relaxers, and pain medicine. I rested a few weeks and seemed better so I went for physical therapy where I re-injured my back on the second visit. This time I was in extreme pain having to sleep in the tub to keep the pressure off my back .I noticed when the problem began numbness and tingling sensation in my right calf. After tests to confirm the fragmented disc I was sent home to prepare for surgery. Over the weekend I developed a spinal headache with roaring in my ears and was taken back for a spinal patch. While there my doctor had my ears tested because of the roaring. I had a hearing test and my ears were viewed through a microscope and was diagnosed with Meuniere Disease. I was placed on a low sodium diet and given a diuretic. After three weeks of all the above medicine and the diet I became ill one afternoon at work like I was getting the flu. My stomach was very unsettled, my vision did not seem right, my balance was off, and I started to develop severe insomnia and anxiety. For the next three months the most sleep I had at night was 4 hours going to bed at 10:30 and waking at 2:30 every night. This problem and the digestive disturbances continued to worsen. initially in Nov I had the back surgery hoping to eliminate that problem and use the time off to deal with my other ailments. While off I visited a clinic in Nashville and had numerous tests and x-rays only to be told I had IBS, given some pills and told I would have to live with it. My stools were getting worse each day the anxiety and depression were worsening and I was worn out from no sleep .I changed my diet and began supplements to help my digestive tract.

I soon started back to work and was exhausted and sinking fast when a friend who was also a PA saw me one day and began discussing my health problems. He told me I was suffering from depression and gave me an antidepressant. It helped my sleep somewhat but the stomach was worse than the anxiety and depression became unbearable. I was referred to a shrink who put me on several medications for depression and anxiety. Now I felt like I was living in hell knowing that if I did not find some help I would not be around for long. Having a three year old, I knew I had to keep me searching, as my child was the only reason to keep living .

I continued searching the net for answers when one day I came across the symptoms for mercury poisoning. It was amazing how many symptoms I had but how could I have been exposed to hg? Then I saw dental amalgams as a source and realized the 12 amalgams I had since about the age of 8 had been slowly poisoning me for almost 20 years . Next I had to find a doctor to treat me. I found a doctor in Atlanta, GA that practices Environmental Medicine and traveled for the testing .A couple of weeks later the results of many tests were in. In a letter the following items were presented: Porphryin levels were shown to be elevated. Amino acid panel revealed elevated

sarcinine and homocysteine. I was also later shown to have toxic renal injury. Chemical level study showed an elevation of tetrachlorethylene at 325% above the adult average population. It is a chemical I was exposed to 15 years ago while working for an outdoor sign company . Stool Study showed geotrichum,klebsiella ,and citrobacter. There was a decrease in lactobacillus and S-Iga was at 1 with low end of normal at 40.Jejunal fermentation test revealed candida in the intestines. Candida blood test revealed candida in the blood stream. Immune neuropathy study revealed damage to the sensory nerves or at least producing antibodies against them. Oxidative stress test showed a decrease in GSH and free radical damage. Heavy metal challenge showed mercury pre-challenge at 2.4 and post at 19.7 lead 1.1 to 2.1 and aluminum 4 to 50.ALCAT indicated several allergies to foods, yeast, and chemicals traveled to Atlanta had my amalgams removed, detoxed the chemicals through a detox treatment a the doctors center, and began chelation along with strong antibiotics for the gut. I was so sick and weak from all of this losing 30 pounds and I began to wonder if I had made a serious mistake. Shortly after the last removal and the final detox session the anxiety and depression left along with the dizziness .Slowly many symptoms began to fade. One year and two months later I can say I am about 65% of the way back to my prior health. I have had to endure melanoma along the way and continue to have headaches, muscle weakness ,digestive problems, and sore joints and muscles .

I truly can see a positive direction and feel my mercury detox is really slow due to very low levels of glutathione .I continue to deal with the gut issues which is the other key to regaining a healthy life. There is no doubt that mercury played a great part in my health issue and many others
I have talked with. I pray each night that God will heal me of the problems the dental and chemical companies have caused. As for me I want to make sure no more unsuspecting people are poisoned to the point that death becomes a better choice than life .I continue to search and live for my now two children and take one precious day at a time.

Al Bellefant
Tennessee
AlBenefonte

E-Mail - albellenfant@yahoo.com (Al Bellenfant

Signature (1)

FROM VANCOUVER, BC

March 8, 2000
to: Dan Burton, Chairman
Committee for Government Reform

Dear Congressman Burton:

This is a personal story about the effects of dentally toxic materials placed in my mouth and the effects they have had and continue to have on me.

I am one of the lucky ones. I did not get MS or Fibromyalgia or Chronic Fatigue or ALS or Lupus or Parkinson's disease. I got "Brain Fog" and memory lapses and numb hands and back, digestive problems and sporadically immovable joints and muliple chemical sensitivites and the worst: a "quicksilver" pain/weight that literally moved around my chest cavity for months. My body was doing its best to deal with an uninvited guest: MERCURY.

This last mercurial (and I know that this quicksilver moving pain sounds strange but it WAS REAL and I did not imagine it), it even occurred when I had the fillings removed and the proper protocol was not followed. It was also a result of taking Chlorella which is thought by some to be useful in re-moving the Hg ....but the Big problem is that it moves the mercury to different places in the body where the body cannot deal with it. When you have remaining amalgam in your mouth it is not a good idea to mobilize the Hg (as I understand now). When all the amalgam is out of the body
re-moving the remaining body burden can never be done in total but DMSA and Lipoic Acid (chelating agents) can help to lessen body burden somewhat and reduce symptoms. (according to Chemist Andy Cutler...see his book "Amalgam Illness: Its Diagnosis and Cure")

There is a HUGE amount of misinformation out there especially among those we trust to help us. The dental community has few dentists who are trained to know how to safely remove the toxic mercury fillings from our mouths, because the people who are in charge of training them will not admit that there is a problem.

I have found a dentist who solved some of my problems and helped me (slowly over time and after removing the toxins) to begin to ameliorate the symptoms.

This dentist is nc longer allowed to practice dentisty in the US. This dentist safely removed all the mercury fillings and other toxic dental remains in my mouth eg. root canals and cavitations.

This total dental revision took place 4 months ago andthe "quicksilver" pain that went flying around my chest cavity has stopped. However I continue to have other mercury symptoms which I treat with DMSA and Lipoic Acid every other week. I find that this method works well for me.

I would be pleased to speak with anyone about the effects of amalgams on the body and my experience of this.
Thanks

Ann Blackmore
sbe@netidea.com

Murlene Brake
146 Laura Drive
Madison AL 35758
256 830-0662

January 12, 2000

Dear Congressman Burton:

My story began at age 9 when my parents got dental insurance and the dentist filled 6 teeth. I developed asthma soon afterward. At age 16 when an amalgam in a lower molar expanded and broke the tooth, the tooth was extracted and the asthma stopped.

By the time I was 20, I had received 12 amalgams and I also began suffering from symptoms that eventually got diagnosed as Chron's Disease. I also suffered from lots of allergies, chronic fatigue, respiratory infections, frequent bouts of colds and flu and frequent kidney and bladder infections. Doctors also suspected that I was developing Multiple Sclerosis. In 1984, I quit my job as a Management Analyst for the Army Corps of Engineers and went home and prayed I would die quickly because I was tired of suffering. I had consulted lots of doctors and everything they did made me worse.

In 1985, I stumbled across information on mercury toxicity and the symptom profile fit me perfectly. However, nothing available to me from the Government Printing Office or the Department of Health mentioned that mercury was in amalgams and I could not determine how I had ever been exposed to mercury. Four months later I learned that mercury was in amalgams.

I was bedridden and nothing had helped my situation so I made the decision to take a chance and have my amalgams removed. I had nothing to lose but money, and I couldn't take it with me. My last amalgam was removed December 6, 1985 and I was extremely ill until sometime in February of 1986 with what I thought was the flu. After that, I improved every single day and the symptoms of Chron's and Multiple Sclerosis stopped. As a matter of fact so did the allergies, infections, colds, flu and fatigue. At age 46, after amalgam removal, I felt better than I could ever remember. I'm now 59 and I'm still symptom free. Life is a joy!

I was one of the original 6 people who established the non-profit organization known as Dental Amalgam Mercury Syndrome (DAMS). Although, I'm not as active in the organization as I once was, I hear from people every day concerned about their health and seeking information on the mercury amalgam connection. I receive phone calls and letters from people who tell me that they have had their amalgams out and have experienced health improvements and/or recovery.

My prayer is that future generations will not be exposed to mercury from amalgams. Human life and suffering is too high a price to pay for professional ignorance and neglect.

Sincerely,

Murlene Brake

Brake

Pete Brake
146 Laura Dr.
Madison AL 35758

January 14, 2000

Dear Congressman Dan Burton:

What do hemorrhoids and amalgam fillings have in common?

After my wife regained her health with amalgam removal in 1985 she began URGING me to have mine removed. I hated going to dentists and since my only health problem was chronic hemorrhoids, I kept refusing. But every time I complained about my hemorrhoids, she would jokingly tell me they would go away if I'd get my amalgams out. Neither she nor I believed there could be a connection.

I finally gave in to her, any price for family peace, and had my amalgams removed. We were both overwhelmed when the hemorrhoids shrunk and never bothered me again. Since then, she has talked with several people who have reported that they were hemorrhoid free after amalgam removal. Anecdotal, I know, but I don't argue with success.

Pete Brake

Ivan Brand
200 E. 9th St.
Pella, IA 50219
515 628-2505
ibrand@kdsi.net

Home of Ivan Brand

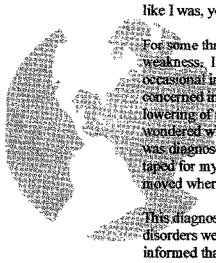
March 9, 2000

Re: **Mercury amalgams and my recovery from**

vocal chord paralysis

Dear Doctors and friends,

Like many people I was a skeptic when told that a solid dental amalgam containing mercury could be harmful. I found it hard to believe that a seemingly hard substance could release mercury. I also found it hard to believe that a substance in such wide usage could be harmful. If you are skeptical like I was, you should consider my own personal experience.



For some three or four years, I had been experiencing progressively worsening condition of vocal weakness. I started out believing bronchitis or a common cold was affecting my voice. I had occasional improvement but the condition became the norm rather than the exception. I became more concerned in 1997 when the condition was substantially interfering with speaking. I also noticed a lowering of my vocal range. I was a trained singer but had given up singing except in groups. I wondered whether a polyp or nodule had formed on the vocal chords, so I visited an ENT doctor. I was diagnosed with a "marked true paresis of the left true vocal chord". This diagnosis was video taped for my benefit and it was obvious, even to my untrained eye, that the left vocal chord barely moved whereas the right one attempted to compensate by moving further toward the left one.

This diagnosis was followed by a series of examinations, blood tests, and a CT scan. Systemic nerve disorders were investigated by a neurologist. All tests and examinations turned out negative. I was informed that there was nothing further that could be done and was referred to a speech therapist. I declined this since I felt I did not need further instruction on the use of my voice.

Since my problems had existed for so long, I was convinced that there must be another cause. I was informed that a viral infection could have been the cause but I was told there was no treatment available if this were the cause. I was also informed that heavy metal poisoning could cause this condition but I considered this unlikely given my clean environment at work and home.

I refused to accept the prospect of no further treatment being available so I began researching other causes. I had heard about mercury poisoning causing paralysis and other problems so I began researching the "silver" dental amalgam controversy. I found that mercury does in fact escape from seemingly solid dental fillings and slowly accumulates in the body. I became convinced that, at least for some people, mercury can cause serious health difficulties. This fact struck close to home when one of my sisters became sick with headaches, severe pain, muscle weakness, partial numbness, tremors, and other difficulties. Despite her consultations with many doctors, including a visit to Mayo clinic, no diagnosis and treatment was successful. Finally, after removal of her mercury amalgams, her difficulties all but disappeared. Her experience in addition to my own research led me to my last option, which was to remove my 14 dental amalgams. In October, 1997, all of my mercury dental amalgams were replaced with non-metal material.

Brand (2)

I received no other medication or treatment of any kind since the diagnosis. Two months after my amalgam removal I scheduled an examination with a doctor at Mayo who had not previously seen me for this condition. I was surprised when he commented after this examination that he did not see a paralysis. I had noticed before seeing him that my voice seemed stronger - yet I was surprised to hear his report because I was still skeptical of the mercury poisoning possibility. I decided that I should return to the doctor who originally made the diagnosis because I wondered whether there was a possibility of a wrong original diagnosis. When I returned to him I did not inform him of the Mayo diagnosis nor did I inform him of the amalgam removal because I did not want to produce any bias during the examination. It was time for a follow-up examination according to his original instructions so that was the reason I gave for requesting this examination. I asked him to video the laryngoscopy so I could see the results with my own eyes. After the laryngoscopy, he reported that he was surprised to see a near normal left vocal chord. When I personally viewed the video, I could also easily see what appeared to be a normal left vocal chord. I could see the left chord moving almost the same as the right one. **This was very much different from the results of the original laryngoscopy.** It was at this time that I informed the doctor that I had undergone removal of my dental amalgams and that I had received no other treatment. He indicated that the effect of dental mercury amalgams is controversial. Nevertheless, he was also very attentive when we discussed the amalgam removal. At the conclusion of the consultation, he commented "you've made a believer out of me". **It was at this time that I was finally convinced that the dental amalgam removal was the cause of my marked improvement.**

One might argue that the above evidence is circumstantial - but considering all the facts, I am convinced that if there were another unidentified cause, it was only a remote possibility compared to the probability that mercury poisoning from mercury amalgams was the cause of the "marked paresis of my left true vocal chord".

My only request of you is that you have an open mind to the possibility that mercury amalgams can produce serious nerve disorders among some people. When conventional medical investigation fails to reveal a cause (as in my case), consider mercury amalgams as a possible cause - especially if the patient has several amalgams containing mercury. I am convinced that many people today are living with serious and disabling illnesses due to mercury poisoning. **Those of you in the mainstream medical profession are the ones most able to help them if you will only be alert to the real possibility that mercury poisoning is the cause of their difficulties.**

Some argue that there are risks in the amalgam removal procedure - but imagine how hollow those arguments sound to me and to my sister who "has her life back" after it had approached a state of being unbearable. For some people, the risks of retaining their mercury amalgams clearly outweigh the risk of removal. Without help from their doctor, many people will suffer from the effects of mercury poisoning if no intervention is taken. **Doctors, can you be counted on to at least inform your patients suffering from symptoms consistent with mercury poisoning that their silver amalgams could be the source?**

Sincerely,

Ivan Brand

P.S. I have all of my medical records from which much of the above information was taken.

Carter

Subj: **Rosemary Carter - my story**

sinusitus; tinitus; stomach and intestinal problems; inability to concentrate; brain fog; depression; rage; severe hormonal imbalances; chronic split lips; burning swollen toes; misshappen and paper thin nails; changes in my voice; hair went white

About 10 years ago, at the age of 42, my health started to deteriorate rapidly. Until that time had been an athlete, running several every day as well as training horses. And I taught philosophy at The University of British Columbia. I had episodes of severe muscle weakness, episode of very low heart rate (down to about 40 bpm;), episodes of severe fatigue, exercise intolerance, severe lactic acid after doing less than my usual exercise, severe muscle cramps and spasms. These symptoms progressed in severity and length until I had full-blown chronic fatigue and fibromyalgia. The low heart rate episodes where replaced with tachycardia. I had sinusitus; tinitus; stomach and intestinal problems; inability to concentrate; brain fog; depression; rage; severe hormonal imbalances; chronic split lips; burning swollen toes; misshappen and paper thin nails; changes in my voice; and my hair went white. I was so exhausted that I couldn't even sweep my floor. I spend 6 months virtually in bed.

My husband and I spend hours and hours searching on the NET for research that might help me. My brother spend hours and hours in the medical library at UBC. On the basis of what we found, I went on a very extensive supplementation program that relieved many of my symptoms and got me back on my feet, but I was not well. As I continued my search, I found an article on the NET that made the connection between the problems I had and mercury poisoning. I followed this up and was astounded at what I found. There can be no doubt that mercury from amalgam fillings is a severe health hazard, and is responsible for thousands of deaths and millions of peoples' ill health. I also discovered that the supplementation program I had developed for myself is one that helps mitigate some of the effects of mercury poisoning.

I had my amalgams removed and went on a detoxification program. I am now symptom free, though I have not finished removing the mercury from my body and am still on an extensive supplementation program. I am training horses and running or cycling.

I am on the Faculty of the Open University of British Columbia and received my Ph.D. in philosophy from the University of British Columbia. In order to understand the technical scientific article, I had to do a crash course in molecular biology. And now that my brain is working again, I am embarking on a B.Sc. in molecular biology, and am considering doing a second Ph.D.. I am particularly interested, of course, in how toxins like mercury mess up the body.

LEO CASHMAN
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MINNEAPOLIS, MN 55407
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MY BRUSH WITH CHRONIC MERCURY TOXICITY

Summary: My story is different from that of most people who have had chronic mercury toxicity. I only had one amalgam filling; various things deteriorated, health-wise over the next few months. I wracked my brain and studied all angles to figure out what went wrong, in my lifestyle or my environment, and then I realized that it must have been the one amalgam filling that I'd had placed. The amalgam filling was replaced by a composite filling just four months after the amalgam had been placed; my thinking ability seemed to have a subtle but definite improvement right away. Other problems flared up for a while, but after about two years, my health turned the corner and I was definitely on a healthier track.

Now here are more details. I was 40 years old before I had my first dental filling, a reflection of a very good lifestyle. I ate exclusively natural, organic foods, I exercised, I was thin and active, and very engaged in my work. Further, I was highly educated in the sciences, with a BS degree in physics and an MA in mathematics from a top graduate school (UCSD).

1985, January 9, a dentist who pooh-poohed my questions and concerns about mercury in amalgam (he didn't discuss alternative choices!) convinced me to allow him to use amalgam for my first dental filling. After that discussion, I convinced myself that I didn't want to be a wimp and that I would have no health problems from the amalgam. After all, I reasoned, they are putting this stuff into the teeth of children and pregnant women. A healthy 40 year old guy should have no concerns.
That night, the sore throat that I had recovered from seemed to have come back. "What's happening?" I noted in a health journal.
In the days that followed I noticed a metallic taste in my mouth. Not very pleasant.

January 21. Woke up not feeling well. Rapid heart beat ....heart fluttering. First thought: the organic cider that I had been drinking that is poisoning. ..something is poisoning me. I was OK at _____, drinking grape juice. But I came over to _____ house where I live, drank a lot of cider and now fee ill! What is it about cider that is poisoning me? Now have uncontrolled chills and shivering ... feel nervous and shaky. Pulse rate = 66...funny, muddy taste in my mouth.

Next morning: I settled down and slept. I feel OK in the morning – but still muddy taste.

In the weeks that followed, there began a pattern of intermittent waking up at night, shivering even though I wasn't cold. When I got up and turned on the light, that would help stabilize me and make me feel better. What was my body trying to tell me? I examined the logical possibilities: a deficiency, an infection, or toxicity. I didn't seem to have an ordinary infection illness, my diet and lifestyle were unchanged and I should not have a deficiency. My mental health was good; in fact, it had always been excellent and I had a great attitude. My symptoms seemed like a low level toxicity ... but of what? What could it possibly be? I was determined to find out. Lead? Mercury? Something in the water? Or in my favorite foods?

january 14, 2000

toxicological effects of mercury committee meeting, january 20, 2000
national academy of sciences,
2001 wisconsin ave, n.w.
washington dc. 20007

esteemed scientists,

i am most grateful for the opportunity to participate in calling your attention, i dare say with the utmost urgency, to a national and worldwide epidemic.

as i have only just today been made aware of your conference, i must apologize for not being able to tailor the enclosed materials specifically for your consideration, said materials which i had originally prepared to send to lawyers for the purpose of bringing a class action suit against the american dental association and the manufacturers of amalgam. i trust that small discrepancy will in no way detract from the validity of the information provided and in fact hope it will underscore the urgency with which it was written.

unbelievable as it may seem, the epidemic at hand has been wrought by a segment of the medical community, and has contributed significantly to the exponentiating decline of public health over the course of the century as clearly evidenced in the health care crisis we see today.

though of course only one of many factors, i believe the amalgam issue is a formidable and critical piece of the puzzle, something quite insidious and pervasive, directly affecting roughly 80 percent of the population.

politicians, medical researchers, talking heads, indeed people in general, are always looking for magic bullets, either in the form of panaceas, or in the form of simplistic causes. in the case of the latter, one easy thing which might be responsible for any number of medical or societal ills. suppose this notion were not as unrealistic as it might seem? suppose there was something which, though not entirely responsible for whatever ills in question, was indeed a prime factor in many of the problems that plague us? it would be nice, wouldnt it, to discover a cause so abominable and far-reaching, that its removal, with one fell swoop, would dramatically improve a wide range of maladies?

i am suggesting to you that mercury amalgam could indeed well fit that bill; a common denominator in over 150 million americans and billions of people worldwide that could be --that i and many experts believe is in fact responsible for a vast array of health problems, many quite serious. it is something for which there has been no fda testing, let alone approval, something which countless studies have indicated is more than capable of producing such consequences, indeed it is a known poison, one of the most toxic substances known to mankind, and it is implanted daily in the bodies of hundreds of thousands of americans, children, the elderly, the already ill, and the as yet healthy.

Docs (2)-

a health crisis induced by doctors is called 'iatrogenic' in nature, and this one has been perpetrated on the world by dentists, and sanctioned, unconscionably, in this country, by the american dental association.

apart from the many ramifications on physical health, as you will see supported by the literature i've provided as well as the substantial literature and documents which will undoubtedly be provided you by the participants of this conference (--all of whom are surely more highly credentialed than myself--), it is my personal belief and the opinion (by implication) of many experts, that mercury amalgam has contributed significantly to one of the most troubling and urgent problems mystifying the nation today, that of indiscriminate violence, --youth violence in particular.

the experts i speak of have merely alluded to this (and unfortunately i mean only mercury experts, none of whom one sees in the media), since there is little clinical evidence with regard to this particular sociological aspect of the danger, and really since their suggestions predate the phenomenon, but i am personally convinced (and am of the specific theory, if none formally exists) that the recent trend of school shootings, workplace shootings, and similar types of public and private violence, including parent-on-child and child-on-parent violence, may be closely linked to amalgam toxicity. i dont know how far-fetched that may sound, but really it makes perfect sense.

most children have their first amalgams placed between the ages of 9 and 15. these young, rapidly developing bodies may be hit with as many as (--or in some cases with at least--) 4 or 5 fillings at once (--i myself had 8 at the age of 12--), --vaporizing mercury, a powerful neurotoxin known to affect behavior, 24 hours a day. i dont think it is at all unreasonable to surmise that this might indeed be a prime factor, not only in the area of violence, but in the general climate of teen angst and related problems, not to mention the adult condition, be it in the arena of crime in general, domestic violence, or otherwise. indeed i would go as far as to make the seemingly fanatical claim that mercury's institutionalization has seen its ill effects tragically incorporated into the very fabric of society.

i know you will be looking into the various aspects of this issue at length, but i urge you not to underestimate the heinous effects of mercury, even in this particular far-reaching regard, and further, i humbly ask that from this moment you consider me at your full service in the matter.

respectfully,

smith jones
5504 kalmia dr.
orlando, fl. 32807

407 282-2199 late-afternoon/early-evening

To: Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn HOB
Washington, D.C., 20515

CALL FOR ACTION:
The Banning of Toxic Heavy Metals from Being Used in Dentistry

After 130 years of debate and the waging of three wars against the ADA, the main stream dental community and manufacturers of dental materials (specifically heavy metals) by an elite group of dentists, medical physicians and scientist we are still practicing dentistry in the dark ages. The myth of the safety of these materials lives on even in the twenty-first century thanks in part to the stamp of approval by the American Dental Association. No matter how much research has been done, no matter how many books have been written by experts warning the dental community of the dangers of this practice, it still continues on today in the year 2000 as though it had a life of its own.

Thirteen years ago I would sit down in a dentist chair and place my health and my life into his hands not knowing any of the information that I possess today. I was told that if I did not have $13,000 worth of work that I would loose all my teeth within ten years, I was only forty at the time and the last thing I wanted to imagine was wearing dentures. He supposedly did bone and gum surgery (which ended up being nothing more than a cleaning), he placed an implant in my lower right jaw (made of god knows what) and proceeded to file all my teeth down to nothing more than a cone shape. Placing 28 crowns on top of them, according to this dentist he was having the lining of the crowns made of gold, due to the problems with plain metal. I left his office thinking the world was great and went on my merry way. All these extensive procedures he did in three visits, which I would find out later would account for the all the jaw pain I was having. His work would prove to be so below dental standard that it would create a severe TMJ problem that plagues me to this day.

But this would be only the beginning of my night-marish tale that would take me eleven years and thousands of dollars to uncover. Through the years I would come up with an enormous amount of symptoms and maladies starting with in the first couple of months I was experiencing low grade temperatures sometimes reaching as low as 95.6, flu like symptoms that only lasted 12 to 24 hours. Sinus and ear pain that I had never experienced before. My legs and head would hurt so bad sometimes awakening me from my sleep, that would escalate within a two week period that no pain killer would tough. With migrane like pain, I would find myself in a fetal position laying in the middle of the floor. Even laying my head on a piilow was impossible because my head would swell up with knots the size of golf ball if you cut off the top would be all over my head. The inside of my mouth would become blood red as well as irritated, constant flairing up of my gums from the irritation from the mercury/base metal combination, my tongue would swell and

get spots all over it, at times actually turning black. I was in the throws of a full-blown reaction to the toxic heavy metals placed in my mouth by my dentist and could find no help or answer anywhere.

I of course left this dentist immediately due to the opinions of another dentist that his work was so shoddy that it all had to be replaced at a cost of over $39,000, this only months after I had put out $13,000 in cash to have this work done. Later I come to find that gold was not what was lining my 28 crowns but the cheapest base metals known to exist in the field of dentistry. I would find though extensive testing to have fourteen toxic metals in my system, three of them poisons. Enough Arsenic, Cadmium and Balinium to kill me if it had not been for the fact that it had taken years for these toxic metals to seep out of my crowns. Their passage way into my systems would be through the root system into my blood supply and from there be transferred throughout my body wherever the blood would take it. Which by the way is everywhere!

It would take so many years to find this information, not that it was not already known by the dental community. It would take eleven before I would run into an Oral Toxicologist who would run the test needed to diagnose me with full blown HEAVY METAL TOXIC POISONING complicated by the presence of an even more deadly material used to bond these metals together "MERCURY".(ALLOY) and is 50-70% of the measured ingredients used to hold these deadly Heavy Metals together). By this time these deadly materials had all but destroyed my AUTOIMMUNE SYSTEM, impossible to stand its own against the constant attacks through the eleven years that passed as I was reaching out to the dental and medical community for help. In 1999 I would go to the Center for Immune, Environmental and Toxic Disorders and show him all the tests I had been going through. I laid before him a longer list of symptoms complete with extreme lethargy, brain fogging, and weakness in hips that would occasionally force me to walk with a cane. Upper respiratory problems that would last for months, allergic reaction to antibiotics, rash from hell that would last for over eight months in 1997 and continues till this day. I am forced to consume from 25-50 mg of Benadryl daily to able to wear clothes. I have become allergic to all of the products I use on a daily basis. Anything with chemicals or perfumes except for basic oils like mineral oil or Crisco grease were out. Shampoos and conditions had to have a limited amount of ingredients in them; EDTA additive was completely avoided at all cost. I found that my condition worsened with every front that came into the state of Oklahoma, which is a lot since we live in tornado alley. A metallurgist would tell me that this because as the barometric pressure would rise the heavy metals would react by swelling up inside my body wherever they lay. The mercury released into my system would react in a manner in which I would feel as though I were going to stroke out, the pressure was so great from my chest up. At times I thought for sure I would die and many times during this prayed to God that I would.

Since this time I have been diagnosed with Atypical Rhuematory Arthritis and according to the clinic in Houston, Texas I am now showing the signs of Multiple Sclerosis as well as Fibromylasia. If this were not enough my heart and kidneys are now being affected. There is no limit to where this poison can go or the damage it can do. Once the immune system has been as compromised as mine is, due to the effects of these TOXIC HEAVY

Page (3)

METALS placed into my mouth by the senseless acts of an irresponsible dentist it begins to turn itself against it own and goes to destroy everything including itself. According to the doctors this is what the rash and skin sensitivity is all about. If matters were not bad enough I am one of many patients who falls between the cracks of the system who possesses no insurance and due to the effect of these TOXIC METALS in my system have had my income taken away due to my inability to work.

If I cannot find help I may surely die but not before experiencing an agonizing life locked into a wheel chair with nothing functioning but my brain. I am only fifty-three years old; I am the grandmother of seven beautiful children who lives I have been forced to miss due to the pain and suffering by which I have been afflicted with. This due to the irresponsible acts of the American Dental Association and the main stream Dental community who continue to put their stamp of approval on these dental materials. Who refuse to admit the truth and take responsible action by banning the use of these TOXIC HEAVY METALS in the field of dentistry when for years and years other non-toxic materials have been available to use. Their reasoning being for the continued use is always been the affordability and easiness of placement by the dentist. It is hard to understand that saving the dentist a few dollars (not the patient) and his ability to place these materials in shorter span of time is not worth the destruction of our immune systems and they're by our health and destruction of our lives..

During my research on this subject I have found that for over 130 years we have fought this battle against the American Dental Association and main stream dental community only to lose time and time again. Each time under the delusion that these materials are safe for human consumption when in reality the handling, disposal and containment while in the dental office is falls under the codes of the Environmental Protection Agency due to the fact that they are so deadly. Yet we are led to believe that they are safe to put into the humans mouth where they will live sometimes for lifetimes seeping poisons into the life giving organisms destroying them, this happening daily at an alarming rate. I ask you with the knowledge we have is it worth the risk?

You ask yourselves why must I put trust into the words of this person? I say to you because I live this nightmare everyday. I say because for over three generations experienced medical practitioners and scientist have warned of the consequences of these actions. That even dedicated dentist were willing to give up their license to practice, as others would end up forcibly having their license taken away by the actions of the American Dental Association, to bring the truth to the ears of the mainstream dental community. All in hopes of preventing what is happening here and now, the possible destruction of the human race! By damaging generation by generation the cell destruction that forms our very being, as we pass this deadly poison onto our children through the blood supply as the mother carries them in her womb. We pass this deadly poison through the very breast milk that the baby nurses on, and last but not least we all sit down in that dentist chair. Where "we UNKNOWINGLY" have this DEADLY COMBINATION OF TOXIC HEAVY METALS PLACED INTO OUR MOUTHS YEAR IN AND YEAR OUT ALL THROUGHOUT OF LIVES. Which one of us exists without the companionship of husbands wives mothers, fathers, sisters, brothers, friends

and most of all our innocent CHILDREN. The American Dental Association, who own the patient rights on these dental materials, has made their organization rich off the LIES that these Toxic metals are safe. As have, the manufacturers and dentist who have grown wealthy off the tears, the suffering with deadly diseases attributed to the use of these toxic materials; finally the deaths of the trusting uninformed patients who were never even advised of the possible dangers of these TOXIC HEAVY METALS.

If you have crowns, root canals, filling, bridges, some implants (other than titanium), metal anywhere in your braces, dentures then you are at risk. The larger the selections, combinations or amount of the above the more at risk you are. The longer the exposure the more deadly the damage. As you sit by that next deathbed of a loved one will you not remember that you had the opportunity and choice to turn this deplorable situation and injustice around for the innocent victim (the patient)? On this day it is I, on the next it could very well be YOU or your loved one!

I implore you to search deep in your souls and do what is right "BAN the use of these TOXIC HEAVY METALS in the field of dentistry.

It is said by many but quoted by one"THAT ORGANIZED DENTISTY IS PROBABLY THE MOST DANGEROUS OF ALL HUMAN HEALTHCARE PROFESSIONS" and that "DENTIST ARE CONTRIBUTING TO THE DECLINING HEATH OF THE MASSES". Dr. F. Fuller M.D.,H.M.D. made these statements and one more compelling one. "THE ROLE THE DENTIST PLAYS IS DIRECTLY OR INDIRECTLY RELATED TO THE ETIOLOGY OF A LARGE NUMBER OF DISEASES, SOME OCCURING AT SITES FAR DISTANT FROM THE TEETH" end quote.

Joyce

Cammarano

Hon. Dan Burton
Committee on Government Reform Because

Dear Congressman Burton,

I was very gratified to hear of your interest in the toxic effects of mercury in dentistry--on patients, dentists and allied dental personnel.

I hope my experience can prove useful to you. I have a Ph.D. in Technological Hazards, and wrote my thesis on mercury poisoning from dental materials as an unrecognized cause of degenerative illness. I was motivated to do this study from my own experiences as a patient struggling for 40 years to get a diagnosis.

I was a sickly child, my illnesses never correctly diagnosed. In young adulthood I began to receive a cascade mitral valve prolapse, glomerial nephritis, Raynaud's Syndrome, Sjögren's Syndrome, rheumatoid of diagnoses from an expanding list of medical specialists: multiple sclerosis, lupus, heart attack, arthritis, Because candidial infection of the brain, skin cancer, pre-cancerous lesions in intestines and breasts, suspected pituitary adenoma (brain tumor), loss of thyroid function and psychiatric disturbance. You name it--I had it!

No doctor offered me a diagnosis of systemic poisoning, but all doctors treated me as one of those strange cases that never gets resolved. I'm sure they suspected a textbook case of Munchausen's Syndrome.

In 1985 I accidentally stumbled across a dog-eared 1982 copy of Psychology Today. An article titled "Neurotoxic Follies" described a man's detrimental experience from toluene poisoning (toluene is what gives nail polish its smell). The symptoms the writer described were almost exactly the same as mine.

Knowing I had no exposure to toluene, I deduced that my symptoms were most likely due to exposure to a different toxic substance. I thought that my 17 mercury fillings might be the cause.

Since I was by this time totally incapacitated, I sent my daughter to the Library for Medical Consumers to gather whatever research she could find on the effects of mercury dental fillings (described in the literature as "silver amalgam dental fillings"). The information she brought back was not medical research, but reports from lay people on their ill health, which they connected with their own mercury fillings or their exposure to mercury while working in a dental office. This information indicated that I could have a problem that was obscure in medical literature.

In August of 1985 a physician at Columbia-Presbyterian Hospital confirmed that I did have mercury poisoning. My condition was so bad that he said little could be done for me. I decided on my own to have the mercury fillings removed and to go on a macrobiotic diet. (In looking over my early life, I came to recognize that my mother had had many dental fillings, and that I started receiving my own fillings at the age of four.) Over 4 years I recovered enough to re-enter my doctoral program, changing my studies from technological development to technological hazards. I received my Ph.D. from New York University in 1989.

Karimian

Since that time I have been working closely with DAMS (Dental Amalgam Mercury Syndrome Support Group – a national and international organization) and with physicians and dentists practicing conventional medicine and dentistry. I lecture on a regular basis to graduate physicians explaining these syndromes. Often the attendees come up to me afterward and share their concerns for themselves and family members. I also work directly with dental consumers and dentists on an individual and group basis. Because of my visibility and knowledge in this area, I get calls from people all over the world seeking current information, support and the benefit of my experience and research.

There is ample evidence that pregnant women exposed to toxic metals and other substances give birth to children with a higher rate of birth defects, particularly neural tube defects. There is research that makes the connection between mercury and these birth defects. I can see it in my children's problems in functioning and their hard-to-diagnose health problems.

In addition to my participation in national conferences, I represented DAMS, and gave four presentations, at the European Parliament Conference on the Dangers of Amalgam Fillings and their effort to introduce legislation to protect the public. As you can see from the enclosed literature, and the list of countries represented, there is a great deal of attention focused on the problem in Europe. Research, funding and attention here in the United States is sparse, with just a few sporadic efforts to sustain inquiry in this highly unrecognized area. On 12/09/90 CBS *60 Minutes* presented a double-segment on the meercury fillings issue and reported receiving the most letters ever.

Controversy about the use of mercury in dentistry has gone on since 1829. As we have learned more about the human body, it has been recognized that these fillings can have a disruptive effect on the immune system and cause birth defects, genetic damage and death. Deaths attributed directly to mercury are very low, maybe 6 a year,the rate of illness and death from hidden causes possibly related to mercury is much higher.

Not wanting to overwhelm you with cartons of paper, I am sending along a small sampling of documents for your review. I would like to put myself at your disposal in the research and investigations you may be contemplating. I include my address and phone number; I hope you'll contact me and tell me how I can help. I am a high school math teacher as well as a dental medical researcher; even with my hectic work schedule, I would make every effort to come to Washington, D.C. to meet with you if that could in any way assist in your efforts.

Sincerely yours,

Anita Karimian, Ph.D.

List of enclosures:

My mercury story

Mercury poisoning is a real happening!

Memory Loss, Staph Infections, shooting pains from the base of my head, severe fatigue, skin rashes, stuttering, chronic sinus and bronchial problems, depression, brain fog and ringing in the ears, tremors and muscle spasms)

To: The Committee - The Toxicological Effects of Mercury

When I was in my early forties, having already had umpteen amalgam fillings, and five gold crowns my immune system bottomed out on me when a small mariland bridge was placed in the right side of my mouth. The bridge, containing mixed metals, put my immune system overboard. It was clinically recognized that my health problems were stemming from my mouth.

After a two-year duration I was in crisis..... staphyloccoccus infection (boils)developed on my left side. Prior to and continuing I had acute headaches, so severe that I thought I had a brain tumor. I experienced frequent shooting pains from the base of my head to the top and experienced gross
fatigue. I had memory problems, rashes on my hands, I stuttered, and had sinus and chronic bronchial distress. Acute anxiety and serious depression set in as my joint problems increased.. I experienced constant ringing in my ears and brain fog. Life was becoming quite unbearable..to add
to this potpourri of symptoms, I developed neck tremors with muscles pulling to the left side. I was a mess!!!

A doctor who specialized in pulse testing (diagnosed by changes in the pulse) observed I that I appeared to be "one-sided". This meant I had a staph infection on one side and my joints were wearing out on the other.

I suspected that my troubles were coming from my mouth. When I told the doctor what metals I had in my mouth, he referred me to a dentist who specialized in metal sensitivity. This dentist confirmed that I was highly reactive to the metals in my mouth. The small bridge had to be removed ASAP. He removed all the visible amalgam fillings, but I was still testing badly. As he removed one of my gold caps he discovered a mercury core requiring all of my five gold caps to be removed.

The results were dramatic, just from removing the bridge and visible mercury. My depression lifted, the rashes on my hands cleared (havoc for a registered nurse) and most notably my stuttering wasn't as troublesome. It was like witnessing my own little miracle. I knew I was onto something exciting. The metals severely hampered my neurological system!. I still had to bare
(2) From: Marilyn Kiefer,RN - 1/18/20
to: the Committee for Toxicological Effects of Mercury

Kiefer (D)_

the painful neck spasms and tremors. My dentist has told me that the last symptoms to surface are the hardest to rid the body of.

I'm much better now. That was thirteen years ago. I've been detoxifying the metals out of my body ever since. My brain is still affected as I make many cognitive mistakes. I'm very slow in my thinking. My memory, especially short term is poor, and my concentration has been affected. I'm also somewhat hyper-active.
The neck spasms diagnosed as Spasmodic Torticollis, are much better but I do subject myself to "Botox" botulinum toxin every three months to control the pain and help my back. My Degenerative Disk disease is considerably better since I've been prescribed a back brace with metal supports. Prior to that I required physical therapy every spring and fall like clockwork. Overall , removing the metals was the best thing that happened to me. I don't know where I would have been today if I hadn't done so.

Please, Please, work to eradicate toxic metals in the mouth. Illness caused by dental metals are bankrupting the health system! If seven other countries are either banning or warning their people, we deserve the "Right to Know" what toxic materials are being put in our bodies....the dental offices presently withhold this information from the patients.

Marilyn Kiefer,RN
DAMS Michigan Coordinator
Michigan

To: the National Academy of Sciences Kelsey(1)

I tell this story with the hope that it might help to spareothers from the painful and costly experience I have had.

About five years ago, I had a period of extreme vertigo, confusion, disorientation, brain fog, spaciness, forgetfulness, inability to focus, unable to function in the usual manner, which had always been active, alert, involved with life. I went through all the tests suggested by the doctor and nothing was found. Eventually, most of the symptoms abated but would come and go. Looking back, I could see that this had been happening gradually for many years.

My energy level gradually diminished - and always the mental and physical fatique went together. I couldn't think clearly and I had no physical energy to perform the ordinary tasks of my life. I had long practiced preventive health care, leading a healthful life style, and keeping myself informed about health issues which I believed were my responsibility to be informed about and to attend to. After some time, I thought that the extreme fatigue could possibly be hypothyroidism. I was tested and this was the case. I was put on a thyroid supplement - never needing a drug before. This was early 1997.

My energy level improved some and I thought the problem had been taken care of. But again, the fatigue slowly consumed me. Again, I sought medical help - which had never been a part of my life due to my health-conscious lifestyle. It was discovered that I had a severe polysystemic candida infection - the yeast had invaded my entire body. I went on a very limited diet to address this. Slowly, slowly, there was some improvement but it seemed to leave me vulnerable to yeast infections. I didn't dare eat anything sweet, not even fruit.

But again, that only gave me some relief; it did not take care of my diminished energy and over-all feeling of unwellness. I had tests for food sensitivities and allergies and discovered that I was sensitive to 33 foods in my diet - many of them fresh, organic vegetables from our garden. What I could eat was getting less and less. I was losing weight, which I could ill afford since I was thin to begin with.

Kelsey Q1

By early 1999, I was sure that we still had not gotten to the root of the problem - we had only been addressing symptoms. I was getting desperate. My life of vitality, activism, joy and optimism had all but disappeared. My husband had taken over most of the household tasks; I saw few people anymore. There was not the energy for social relationships; many days I could hardly drag myself out of bed. I could not carry on an intelligent conversation with anyone. My mind (or brain) simply wasn't functioning very well. My memory seemed to be going and there were periods I wondered if this was what alzheimers was like. Rarely, could I drag myself out into our lovely garden, just to sit and enjoy a pleasant day. I was attempting to integrate this experience as part of my spiritual journey, but there simply wasn't the mental or physical energy to focus creatively. I was just existing. I decided that if this was the way I had to live, unable to make a contribution, no quality of life, I simply didn't care to survive like this. My friends and family were deeply concerned.

Then I decided to call a physician whose work I had followed for years to see if I might be able to see him, not really sure how I would manage to get there on my own, since he was out-of-state. But I was able to make an appointment and I went. We spent four hours one morning going over my history and making numerous tests. At the end of that time he was pretty sure that my problem was heavy metal poisoning. This was confirmed by a lab that specializes in heavy metal testing. It revealed that my body was dangerously toxic with mercury, caused by the mercury amalgams in my teeth. At least I now knew what I was dealing with.

Since that diagnosis (and before), to say that I have been through the valley of death is no overstatement. It has been (and it is not finished) a long and difficult journey. Sometimes it seemed that it might be easier just to abandon all the effort and commitment that was required in order to recover. But I was determined that my life was not over - there were things I yet wished to do.

Kelley

I have been on many supplements and homeopathic remedies to restore my health. I had to find a mercury-free dentist, one trained in removing mercury amalgams. I located one some distance from my home which meant driving some distance in heavy traffic into a heavily populated area. I could not have managed without the help of my friends and family. These trips went on all summer (1999); I thought it would never end. After the mercury was removed from my mouth then it had to be chelated from my body (and brain - the target for mercury). Since chelation also removes minerals from the body, I had to have intravenous mineral replacement. We have suspended chelation for six months and then will check the mercury level again. I continue oral chelation, as well as the many supplements and remedies which address the many systems in my body that were compromised by the mercury. My body simply has been unable to use the nourishment provided. I'm slowly regaining some of the over 20 pounds that I lost. Eating has been a stressful experience because there seems to be so little that my body can accept.

But I have hope and I know that I am on my way to recovery. In February (2000) I will attend a program sponsored by the out-of-state physician I've been working with. We have high hopes from this program which will address many of the health issues I have been dealing with as a result of the mercury toxicity.

This experience has been costly in many ways. Our "health-care" system, as it exists, does not cover what I have been through. We have had to dig deep into our savings. I feel fortunate that we were able to see this through, financially. There would be many who simply would be unable to have the care that was necessary for recovery. Because we have not acknowledged that mercury is highly toxic (more so than lead or arsenic), we continue to put it in people's mouths and cannot get health-care coverage for removing it, even when a life is at stake. My physician is an M.D., trained in many different healing modalities, one of which is homeopathy. He and all

Kelsey 9

his patients are penalized because the system does not recognize the more natural and gentle approaches to healing. So there is no coverage for such expenses. I hope that our health-care system can become more enlightened and brought into the 21st century. And I hope that my story might help to move that along so that others will not have to go through what I have experienced.

Ernestine "Kelley" Kelsey
(Mercury Dental Amalgams)

Jan. 13, 2000

Ms. Kelley Kelsey
19554 Glendale Ave
South Bend IN 46637-1814

Kevin (i)

July 10, 2000

Dan Burton, Chairman
Committee on Government Reform
102 Cannon House Office Building
Washington DC 20515

Dear Congressman Burton:

MERCURY AND ANGER/ EMOTIONAL DISTURBANCE

Has anyone had the experience where they had many years of being short-tempered, and quick to anger, and being prone to rages, and then had their fillings removed--and found that they were not so quick to anger or rage, or even fear?

I have a very short fuse, am very defensive, and quick to anger. Now, for years I have attributed it to psychological origins from typical dysfunctional family stuff. But I've been reading in Huggins book, and I wonder if maybe mercury has something to do with it?

I've got 14 amalgam fillings, and my mother worked as a dental assistant for many years when I was a child (from age 5 to about 13.) I wonder if Mom could be exposed to mercury all day and then bring it home to kids? I think it's obviously more likely that my mercury is it's from my own fillings.

But what about the rage reduction theory. Anyone find they were calmer and less inclined to tears/outbursts, etc. after they had their fillings taken out?

Kevin
Kevransom@aol.com

Kimberly

July 10, 2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Bldg.
Washington, DC 20515

Dear Congressman Burton:

This is a message I sent to the internet group I belong to. They have been so very helpful to me with the advice and information that's offered.

I have had six of my 10 amalgam fillings out so far and boy do I feel really great!! First I have been able to say this in years and years - I even feel better than I did before I got my chemical injury summer 96! How cool!! I even was able to muster a little Christmas shopping tonight dealing with people smoking and perfume and all the synthetic Christmas smellies and I also went to Kinko's - and NO REACTIONS!!! I actually feel like I can someday be well. I never realized the impact that my mercury had on me. Was talking to someone the other day and realized that I started getting really depressed the same year I started getting fillings. But then that was also the year I got my period so maybe the mercury has nothing to do with it.

Anyway - I guess I am babbling but I just wanted to share my fabulous news and to thank you all for your fabulous advice and support.

Kimberly
Ikmweeks@juno.com

AUTOIMMUNE DISEASE CAUSED BY
AMALGAM MERCURY TOXICITY
Diagnosed with Multiple Sclerosis, Lupus and Myasthenia Gravis

July 17, 2000

Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn Bldg.
Washington, D.C. 20515

Dear Congressman Burton:

I am a 58 year old American female with three children who had been healthy for most of my adult life, until I realized that I had been poisoned by the mercury leaching from my "silver" dental fillings. The following is my personal story, and how I discovered the cause of chronic symptoms and illness.

I was struck by double vision instantly on March 16, 1998, seven days after having an old amalgam filling drilled out of an upper molar and replaced with high copper mercury amalgam, specifically NOGAMA-2, (containing 50% mercury and other metals) a product which has the American Dental Association's "Seal of Approval." The product was mixed by my dentist with liquid mercury.

Diagnosis Multiple Sclerosis or Lupus
I was referred by my optometrist to a resident neurologist at the University of Pennsylvania Hospital, who ordered a series of blood tests and an MRI. The following week I saw a neuro-opthomalogist at U of P, who diagnosed me with Multiple Sclerosis or Lupus because my blood studies revealed an extremely high ANA titer, high rheumatoid factor and high liver enzymes, although the MRI did not exhibit brain lesions ordinarily seen in MS. He assured me that my eyes could be "fixed" with steroids (Prednisone), but I would just have to live with the illness. Needless to say, I was shocked and traumatized by this diagnosis, as I knew that either one of these diseases equated a life long sentence of immune suppressing medications (with their nasty side effects), and some degree of disability.

How I discovered Mercury Toxicity from Dental Amalgams
It was on the Internet that I discovered what had happened to me.....the silver mercury filling which had been implanted in an upper molar seven days previously was the cause of the sudden onset of double vision. Thanks to the research opportunities of the Internet and a woman from England who described her ten years of MS followed by double vision occurring seven days after having dental work. That was my first clue! I later read studies and incidences of acute mercury
poisoning where the victims' symptoms appeared seven days after mercury exposure. (American J Indust 5:251-258, 1984, Out of 41 intoxicated people they ate loads of ethylHg treated rice containing ca 50 mg Hg per 1 kg rice) 15 were severely ill and 8 were admitted to the hospital

Koss (2)

where they died. There was a lag period of 7 days before the disease onset. Muscular weakness was among many symptoms.)

No doctor could impart information as to what may have caused the double vision. Many months later I found the answer in the work of Dr. Patrick Stortebecker (a Swedish neurologist-since deceased). His studies and research can be found in his book, *Mercury Poisoning from Dental Amalgam - a Hazard to Human Brain.* His research proved that toxins and infection from an upper tooth pulp can travel along the nerves through the cranial venous system to the trigeminal nerves, ocular branches, ciliary ganglion [nerve junction] behind the eye, the brain stem and spinal cord. Symptoms as seen in Myasthenia Gravis can occur due to mercury-induced blockage of the acetylcholine neurotransmitter receptor. Not one doctor who I have consulted with was able to give me this information, in fact, they rejected any inference to mercury toxicity as a possible cause of the double vision or autoimmune disease even though they had no ideas what caused any of my symptoms. WHY don't doctors want to learn the science they weren't taught? WHY don't they want to CURE patients? Why do they ONLY treat symptoms.?

As the disease progressed, within the next few months I developed drooping eyelids, loss of equilibrium, muscle weakness, Raynaud's syndrome, below normal temperature, intestinal problems, voice weakening and fluid retention. I discovered that varied symptoms and illnesses which I had been experiencing on and off for years such as arthritis, muscle cramps and spasms, skin rashes, severe depression, anxiety and short term memory loss were also common symptoms of chronic exposure to mercury from dental fillings. To my surprise, upon removal of the twelve metal fillings by a dentist specializing in biological dentistry, the three year rash on my legs disappeared within two weeks, as well as the neck and shoulder spasms within days. However, the double vision has not disappeared but is not as severe.

Rather than steroids, during the following year I gulped down hundreds of supplements including daily intake of 9,000 mg of buffered Vit. C, Vit. B complex, Vit. E and A , selenium, B6, MSM (sulphur), trace minerals and many more in addition to Vitamin C and mineral IV infusions. One year after removal of all the fillings, a urine challenge test (24 challenged urine analysis, (a chelating agent which binds to mercury.DMSA was taken orally), revealed high levels of mercury and lead. Blood, urine, fecal tests, x-rays, SPECT scans , MRIs and Gallium scans have shown low immune system killer cells (NK) , low levels of the mineral lithium, vitamin deficiencies, jaw infection and osteonecrosis of the jaw, adrenal insufficiency, oxidative stress, high levels of free radicals, avascular necrosis, degenerative joint disease in hip and sacrum, and enzymatic disruption along with many other signs and symptoms typical of mercury toxicity.

In an effort to understand the health hazards of mercury from dental amalgam, how the associated illnesses can be cured and the best and safest protocol to detoxify mercury, I attended conferences in Europe and the United States, and have communicated with scientists, doctors, dentists and researchers all over the world. As reported by international scientists and practitioners, the information is clear....Amalgams must be banned. Sweden no longer uses amalgams,(their Health Insurance Agency will no longer pay for the placement of amalgam), Japanese dental schools no longer teach placement of amalgam and their environmental mercury standards have changed to such a degree that amalgam refuse no longer fits into their standards of allowable mercury levels, France, Austria, Australia, Germany, UK, Finland, Norway and

(3)

Australia have issued governmental advisories not to place mercury amalgam in children, pregnant women or those who have kidney illness. The Environmental Protection Agency in

U.S. has issued a Virtual Elimination of Mercury proclamation. Several states have issued environmental mercury resolutions to ban the use of mercury in industry and products.

I was very lucky to have discovered within a few weeks after the double vision developed that many of my problems were in all likelihood due to chronic mercury toxicity, as most people are misdiagnosed and never discover the cause of their illness.

I had my first amalgams removed within a month of being struck with the double vision, but I have realized that many , psychological, neurological, neuromuscular, visual and skeletal symptoms that I developed during the last fifteen years were most probably due to mercury toxicity. Recent tests have also revealed a degree of adrenal gland dysfunction.

I have been unable to work since becoming ill two and a half years ago, I have chronic muscle and joint pain and I still have double vision and a pain in my head. I am outraged at the unnecessary illness and suffering due to mercury toxicity from dental amalgams. Amalgams were never approved by the FDA, they were grand fathered in. Greed, money and power regulate the health of our society. How could this have been permitted for over 150 years?

Please, as a government committee and representative of the citizens, examine the science and take the law into your hands to save future generations, our children, from this unnecessary cruel suffering, illness and death.

Sincerely yours,

Freya B. Koss
MERCURY FREE PRESS
519 Sussex Road
Wynnewood, PA 19096

Phone: 610-649-2606
Fax: 610-649-1938

E-Mail: FreKoss@aol.com

Koss

Elemental Analysis Urine (24 Hour)

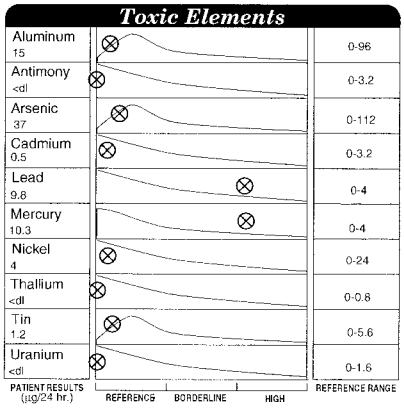
Great Smokies Diagnostic Laboratory℠
63 Zillicoa Street
Asheville, NC 28801-1074

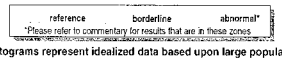
Andrew Lipton, DO
822 Montgomery Ave #315
Narberth, PA 19072

Patient: Freya Koss
ID#: 021199-0440 Age: 57 Sex: Female

Collected: 2/10/99 Received: 2/11/99 Completed: 2/24/99

Toxic Elements





Histograms represent idealized data based upon large populations

24 Hour Urine Total Volume (ml)	1420

Post-provocation laboratory results.

Results Pending Submission of Total Volume, 021699, FJB. 'Toxic elements only as per requisition, 2-11-99, jb' Amended report , total volume of 1420ml submited on 2/18/99. jwh

Patient: Freya Koss ID#: 021199-0440

Comments

This report of urine element levels includes microgram concentrations of elements generally regarded as toxic. If a 24-hour urine specimen was collected, toxic elements are reported as micrograms per 24 hours (ug/24 hr). If a random or less than 24-hour specimen was collected, toxic elements are reported as micrograms per liter (ug/l). Please note: "<dl" denotes less than the detection limit of the instrument.

Occasionally, it is desired to convert the reported units of measurement into other units for comparison purposes. If this is desired, the following formulas can be used.

. To convert ug/24 hr or mg/24 hr to ug/l or mg/l, multiply by (1000/24 hr volume in milliliters)

. mg/l is approximately equivalent to "ppm"

. ug/l is approximately equivalent to "ppb"

. (mg/l) X 1000 = ug/l

. To convert reported units into ug/hr or mg/hr, use the following formulas. The volume (ml) and the time period of urine collection (hrs) must be known to make conversions from ug/l or mg/l.

ug/hr = (ug/24 hr) / 24

mg/hr = (mg/24 hr) / 24

ug/hr = (ug/l) x ((ml collected / 1000) / hrs of collection)

mg/hr = (mg/l) x ((ml collected / 1000) / hrs of collection)

Lead, Pb, an element with multiple toxic effects, is elevated in the urine, Possible sources of lead include -

. Leaded or soldered joints in water systems
. Contaminated herbal preparations and teas
. Chips of old lead-containing paint
. Art supplies, colored glass kits, etc.
. Bullets, fishing sinkers, balance weights, radiation shields
. Lead-acid batteries
. Bearing alloys, babbitt metal
. Some ceramic glazes or pigments
. Sewage sludge and "earths" from sewage treatment
. Soils and vegetation along highways

Historic uses of Pb - housepaint, antiknock gasoline additives, and soldered joints in water systems - have been discontinued for the most part, in recognition of lead's toxic properties. In the body, absorbed Pb soon leaves blood plasma and accumulates in erythrocytes where it binds to hemoglobin, thiols and to the cell membrane. Eventually, Pb deposits primarily in bone tissue and also in the aorta, kidney, liver, adrenal and thyroid glands and brain. Lead can pass the placenta, such that fetal and maternal blood levels equilibrate. Calcium, zinc and/or iron deficiency conditions enhance uptake of ingested Pb. This element can bind to enzymes, proteins and membranes that present sulfhydryl, phosphate, amino and hydroxyl groups. Pb interferes with enzymes that form heme, shortens erythrocyte lifespan, disrupts iron transport in erythropoietic cells, affects renal transport of uric acid, significantly reduces cytochrome P-450 activity in children, and is synergistically toxic with cadmium and mercury. In children, manifestations of lead excess may include encephalopathy with loss of IQ, and behavioral disorders. Adults and children may

Results Pending Submission of Total Volume, 021699, FJB. 'Toxic elements only as per requisition, 2-11-99. jb'
Amended report , total volume of 1420ml submited on 2/18/99. jwh

Patient: Freya Koss ID#: 021199-0440

Comments

present anorexia, metallic taste, insomnia, headaches, fatigue, anemia, reticulocytosis, and uricemia. Erythropoietic porphyria or coproporphyrinuria may occur.

Mercury, Hg, a toxic element, is elevated in the urine. Possible sources of mercury include -

. Contaminated shellfish or seafood
. Contaminated water supplies
. Dental amalgams - recent dental work
. Electrical switches and relays, explosive detonators
. Batteries and electrodes (calomel electrodes)
. Laboratory equipment, barometers, thermometers
. Some specially-formulated fungicides
. Old paint containing Hg fungicide
. Chemical process industry, "chloralkali electrolysis"
. Mining and smelting operations

Mercury has strong affinity for sulfhydryl (-SH) sites on proteins and enzymes throughout the body and deposits in many tissues and organs. The kidneys eventually carry much of the body burden regardless of route of exposure or chemical form of the Hg. Elemental and inorganic Hg distribute predominately to liver and kidney. Excretion is slow - kidney Hg via urine and liver Hg via feces. Elemental Hg vapor may be dissolved in blood and can deposit in brain tissue. Organic Hg (methyl, ethyl) binds to enzymes, proteins and glutathione in blood and various tissues, circulates rather freely, and has a long retention halftime in the body (approximately two months). Hg interferes with catalase, monoamine oxidase, mixed-function oxidases and P-450 (in liver tissue), glutamic acid decarboxylase (in brain tissue), and other enzymes. In the kidneys, Hg stimulates thionein formation and is distributed there partly as mercury-metallothionein. In cell mitochondria, organic Hg, especially methylmercury, disrupts respiration, decreases synthesis of RNA and can be mutagenic by altering chromosome structure. Symptoms consistent with Hg contamination are variable and may include: metallic taste, increased salivation, paresthesias with decreased senses of hearing, touch and vision, hypertension, headaches, fatigue, insomnia, and fine muscle tremor possibly displayed as poor handwriting. A hallmark symptom is emotional disturbance, sometimes a bipolar depression but often a form of excitability and lack of ability for mental concentration.

Results Pending Submission of Total Volume, 021699, FJB. 'Toxic elements only as per requisition, 2-11-99, jb'
Amended report , total volume of 1420ml submited on 2/18/99. jwh

Susan Kreider
169 W. Queen Lane
Philadelphia, PA 19144
(215) 849-1698

July 25, 2000

Ms. Freya Koss
519 Sussex Road
Wynnwood, PA 19096

Dear Freya,

Thank you for contacting me following your receipt of the letter I sent to my state senators on the Government Reform Committee regarding the July 15th, 2000 congressional hearings "Mercury in Medicine." I am sending you a detailed account about how I became mercury poisoned. It is especially lengthy because, as you know, mercury is difficult to assess by way of the usual examination of blood and urine. Moreover, there seems to be a conspiratorial cover-up on the part of the American Medical Association and the American Dental Association to keep this major public health tragedy under wraps.

In fact, I am as outraged by the shabby treatment I received by the medical/legal establishment following my injury as I am by the disability I have sustained. (Note that I am excluding in this statement my relationship with Clifford J. Shoemaker, Esquire who is representing me in my claim to the National Vaccine Injury Compensation Program. He is no less than a hero, in my estimation.) I understand that you are in contact with Charles Brown, Esquire in behalf of the Consumers for Dental Choice, and ask that you include my story among those presented to him for his consideration.

Key points and recommendations regarding my personal account involve the following issues:

- Biocompatibility tests should be a standard of care prior to the installation of dental materials and orthodontic appliances (just as you would not transplant an organ without providing immunosuppressive therapy to prevent rejection.)

- All mercury-containing products available for internal use should be banned and immediately recalled from the market.

- Products should not be 'mandated' until they have been thoroughly researched in a wide demographic sample to ensure that the benefits outweigh the risks – particularly if the benefits are primarily to industry in terms of profits.

- Consent forms are useless if thorough studies have not been performed and the forms do not convey the severity of some rare possible adverse effects, especially if procedures are mandated.

- The American Dental Association and pharmaceutical industries should be subjected to the same scrutiny and accountability as the recent tobacco industry litigation. It is ludicrous to even compare the health consequences to smokers, who were fully warned at least during my lifetime, to the innocent victims of mercury-toxicity.

- If one were to humor this ludicrous comparison, however, consider the status of the infirmed National Vaccine Injury Compensation Program, established in 1986 to protect the pharmaceutical industry from litigation:

  - $140,000,000,000 tobacco settlement vs. $1,400,000,000 available in NVICP

  - A judgement levied against tobacco manufacturers vs. the $1.4 billion in NVICP that was accrued as a result of a surcharge on vaccines administered (i.e. the victims are the very ones who paid into the fund.)

  - Class action suit vs. individual claims taking years to resolve. While it was supposed to err on the side of compensation of persons whose injuries had at least a temporal association with the administration of a vaccine, 86% of claims to the NVICP are being rejected.

  - Well known correlations (such as coronary artery disease or lung cancer) vs. severely whittled down (by DHHS in 1996) NVICP Table of Compensable Injuries, made ridiculously narrow for purpose of use and interpretation. Long-term effects of vaccine injury (>72 hours after administration) are not even given consideration. This is not adequate considering that autoimmune problems may not be apparent for months.

- Costs for safely excavating and replacing the toxic materials from my teeth -not including medical and possible future surgical intervention to remove a cavitation, amalgam tattoos and detoxifying my tissues -represent 25% of my gross annual income. This money should be reimbursed to me from a claim related to the dental amalgams issues, separate from my claim to the NVICP, in addition to compensation for my grave inconvenience and the far-reaching impact that it has had on my health.

- Dr. Harold S. Buttram agrees that it is unlikely that I could conceive, carry and deliver a healthy baby considering all the damage that has been done to my immune and neurologic systems. It is appalling that in this country dental amalgams are still used for females of childbearing age. One cannot help but consider the fact that the United States has dropped in world standing for lowest infant mortality from 3rd place in the 1950s to 25th place currently.

- Abington Memorial Hospital should be held accountable for their incomplete documentation that prevented me from being able to file a full report to the Vaccine Adverse Event Reporting System. In the very least they might have pulled old invoices to ascertain what manufacturer was providing the vaccines during the time they were forced upon me at their institution.

- All vaccines available on the market should be included under the NVICP; it is beyond comprehension that it took >5 years and many thousands of VAERS reports before the hep B vaccine was included under the umbrella.

I appreciate that many of my issues are beyond the scope of Consumers for Dental Choice, but under my circumstances I have difficulty separating one from the other. Thank you, in advance, for any help you can give me -and society at large -in reaching satisfactory resolutions.

Truly,
Susan Kreider, RN, CPC

according to a strict schedule: the 2nd shot one month following the 1st shot, with a 3rd shot 6 months later. Having a strict schedule to follow to ensure vaccination effectiveness gave me a sense that this standard of practice was supported by extensive clinical trials from a wide demographic sample.

I was never provided a manufacturer's package insert, nor offered so much as a peek into a Physicians' Desk Reference, (although that is not something a 1st semester nursing school student, generally speaking, can fully comprehend.)

The consent form didn't list potential disastrous outcomes of an acute or chronic nature. Several benign conditions such as transient malaise, low-grade fever 'usually < 101 degrees F,' and inflammation at the site of the injection, etc., were listed.

I signed and dated the consent form with each of my presentations to Student Health for my scheduled injections. The nurse who administered the injections was not thorough with her documentation. The manufacturer of the 1st dose was SmithKline, product name Engerix, according to my immunization record. No manufacturers were listed for the 2nd and 3rd injections. Not one lot number was documented for any of the three doses I received.

Within a few of days from the 3rd shot (March 18, 1991) my hands turned cadaver blue. An astute nursing instructor encouraged me to visit the rheumatology clinic. I had, since she mentioned it, noticed a vague tingling in my right hand. Because I was not expecting any neurologic events and because the tingling was insidiously vague, I was not especially alarmed about my health status at this point. There were no grand mal seizures, or gastrointestinal complications, no fevers or outstanding psychiatric moments.

Ironically, it was April Fool's Day 1991, two weeks after the third shot, that I was evaluated. Most bizarre was my serum anti-nuclear antibody (ANA) titer, positive at 1:2560. March 15, 1993 they were 1:5120.

Over the next few months and years I was increasing ambulatorily- challenged. I lost my reflexes, sensation to light touch, and proprioception. I developed glove-and-stocking paresthesias, which continue to this day. My movements lost fluidity. I lost proficiency in participating in step aerobics class.

While in nursing school I presented from time to time to the Rheumatology Clinic as per their recommendations. Both house staff and supervising attending Charles Pritchard, MD were inclined towards a diagnosis of systemic lupus erythematosis, but seemed less than convinced. X-rays of my hands were done; my hands were increasingly swollen and my ring fingers changed from size 6-1/2 to 8-1/4. An EMG was performed and verified sensory nerve damage. Bio-feedback therapy was attempted a few times; I was hooked up to a thermometer attempting to raise the temperature in my cyanotic 'sausage-like digits,' but I felt little control over the reduced temperature in my extremities.

The only medication offered to me was Procardia XL 30. I was advised to wear gloves even in moderate weather, although mittens prove to be far superior. I was warned about the 2-cups daily coffee habit I have. I was especially warned regarding the fact that I smoked a pack of cigarettes a week, although in one of the progress notes my habit was significantly over-reported as a pack a day. I quit this habit in 1994 -becoming so spastic after smoking one cigarette that I couldn't take a few steps without falling.

Second semester I took a part-time job as a nurse-extern at Chestnut Hill Hospital. They evaluated my Hepatitis B antibodies; I wasn't given a booster. Despite vocalizing my concerns about my massively

elevated ANA, the employee health nurse encouraged me to receive the MMR vaccine in May and June 1991.

I graduated May 1993, concerned about climbing and descending bleachers, unassisted, as I became more and more awkward and accident-prone. Jobs for nurses were tight at this time; the majority of my classmates didn't have offers. I accepted a full-time position as a graduate nurse at Eagleville Hospital, providing care to drug addicts and alcoholics. The pay was low, but it offered benefits.

During the fall of 1993 I experienced an acute illness. I had a severe sore throat and could see some kind of gray lesion on one of tonsils. A culture was taken and I was given a prescription for penicillin. I had no appetite. After several days I was informed that the penicillin would not be effective. I stopped it. That night I had such intense vomiting that I considered taking myself to the emergency room. I even had a 'black hairy tongue,' which I had only heard about. Somehow I survived, but I was out of work two weeks and lost about 10 lbs. (9% of my usual BW.) I continued to have no appetite.

My walking was getting worse and worse. I started to panic. Instead of covering various units and Detox on weekends, the supervisor moved me to the PEP Unit (Program for Employed Persons) full-time. They thought I would have less chance of getting knocked down than on a volatile unit such as Detox, where fights break out regularly among patients who are miserable. The PEP Unit Manager told me that I was a good role model; many of our clients scammed to claim disabilities.

I saw another rheumatologist, Charles Selby, MD. He didn't believe that I had SLE because my cardiac, liver and renal functions were intact. He suggested that I might have a limited form of scleraderma, affecting only my hands and feet, and described my 'sausage digits' in his report. He rendered a diagnosis of 'undifferentiated connective tissue disease.' He concurred with the prescription for Procardia.

Judith Bronstein MD was frankly uncomfortable treating my neurologic damage. She stated that it was not what she was used to seeing. She gave me a referral to a neurologist at Germantown Hospital, Stephen D. Silberstein who specializes in headaches. He gave me one. He performed an EMG, confirming sensory nerve damage. He evaluated serum B12 and folate levels.

A month later I had a follow-up appointment with this neurologist. He clearly hadn't prepared for this scheduled appointment. He sucked on his soda straw, distractedly, like I was interfering with his lunch break. My serum B12 and folate levels were normal. He told me to come back in a month because he had to 'make some calls around the world to people who specialize in these kinds of things.' Clearly, not him. I was so disgusted with his attitude, I made a formal complaint to my HMO provider a few days later when I was in one of those kick-the-dog kind of moods.

Early 1994 a doctor who made weekly rounds on the PEP Unit, Elizabeth Carroll, DO asked appropriate questions regarding my obvious impairment and need for treatment, 'have they evaluated for heavy metals?' etc. I appreciated that she was clearly concerned and thoughtful. I asked if she would manage my care.

With a competent and concerned medical professional to manage my care, I was provided numerous referrals to a variety of specialists. A blood sample ruled out serum metals toxicity. (I have since learned that serum mercury tests are inconclusive one year following a significant exposure.) An MRI of my brain and cervical spine ruled out MS, but showed that I had some herniated cervical disks.

I was evaluated by another neurologist, Matthew Stern, MD known for his expertise in movement disorders. He confirmed that while the disks are herniated, they do not compress the spinal cord. He referred me to Shawn Bird, MD a neurologist at the Hospital of the University of Pennsylvania for further work-up. I was concurrently evaluated by a third rheumatology practice, Bruce Freundlich, MD initially. It was Kendra Kaye, MD who managed my care.

Another EMG confirmed sensory nerve damage and ascertained that it was a non-demylenating variety. Dr. Bird stressed to me how rare this type of neuronopathy is. He said that only 4 things are known to cause this type of nerve damage: (1) B6 toxicity, (2) Sjogren's Disease, (3) Cancer, or (4) ideopathic.

Blood tests, MRIs, CT-scans, mammography, CXR, minor salivary gland bx and other ophthalmic tests ruled out these conditions. The minor salivary gland bx confirmed a chronic inflammatory process, but no attention was paid to this finding to explore the cause.

One of the CT-scans revealed a suspicious 2 cm. lesion in my RLL. A thoracotomy was performed. It was an enlarged lymph node.

A sural nerve bx. confirmed a diagnosis of 'severe sensory neuronopathy of idiopathic origin.'

After the diagnostic tests were performed I was prescribed 60 mg. Prednisone daily for two months. I felt worse while on the steroids, specifically more ambulatorily-challenged.

I was next prescribed a course of pulse-steroids. I tolerated 3 days of IV Solumedrol, and started another course of Prednisone but soon weaned off of it, becoming non-compliant because it wasn't helping.

An Rx for methotrexate, a chemotherapy drug, was offered by Dr. Kaye and declined. Childless, I was afraid of this chemotherapy drug that can cause horrible birth defects.

In 1995 I had migraine headaches that occurred monthly. Usually they did not last for more than a day. A diagnosis of borderline HTN was also made. I noticed that while taking a diuretic my gait improved. I gave up the cane for a while. For a few years (1994 - 96) I had painful neuralgia in my toes. I tried a prescription for Elavil and evening primrose oil, because I had heard that it might be helpful with neuralgia associated with diabetes. Nothing seemed to alleviate the pain, intermittent in nature.

My neighbor, a licensed acupuncturist, provided a few treatments but I was unable to support the expense for the intensity of treatments I suspected I would need for significant improvement.

The pain has since abated.

In late 1994 an administrator at Eagleville Hospital referred me to the dental hygienist, because "She walks like you do. She believes that she was injured by the Hepatitis B vaccine."

At that moment of cognitive association, I realized that my profound decline in immuno / neurologic status was at least temporally associated with vaccinations I had received. I attempted to gather complete medical records from the AMH Department of Student / Occupational Health.

I filed with the Vaccine Adverse Event Reporting System. They contacted me twice, seeking lot numbers and manufacturer names. The hospital that had administered the shots couldn't provide the information. A nursing instructor who had taught a class 'Legal Aspects in Nursing' refused to respond to my phone calls / letter.

Unbelievably, VAERS informed me that the hospital was not remiss by this lack of detail. The official documentation provides vague information about a PPD administration, aside from the aforementioned limited details.

VAERS assured me that my report was 'among the most serious they have received,' and that the hepatitis B vaccine was not covered by the National Vaccination Injury Compensation Program. They cursorily corresponded once again to evaluate complainant progress, to pretend to be performing a service. That was years ago.

I spoke with the dental hygienist, Ann Paul and her husband on numerous occasions. We met with Michael Hugo, Esquire of Boston while he was visiting Philadelphia. He said that he would provide legal counsel. Months later, however, he returned my medical records, explaining that he was overwhelmed with breast implant litigation.

Ann became more angry and disabled. She went out on total disability -the day of the OJ Simpson verdict, coincidentally. We lost contact sometime in 1995 because she didn't feel that I was angry enough.

I expressed my concerns regarding my immunization history, especially the hep B vaccine, to Dr. Kaye. To her credit, she contacted the CDC. They assured her that there were no relationships between the hep B vaccine and rheumatoid conditions and autoimmune disease.

By 1995 I had to have hand controls installed in my car. I was having 'panic attacks' (self diagnosed) while driving. If I gave myself plenty of room for reaction time, cars cut me off. Sometimes when I would go for the breaks, I would wind up with my foot on the accelerator. Sometimes my foot would end up underneath the pedal. I became diaphoretic, my heart raced.

I maintained employment, working at least 4 hours over-time a week.

When he brushed me off, Michael Hugo referred me to a female lawyer in Maryland. She stated that she had handled one Hepatitis B vaccine injury claim, but explained how difficult such litigation was due to multiple factors. She referred me to a neurologist who had provided testimony as an expert witness.

This neurologist was kind enough to return my phone call. He stated that it is very difficult to prove causation in such matters, and that he wouldn't be able to take me on as a client because –coincidentally - he was retiring from practice that very week and had most of his professional belongings in moving boxes. He added that he believed that there had been a settlement in the case that he provided testimony. He was, however, under a GAG ORDER not to discuss it!

I went on with my life. I took a desk job. The pay was still lousy, but I could commute less, avoid working weekends, use my medical knowledge, and learn a new skill.

HomeNurse, Inc. in Wayne, PA provided supplemental employment opportunities. Despite making full disclosure regarding my physical limitations, occasionally to meet their scheduling needs they would

inappropriately assign me. Once or twice I was removed from an assignment because a client required care I was unable to provide.

Through networking I learned of an employment opportunity at Children's Hospital of Philadelphia. I accepted the position at the end of January 1997. Because of the improved pay I was able to lose the second job. I had earned additional certification, and so pursued employment at the Hospital of the University of Pennsylvania, my present employer.

In September 1998 I revisited Dr. Shawn Bird. I was curious whether he thought it was plausible that the Hepatitis B vaccine caused my injury. He stated, "We know of no toxins that can cause the kind of nerve damage you have." He added, "It could have been caused by a virus." He reiterated how rare the type of nerve damage I have is: "My colleagues at Johns Hopkins University and I see 20 cases of sensory neuropathy a week. Collectively we may see a case like yours once every 3 months."

In late 1998 my PMD treated me for a polysystemic yeast infection that I probably had had for a number of years, especially considering that the Hepatitis B vaccine contains DNA from some and the fact that I had been on steroids for a prolonged period. Finally, a persistent fungus under my thumbnail led to treatment with a strong oral medication, Lamisel. I took the medicine as prescribed for two months. These symptoms abated.

In November 1998 I participated in a research study looking for subjects with borderline HTN, funded by the NIH, for a period of 14 months. It was to evaluate the effects of exercise on blood pressure.

As a condition of the study, I had to give up the diuretic and calcium channel blocker. As I suspected, my walking deteriorated again. The long-term benefits of exercise outweigh the temporary disadvantage of increased difficulty with ambulation due to giving up the diuretic, I reasoned.

The only other prescription medicine that I take regularly is Flonase nasal spray for relief of seasonal allergies May through October. Thanks to this steroid spray I suffer from far fewer headaches.

At least twice a year since approximately 1996 my back goes into spasm. In addition to alternating wet heat compresses and ice packs, I use Skelaxin 400 mg. t.i.d. with ibuprofen 600 mg. for a few days. When evaluated by the ED for one of these incidents, they agreed that they are likely a result of my gait irregularities.

I still use a cane in bustling places such as at work. My coworkers assist me when we go to the cafeteria; I am unable to walk while balancing a tray of food. Highly polished floors look slippery and this increases my nervousness, adding to my spasticity. Once a month or so I fall. I usually don't get hurt.

At my 8 month medical check-up for the HTN study I qualified to be taken off the Vasotec 2.5 mg.

I consulted a registered pharmacist about my condition. Vitamin and herbal supplements have cost me in excess of $100 per month.

VAERS didn't call me, although I 'should have known,' in August 1997 when the Hepatitis B vaccine was added to the NVICP. Likewise, they did not inform me about a statute of limitations August 6, 1999 for folks like myself.

January 22nd 1999 a neighbor lady / friend called me to alert me to the fact that she had heard 'out the corner of her ear' that ABC's "20/20" was featuring a story about Hepatitis B vaccine, airing concerns

about public health. I learned of victims other than the dental hygienist and myself. I became aware of the National Vaccine Information Center and Bonnie S. Dunbar, PhD of Cell Biology at Baylor College of Medicine, whose brother was injured by the hepatitis B vaccine.

I attended the May 18th Congressional Hearings of the Subcommittee on Criminal Justice, Drug Policy, and Human Resources of the Committee on Government Reform, and submitted written testimony to the Chairman Congressman John Mica (Rep., Fl.)

I have learned that there have been some 25,000 VAERS reports about the hepatitis B vaccine in the 1990s. Of adults, 77% are females, predominantly of European lineage. The CDC claims nurses 'over-report'. Fifty percent of these reports represent 'serious' events, vs. 15% of VAERS reports for other vaccines. The FDA admits that 9 out of 10 doctors are reluctant to report these suspected temporal events.

I am enrolled as one of 100 subjects in Dr. Dunbar's study "Mechanisms of Adverse Reaction to Hepatitis B Vaccine," and contributed blood samples to each of the three laboratories. At the August 3rd hearings I heard Dr. Dunbar's colleague report that a 3rd grant proposal has been rejected by the NIH.

In September 1999 I was evaluated by an immunologist who confirms that my autoimmune disorder was likely caused by the hep B vax. I learned that my IgE immunoglobulins are 2,041.2 indicative of a severe allergic event.

In February 2000 I was evaluated by Harold Buttram, MD, FAAEM of Quakertown, PA. I had heard him speak on the radio about vaccine-related injuries. He noted that an analysis of my hair demonstrates an elevated mercury level. Reading the "comments" provided by Great Smokies Laboratory, I realized that I had many of the health problems associated with chronic mercury toxicity. I remembered meeting Anne Ferreira at the two congressional hearings I had attended. She had given me information about mercury in dental amalgams, and I reviewed the information carefully, although > 6 months later. I became very concerned about all of the dentistry I had had in my life.

In April 2000 I completed the HTN Study, and was found not to require medication.

Dr. Buttram advised me to see a biologic dentist. I consulted Andrea Brockman, DDS in March 2000. We were surprised when the mercury vapor reading registered "0." She noted that I have amalgam tattoos on my gums, and what appears -on xray- to be a cavitation in my alveolar bone. There was galvanic energy as a result of juxtaposition of dissimilar metals, e.g. a crown with –150 charge next to a filling with a charge of +6 creating a battery effect.

The day I saw her my back was in spasm. Dr. Brockman eyes were wide when I told her that I ate fish a couple of times a week. I had had broiled filet of salmon stuffed with crabmeat, two nights consecutively. That night my spasm got worse. I was out of work the whole week, unable to straighten up.

Since giving up seafood entirely for three months my back hasn't gone into spasm.

Dr. Brockman also made me aware that when I had allergy desensitization shots, weekly for two years in the mid-1980s, there is a strong chance that these shots also contained thimerosal.

In April 2000 a Cliffords Materials Reactiviy Test confrimed sensitivity to 16 of the 83 chemical groups and families of compounds evaluated, including: aluminum, formaldehyde and mercury. I noted that 71% of the orthodontic materials on the market are considered "not suitable" for me. I suspect that the fact that

I wore braces for 4 years in the early 1970s with materials that were (likely) biologically incompatible contributed to the fact that I had required such extensive dental work in the 1980s.

In the first two weeks of May 2000 I had my dental fillings and crowns removed. It cost almost $12,000 because my dentist used hi-tech precautions to prevent me from further mercury exposure. After the removal of each quadrant I visited Dr. Buttram's office to receive IV vitamin C in case any mercury was inadvertently released into my bloodstream.

The fillings and crowns had been manufactured and installed using approximately 7 – 9 grams of mercury (for the sake of reference, it takes only ½ gram of mercury in a 10-acre lake to warrant posting a fishing hazard warning.) Dr. Brockman suspects that nickel was also removed.

My new friends at DAMS (Dental Amalgam Mercury Syndrome support group) advised me not to take the urine challenge test recommended by Dr. Brockman. They said that it can cause permanent injury. Dr. Buttram agreed, when I conveyed their concerns. In fact, he refused to order the test for me after the amalgams had all been removed. He said the results would be "academic." He stated that there was enough physical evidence of mercury toxicity, and that the test would be unnecessarily dangerous. In fact, he refused to order IV chelation therapy for me for the same reason. Instead he has prescribed: chlorella, methylsulfonyl methane, zinc, and selenium to help me detoxity slowly and deliberately. He explained that the sulfur changes the form of the mercury from solid to gas, so that it is more easily excreted in feces.

On my first visit for the IV vitamin C therapy, the nurse drew a blood sample for a detailed analysis of my red blood cell essential fatty acids by BodyBio in New Jersey. It cost $300. I received the results at my June visit. They indicated severe metabolic dysfunction and were supportive of a diagnosis of heavy metals toxicity. In particular, arachidonic acid is 164% deficient. (The brain is 60% lipid, and arachidonic acid should make up 12% of these.) Conditions associated with an arachidonic acid deficiency include: chronic fatigue syndrome, metal toxicity, schizophrenia, and ADHD (attention deficit hyperactivity disorder.) Arachidonic acid is critical for cognitive function, mental stability, cell membrane fluidity, and other important metabolic functions. In fact, the decreased fluidity index explains to me, on a cellular level, why I lost reflexes and experience stiffness in movement.

Dr. Buttram explained that good dietary sources of arachidonic acid are butter and eggs, and that I should really load up on these things. The report gave me a variety of specific suggestions for my optimal rehabilitation, such as: venison, thyme oil, kiwi, avocado, parsley, nutmeg, hearts of palm, mushroom and papaya. Since Dr. Buttram advised me to stay away from shellfish, especially –he says moderate size fish are okay once in a while –I cannot take BodyBio's suggestion to eat lobster and shrimp. DARN!! The report stated that I should avoid peanut butter and canola oil, but encourages me to eat raw pecans, almonds, pistachios, etc. This is a diet I can follow!

Dr. Buttram also prescribed trace minerals and electrolytes, based on my specific BodyBio findings. It is a relief having dietary suggestions specific to my needs; I plan to repeat the study in 6 months, per Dr. Buttram's recommendation, of course.

I have since learned that many newborns have an elevated mercury level proportionate to the number of their mother's 'silver' dental fillings. To say that these fillings are stable while the scraps are treated as hazardous wastes is absurd. The Lorsheider-Vimy experiments conducted on pregnant sheep in Calgary in the late 1980s using xrays of radiographically-tagged 'silver' dental fillings proved that in only 29 days the mercury does indeed travel throughout the respiratory and digestive tracts. When the experiment was

challenged, using pregnant primates, the results were confirmatory. The fetuses had significant mercury exposures.

It is likewise absurd to include mercury, aluminum, formaldehyde and MSG in vaccines whether they are used in the manufacturing process to deaden an antigen, used as an adjuvant, or added as a cytotoxin to prolong shelf-life. In 1990 the World Health Organization declared that there are no acceptable levels of mercury exposure. How can the pharmaceutical manufacturers assure us that this "cytotoxin" is only going to prevent mildew from forming in the vials, and will have no untoward effects on tissues in the neonate's central nervous system?

Instead of just manufacturing new vaccines that contain less mercury (aka thimerosal,) old vaccines in stock should be recalled and trashed –in a manner such as one would dispose of other biohazardous wastes.

Likewise, with all the stronger, more aesthetically pleasing biologically compatible dental materials now available, there is no place for amalgams with high mercury content in the market. What's the financial difference of $20 of so, compared to preserving one's health?

Sharon Lallman
812 NE Poplar
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785-233-4941
email- RoseSL40@aol.com

Date: 1/10/00 2:51:49 PM Eastern Daylight Time
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Carol A. Maczka, Ph.D.
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Subject: Committee meeting on methyl mercury.

Dear Carol,

I am submitting the following information from my personal experience with mercury toxicity due to mercury fillings.

My personal experience in dealing with the effects of "silver fillings and mercury toxicity" as a result, came after 9 years of disabling illnesses, with no one direct connection, until I was properly diagnosed. I am a 39 year old female, with a Bachelors degree in Communications. I have been suffering with many illnesses which are interconnected, and until I had the mercury fillings removed and replaced with compatible materials, I continued to get sicker. At the time that I chose to have the fillings removed, my physicians said that my condition was life-threatening, and that I needed to have the mercury removed due to "medical necessity".

Among the diagnoses that I have had are: overuse syndrome, tendonitus, endometriosis, fibromyalgia, depression, chronic fatigue syndrome, migraine headaches, toxic brain syndrome, systemic candidiasis, food allergies, chemical sensitivities, and difficulties with my memory. Before I had the fillings removed I also experienced suicidal thoughts which are now completely gone. The original diagnosis was overuse syndrome and tendonitis. I was working for a printing firm and had a vast array of symptoms. One of the benefits of the job was dental coverage, so I went to the dentist. He began by removing old silver fillings and replacing them with composite fillings. Little did I know that the composite fillings were primarily made of nickel.
As a result, not only did I have some fillings that contained mercury, but I also had bridgework, crowns, and composite fillings that had nickel in them. That's two toxic metals in my mouth.
Along with the aforementioned diagnoses I was also battling painful periods, which got progressively worse after the dental revisions. This developed into endometriosis, and also resulted in a miscarriage. I was placed on 32 pills per day, given multiple labels and diagnoses, and given steroid shots and pills. In an attempt to control the painful and erratic periods, I was placed on the birth control pill.

In the process of all of this, I lost my job. Losing my job and the ability to utilize my Bachelor of Arts degree in communications was devastating. Having formerly worked in the medical, political, media and publishing industry, I found myself falling into the range of the disabled and oppressed group of those no longer able to function in the area that they had worked in before. When the illness seemed to be relentless, and when the doctor's were telling me that this was life-threatening, I found an inner-resolve for survival rise up within me. I had examined and tried every traditional method of healing and only found myself getting worse, or hooked on more

medications just to get through the day. Everyday was a struggle.

I located a physician who specialized in Environmental Medicine. He began treating me for systemic candiasis through the use of diflucan, and diet. While undergoing treatment my condition improved. When I had some dental work done, my condition deteriorated to the place where I was bed-ridden for months. I had a nickel bridge removed and another one placed.
I also had some old mercury fillings removed, but was severely ill after each dental visit. I was left with 12 silver fillings, and was losing weight rapidly because of severe, chronic diarrhea. I was also experiencing tremors, poor memory, depression, brain fog (spaciness), numb fingers and hands, frequent leg cramps, facial twitches, nervousness, frequent urination, chronic fatigue, bloated feeling after eating, ringing in the ears & ear infections, metallic taste in the mouth, suicidal thoughts, headaches after eating, and diarrhea.

After 2 years, and watching for a pattern in my health problems, we finally determined that I was allergic to mercury. This was confirmed through an allergy test, and 2 hair analysis. Two physicians chose to not perform the forced urine test because of the severity of my illness.
I decided to have the mercury amalgams removed. I attempted to have the dental work done here in the US. A battle with my insurance company to pay for the dental revision based on medical necessity was a good example of how most policies divide a persons coverage
into medical, dental, and optical. I was challenged to prove that the procedure was medically necessary. As part of the process, the insurance company sent me to physicians who either denied the existence or mercury toxicity, or determined that I was in need of neuropsychological evaluation. One physician, Dr. John Renner, Independence, MO, who the insurance company
sent me to, informed me that I was likely to face jail time if I had the amalgams removed and submitted the bill to my insurance company. He stated that I would be committing fraud, by submitting fraudulent medical claims. Since the debate on mercury is so controversial, they were unwilling to pay for the procedures.

I began talking to others, mostly professionals, who had successful experiences in having their dental work revised. After much consideration, I traveled to Mexico to have all of the silver fillings removed, a root canal tooth pulled, and cavitations. There were severe infections in my gums and bones, and I reacted severely with tremors and seizures for several days after the procedure due to mercury dumping into my system. They incorporated anesthesia and vitamin C IV's during the procedure, along with accupressure, acupuncture, and nutritional counseling. I have been on DMSA for 6 months now and taking Vitamen C IV's once a month. I am most pleased to report that now 6 months after the procedure, my health is improving on a daily basis. I have been able to return to college in a Masters program and go to work as a substitute teacher. Before, this would not have even been a consideration of mine.

In closing I would like to say that we should have the right to have informed consent, and should not be subjected to the cruelty of those such as Dr. Renner who are hired to keep this issue quiet. I am appalled that I would be threatened with serving time in jail for choosing to have a dental
procedure done. And I am also concerned that this same doctor indicated that he would see to it that my attending dentists and doctors would be investigated, and would also face the same potential of being placed in jail, simply for practicing mercury free dentistry, and treating the after-effects of mercury toxicity. The insurance company sent me to him and has denied
payment of my claim based on their opinion that this is not a medical necessity, and that there is not enough scientific data to support that this condition exists. It is time that scientific findings from other countries be examined, and that we move to have the right to choose treatments that
have proven successful for other individuals.

Respectfully submitted,

July'2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Bldg.
Washington, DC 20515

I'M LIVING PROOF – MY MS WAS CAUSED BY AMALGAMS

Dear Congressman Burton:

Those who feel that MS cannot be caused by amalgams are full of BS.
I'm living proof.

When I was young, I had a LOT of the symptoms of mercury poisoning, nobody knew that was what it was. I wet the bed when I was 10 years old (right after having a filling put in my mouth), I had to go outside when my dad turned on his radial arm saw because my teeth hurt so badly. I always had sensitive teeth and I had no endurance when it came to sports. I could go on and on.

My "MS" attack affected my whole body. I was a vegetable 2 years ago and in a wheelchair. Since I have done the Huggins protocol of Hg removal and chelation, nutrition therapy, I am working two jobs and going to school, working on a computer degreee and am in the least amount of pain that I have been in for 4 ½ years. I can now wear high heels.

I got the best blood report I've ever had last week. I only have to get 3 more things working right and am on the way doing that. My pituitary gland, my stomach digesting food, and balance my hormones. Won't be long now!!!!

Martha Lange

martha_l@hom.net
P.S. I continue to improve. I think in 2 years, I will be totally well. I can also climb the ladder to my attic most days now too.

Subject: **my letter to the ADA**
Date: 6/14/00 3:45:43 PM Eastern Daylight Time
From: cannesdo@yahoo.com (Jennifer Lasher)

To the ADA
Information Officer:

I have been informed that your organization claims that fewer than 100 adverse reactions to dental amalgam have ever been reported.

You people frighten me. More than I can say. So now it's 101. Read on...

Amalgam stole my life. I'm 33 and I haven't begun to live. I've been sick for 20+ years and it wasn't until the spring of '97 that I understood why. At that time I had 7 cracked amalgams removed and on instinct, having heard they contain mercury I decided to replace them with composites. Thankfully I had a parent who could afford to help me do this. The amalgams were removed in three appointments spanning three weeks. After having this hazardous waste (according to you) drilled out of my teeth at high speed and breathing in the vapor I fell completely apart.

I did it as a pre-emptive measure, I didn't expect adverse affects from the removal. But by week two I was twitching like a lab rat. I couldn't stand to be touched, couldn't stand the sound of a human voice -- couldn't be around ANYONE at this time when I needed help the most. I broke into a sweat like I'd never known, drove my car into a pole, and tried to take a shoe off my foot that wasn't there. When the phone rang I didn't know what it was or what to do about it. My head hurt so bad I thought it would implode. I lived half-alive in a haze of absolute and utter terror for the next two years. I slept 2 hrs a day on a good day. I screamed at God and begged for an end, any end, and I attempted, finally to take my own life. Now, 3.5 years later, after 300+ hrs of sauna therapy and $5000 of supplements to keep myself - LITERALLY — alive, I am finally able to see a light at the end of the tunnel. I went through it alone.

Because of your greed. Period. I used to hold onto the kitchen counter for HOURS on end -- drooling on the burner and howling like an animal so I wouldn't kill somebody, or kill myself. I was diagnosed as manic-depressive, medicated for 7 years (quit all the meds 2 years ago), treated like a crazy person and everyone I know believed that. Now, since all fillings have been removed. they are horrified at how wrong they were. I am slowly returning to the person I used to be. I am kind and patient and tolerant. I am no longer depressed or fearful. I look forward to the future and am a pleasure to be around. The result of my DMSA chelation challenge indicated that 2 years ago I had a body burden of 8.3 on a scale of 1-9 of...you guessed it...mercury.

If I didn't have a parent who could have taken on the financial burden your amalgam would have killed me. My fillings were a Cu/Hg amalgam. Funny, isn't it, that when tested for allergies these are the two metals I was allergic to? Try to tell me they're bound. When I add copper to my supplements I get very toxic very quickly. THESE FILLINGS CORRODE AND LEAK. PERIOD In the 1840's dentists lost their licenses for *using* amalgam.

SHAME ON YOU for letting your brothers and sisters suffer so horribly. SHAME ON YOU!!!

I have a list of 60 symptoms that resulted from the toxicity of these fillings. Among them, cognitive difficulty (an understatement), allergies (they started the same summer I got my first filling), neurological problems (tripping down stairs, stuttering, running into

LASHER

doorframes), depression, anxiety, rage, anemia, severe PMS -- YOU NAME IT, I'VE HAD IT. I was a chubby healthy NORMAL child until I got that first filling, then I lost weight, became hyperactive and hitting puberty was the beginning of the end.

I am the girl next door. I'm not some radical raised in a teepee wanting to undo every governmental institution I can. I trusted you, but it's clear now that other governments have declared this material unsafe that I am not alone anymore. Face the music, people. We're out here. We are your sisters, you daughters, your fathers...we don't put two and two together because we can't. Mighty convenient for you.

Everyone I tell about my story says, "There isn't mercury in them any MORE is there???" AT LEAST tell us the truth about what's in them, make it public so people can decide for themselves.

MERCURY IS THE MOST TOXIC NON-RADIOACTIVE SUBSTANCE IN THE WORLD. TESTS HAVE PROVEN IT ISN'T BOUND. GET IT OUT OF OUR MOUTHS!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!

The dentist who removed those first 7 fillings asked me when I told him how ill I'd become that week and asked if amalgams could be the cause, "On the record or off?" He told me when I promised silence that he wouldn't put them in his own child's mouth.

DO THE RIGHT THING.
DO IT.
PLEASE.

Jennifer Lasher

Levy (1)

March 19, 2000

To Dan Burton, Chairman
Committee on Government Reform

From: Maz Levy, San Francisco, CA
Homeless due to mercury poisoning.
"Maz Toothousand" <toothousand@hotmail.com

Subject: Mercury FYI

Dear Chairman Burton:

I have researched mercury for 6 years following chronic mercury poisoning. I want medical professionals to be taught mercury diagnostics and statistics. This is a quickly written account for your information.

re: chronic mercury poisoning and galvanism (micromercurialism) due to excessive replacement of dental materials following domestic violence.

Every material the dentist has used in the past has a toxic element. Mercury being 50% of all amalgam fillings followed by tin and copper.

These all carry a galvanic current that is harmful to natural materials. This galvanic current is sent through the neural system from being implanted to the dental nerve.

Mercury is negative radiation, it promotes uptake of radiation in surrounding tissues often used in medical diagnostic testing.

Mercury and heavy metals promote invasion of microbes, bacteria and viral infections, microbes feed off deceased and toxic cells.

Mercury from dental materials is found to progress along the same paths in the body as cancer, mercury exposure lowers the immune system, mercury causes antibiotic resistance due to the metallic content unable to penetrate the outer layer of the cell coating.

Mercury crosses the blood brain barrier following methylization with bacteria, allowing toxins to move freely into the brain. Mercury is found to cause memory loss, concentration loss leading to alzheimers.

Mercury crosses the placenta to the fetus in pregnancy, creating a higher percentage of mercury in the child than the mother.

Leaf (2)

Mercury effects the neural motor causing repetitive motion fatigue and ALS with the addition of galvanic currents.

Mercury's main route is through fecal matter resulting in high grade carcinoma of anal tissue. Carcinoma of anal tissue often results in stomach cancers.

Mercury causes visual disturbance, seeing patterns, restricted vision, night-time blindness, slow response to dark and light, blurred vision, fluctuating difficulty in reading.

Implanted mercury is the most serious of chronic toxic exposure because if effects the whole body and generations to come. More so because there is no doctor trained in chronic mercury exposure and its non-specific symptoms at an early stage. Many times unable to prescribe for the complaint patients are sent to psychologists who will without medical evidence prescribe a toxic pill that can weaken the system already toxic.

Mercury is a pathogen, pathogens are not treated except by large industrial chemical corporations.

Mercury is the cause of many chronic diseases, chronic because the source has not been considered, the toxin not removed and detox not treated.

Mercury in fish is eliminated by the body after 30 days, mercury in dentistry is accumulative for tens of years and never eliminated.

I am 44 years old, female, I had a massive amount of fillings, my dentist warned that I should seek only very minimal uninvasive treatment in future. Approximately 16 years ago I suffered from domestic violence, fist blows to my face and jaw. I was pregnant and recieved treatment at University of California Dental School, I was concerned with treatment being pregnant. Treatments were ongoing for the next 10 years replacing massive fillings, also 2 gold crowns each side, root canals and pins also in others.

I have 2 eye tooth remaining untouched with double roots.

I never felt the same since. My daughter was born and went under the lights, my contractions were totally irregular, down to 3 or 4 minutes apart then back up to 15 minutes apart. I was exhausted by the time she was born.

My daughter suffered many ear infections and an incident of bronchial pneumondia almost to the point of hospitilization.

In the first 10 years I had neck, shoulder and arm pains, I could no longer

play mandoline, exercise and treatments made no difference. I felt aloof in the evenings, as if communication between brain and speech were not together. I suffered digestion problems without any diagnosis.

By 1993 I could no longer take the replacement of breaking tooth, the galvanic current was so high, my health had suffered many non-specific symptoms. I could not get a diagnosis for the digestion problems. I could not get up in the morning due to nausea, stiffness, fear of passing out. I suffered dysmennorhea, with excruciating pain worse than child birth, vomiting and inability to function, heavy bleeding, frequent and irregular. At this time I also lost my ability to understand the structural databases I had created, I could not see two problems together as a whole. I forgot telephone messages and names as soon as I was told. I could not remember my weekly schedule even if it was the same for each week. I fell asleep during rush hour.
I could not eat anything, until I discovered only protein in the form of a natural bean mixture. I had dermatological problems, dry skin, dry mouth, dry eyes. There were irritating spots along my back and shoulders, these got worse the more I showered.

I installed a carbon monoxide detector, this went off every time I showered, I learned about blue water, the water heater had corroded and given off a galvanic current also, this caused the spots on my back and an inability to raise my arms and resulted in contracting viral herpes from a school child just by pointing. I removed every source of galvanic current except the one I could not afford to in my mouth.

My daughters hair analysis was higher than mine for mercury, this correlated with the science on fetal exposure. She had only recently got small fillings, and could never run the mile in school without joint pain, and now complained of bubbles in her tummy, that the doctor didn't know what to make of without doing invasive treatment.
The removal of her 50% mercury, amalgam fillings, followed the fastest mile in physical education and no joint pain. The digestive disturbance was gone.

At that point I filed for disability unable to afford $20,000 and unable to work. I lost custody of my daughter, my home, and all means of support. I have no visitation or custody to make an accurate follow up at this point. It was acceptable then to call mercury poisoning from dentistry a fraud and subject to ridicule.

The dentists measured a very high current due to galvanism, loss of bite and a neuropsychological report for toxicity and organic syndrome. As an outpatient of Richard Olcesey of NorthCoast Rehab. in Santa Rosa, he understood how easy it was for any psychologist to attempt to undermine my

Leg (4)

mental state that was sound. Anxiety for my daughter and an inability to hold back tears is still mercury etiology considering the chelation of lithium by mercury.

I had reoccurring Epstein Barr, urine and fecal infections, also mercury etiology from a lowered immune system. Concentration loss, short term memory loss, disturbed sleep, frequent urination, fatigue, menstrual problems, problems with toxic exposure and a heightened concentration loss under fluorescent lighting. Ringing ears, weakness all down one side, joint pains, ataxia - difficulty in the hips, pain from walking, standing and staying in one position too long, often standing from sitting results in loss of ability to stand.

I went through a toxemia of pregnancy. At first I slept for days, then I felt suicidal as the hormones raise very high and drop suddenly. Now I was infertile. But I kept insisting that I needed to be checked with a sonogram because the literature shows it leads to cancer. Finally the doctor sent me to a surgeon for anal polyps, these were indeed high grade carcinoma.

All my symptoms are indeed that of mercury under the influence of a galvanic current. Every tooth in my mouth except for the eye tooth have been drilled and filled with an excessive amount many times. The new copper fillings show a yellow surface and breakage next to the gold crowns. These I fear have increased the mercury level significantly promoting chronic exposure to acute levels.

I do not have petty sensitivities like some toxic people, I am immediately aware of mercury exposure, felt in dental offices, some buildings where fluorescent lighting may have leaked or broken. I suffer nausea and difficulty breathing in smog and have to go either up above the smog level on the mountain or out to the ocean. I do not normally suffer from Asthma although many do. I avoid all foods and intake of ethyls, methyls and sulphur.

I appear to be mercury toxic, and prone to viral infections and sinusitis, I can sense a virus in my glands immediately. I have a fine finger tremor.

I have requested disability since acute symptoms since there is no resource for removal of the toxic source of exposure.

Mercury poisoning cannot be seen, smelt, tasted, and there is no obvious physical condition, except possibly the tremor and difficulty handling oneself in public. Those of us who have met each other being mercury poisoned, find that we don't look as bad as we sound, but we have all suffered considerably. Mercury poisoning looks like cyanide, we get weak and

Lay (5).

tired, but since I was very athletic from rowing, gymnastics etc. I still have a certain physical look but there is no stamina, repetitive motion fatigue consumes me, what I do physically now, I suffer for having done. To be able to do something doesn't mean it can be done again and again. When the whole pathology is seen as one condition, mercury poisoning is as the myth we are turning to stone.

Removal of the source of mercury is the only cure for this disease. Mercury is the toxin of all toxins, as it penetrates the blood brain barrier and fetus, or as Newton noted by the silver hair of the furnace workers.

Mercury is an electrical component, it is perfect for completing the circuitry in the information age. In humans mercury destroys reasoning, comprehension, memory, physical ability, the functioning of organs. The toxicity of mercury kills cells, microbes feed off those cells, bacteria, viruses and microbes are the biological evidence of mercury.

M. Levy

Linda M(

134 Winston Dr
Williamsburg, Va. 23185
July 16, 2000

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Bldg.
Washington, DC 20515
Dear Mr Burton:

I'm writing to you, a public servant, to tell you of my experience of being poisoned with the dental (mercury) amalgam placed in my teeth; and also to urge you to become active about this issue to protect all citizens against this serious public health threat. The World Health Organization is recommending that mercury be banned from dental use. Thousands of scientific research papers have been published in various parts of the world verifying its toxic effects. Although the American Dental Association claims studies have been done to prove its safety, it has no list. Meanwhile I myself along with many others have experienced and continue to experience reversal of symptoms and improved functioning felt immediately upon getting up out ot the dental chair.

Six years ago I was having bilateral arthritis symptoms. I took prescription arthritis medications for several years. Conventional doctors could find no cause for the symptoms changing. The symptoms included:

- chronic fatigue
- difficulty walking and maintaining erect posture
- limping
- feeling as though my head was transmitting electricity
- feeling as though my brain was being ripped in half

feeling as though my brain was being fried
earaches or burning ears
aching in most of my teeth - with 16 mercury fillings in my mouth

- feeling as if my head was as big as a large balloon
- swollen, painful-to-the-touch lymph nodes in the neck and back of the head
- allergies to most foods
- burning sensations in various parts of my body

I began doing my own independent research. I requested a hair analysis from an out-of-state health care practitioner. The results showed a toxic level of mercury. I also had a test done showing the negative electrical charges comingfrom my teeth. (I have included this test result.) I first spoke to Catherine Lynn, DDS of Newport News, who treated me for five years. It was she who advised me to have some old corroded fillings replaced, drilled out old mercury to expose me to more mercury and then filled the teeth with a new mercury mixture. She also chose 3 more metals to cover the palate of my mouth as a way of holding a false tooth in place. I now know that saliva mixes with mercury and other metals to produce a battery

Linda M. (2)

effect. I asked her what she could do to help me. She explained dentists have been putting mercury in teeth for 160 years and that she could lose her license if she took it out of my mouth.

I approached the clinic at the MCV School of Dentistry for care. Three gray-haired faculty members who looked briefly into my mouth told me the results of my hair analysis test were worthless, part of a scam. No one would remove any mercury. And as for the mercury -filled tooth that was beginning to get achy off and on - they would probably cover that with a gold crown. More metal!
Fortunately I did eventually find some real health care - compassion and knowledge of mercury, within this state. On four successive occassions I immediately felt relieved of some symptom upon leaving the dental chair. I continue to improve with the use of alternative therapies.

Toxic mercury from dental amalgams is a serious threat to the functioning health of all US citizens. Please become involved in seeing to it that there is a thorough investigation of this issue. I'm also concerned about the safety of other dental materials, as I did a lot of reading before deciding which materials to pay for for my most recent dental work.

ALL HEALTH CARE PROFESSIONALS WILLING TO HELP (FEW IN NUMBER) THOSE WITH TOXIC MERCURY SHOULD NOT BE HARASSED OR PENALIZED IN ANY WAY.

Lastly, why is it that Trigon Blue Cross/Blue Shield paid Dr Catherine Lynn to load me up with more mercury, but won't help pay to take it out as sick as I've been?

I'm sending a copy of signatures I'm forwarding to the FDA and Congress to show public conern about this issue. If you have any questions you can reach me at 757-565-1839 or cifell@widomaker.com

Cordially,
Linda M. Cifelli

Lisa cy

July'2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Bldg.'
Washington, DC 20515

"60 MINUTES SAVED MY LIFE"
Recovery from Multiple Sclerosis

Dear Congressman Burton:

Suddently I had a bad pain in myleft eye and went blind in that eye.

The opthamologist (graduate of Johns Hopkins) diagnosed me with Retrobuldar neuritis. He told me it could be Multple Sclerosis. I rejected that diagnosis. Steroids were my only option of treatment, which I also rejected. After approx. 2 months of complete blindness, in that eye, pain had subsided as the inflammation subsided, but nerve damage was not correctable (so they said).Afer using visualization techniques, it started to clear up. (I read many books on these techniques, and other books, like Norman Cousins, "Anatomy of an Illness.")

The doctors were amazed that I gained sight back. (My theory was, if my brain could tell my hand, for instance, to pick something up, and it would respond, then why couldn't my brain tell my body, internally, to do things, as well. So, I used visualization techniques to tell my brain to send things to blast away the scarred tissue on my optic nerve, so the electrical impulses which allowed me to see could be transmitted down the nerve once more. This did indeed work and although I doubt I will ever get full vision back in that eye (I don't do those techniques anymore) I can see out of my left eye, although it is like looking through a screen, there are holes in my vision field, and colors don't look the same anymore.

The following year, the double vision abruptly interrupted my life and spinal taps, MRI's, and a barrage of nuerological tests "confirmed" the diagnosis of MS. This time I endured the steroids (and the side effects.) The spinal fluid did not show MS, but the confirmation was made by the double vision and the plaque or scarring on my brain shown by the MRI's.The steroids, it is said, do not work for everyone, but I could see the two separate images gradually coming together as one over a period of 3 months, so the doctors claimed I was steroid sensitive and so they did indeed work for me. Next year, my balance was affected and rotary nystgmus (eyes move on their own and shake constantly) set in. Again, steroids, visualization (my idea again, doctors, of course, poo-poo'd that idea) and 2 months of time made it go away.

Through the next few years, I endured depression (attributed to the diagnosis) fatique, blurred vision, nervousness, anxiety, weakness in my limbs, tingling sensations, burning

Lisa C)

sensations and various pain. (All attributed to the MS, but I rejected steroid treatment and opted for just my own method of treatment: distraction in the form of reckless behavior, ie, sky diving, impulsive behavior, drinking to excess, manic behavior, etc.

It was around that time, 60 Minutes reported the amalgam/mercury story. I had 11 large amalgam fillings. My cousin was a dentist and removed all of them, at one time, and replaced them with gold (now I wish I had opted for composite material, but the gold doesn't seem to cause me all that many problems). Within 10 days, I had NO more symptoms of MS! Very few people, including my doctors and my cousin, the dentist, believed me. I didn't care, I KNEW it was from the mercury!! (Thank God for that TV report!)

This has been a long, but educational trek. I HAVE NO DOUBT I was mercury poisoned and still endure some after effects. I did not do any chelation, I didn't know about it back then. I feel extremely strong about getting the message out and making "whom ever it is" that approves mercury use to STOP! I would like to go back to school to become whatever I need to to get the necessary credentials (not sure what they are, though) to do research, writing, etc. to get paid for working against this practice of using mercury, about which I am so passionate, interested and directly affected by.

I wish everyone affected by mercury all the best of luck in beating this thing If there are any questions about my experiences, please send me an email or posting and I will be glad to answer.

Sincerely,

Lisa Cochran
(lisalmccoc@aol.com)

Madronero (1)

2157 Rayburn House Office Building
Washington, DC 20514

RE: **Dental Amalgam Mercury – Spontaneous Abortions**

Dear Congressman Burton:

My interest in the issue of dental mercury amalgam and potential health hazards was initiated by my two spontaneous abortions. Reflecting on the similarities of the events, I discovered that in both instances I had dental work performed just prior to the miscarriages. The correlation of events led me to question the exposure of dental procedures, involving the use of mercury. The information that unfolded in my quest to understand the issues was alarming, to me.

There is convincing evidence that mercury does cross the placenta, causing birth defects and miscarriages. "The Toxicological Profile on Mercury", published May 1994, by the U.S. Public Health Service clearly states that mercury is harmful to humans. Moreover, it states that mercury passes into the body through diet and dental amalgam.

The history of mercury amalgam in the United States dates back to 1833. Under the G.R.A.S.(generally recognized as safe)category, the FDA grandfathered in it's accepability. There is documented research cited to confirm overwhelming health hazards. The World Health Organization speaks out, against the use of mercury amalgam. The American Dental Association contends that the information regarding
health complications related to mercury is anecdotal.

With all of the compelling research coming from other countries, one must wonder why the American body is so different that the same does not apply. Most dentist's for fear fo being deemed unethical do not acknowledge the presence of contentious information about mercury amalgam. According to the amended American Dental Association code of ethics, to make the removal of serviceable mercury fillings an issue of unethical conduct, if the reason for removal is to eliminate a toxic material from the human and if this recommendation is made solely by the dentist. (American Dental Association 'Principle of ethics and code of professional conduct', Section I-J: Representation of care and fees, 211 East Chicago Ave., Chicago Il US, 60611)

Clearly, there are many issues that require more probing research. However, when a patient seeks the professional advice of a healthcare professional, the care of that patient should be paramount. If there is known information that questions the efficacy of current protocol, shouldn't the patient be informed? Is informed consent not to be considered? Especially when there is such controversy about the safety of the treatment, the patient
should be made aware of those dangers.

Respectfully,

Dorice A. Buck-Madronero
4 Regis Court
Suffern, NY 10901

Marquez 1

N. Anne Marquez, Ph.D.
59 Varda St.
Rohnert Park, CA 94928
707-792-2663 Phone/Fax
annemarquez@pacbell.net

July 14, 2000

Dear Senator and/or Committee Member,

I am writing this letter to urge you to investigate the dangers of the use of mercury in vaccines and dental amalgam. As you probably know, mercury is used in a preservative called, Thimerosol, and routinely added to vaccines. These vaccines are given to infants between birth and 6 months of age. So many vaccines are given (31 at last count) during this time period that the aggregate amount exceeds "safe" levels established by the FDA. It is suspected that infant diseases reaching epidemic proportions in this country such as asthma, autism, attention deficit disorder and others may have a connection to this questionable practice.

Ninety-five per cent of Americans have amalgam fillings (50% mercury) in their mouths. The safety of this practice has never been established and many suspect that it is a dangerous practice indeed. Neurological/autoimmune disorders such as multiple sclerosis, lupus, als, chronic fatigue syndrome, Alzheimers, Parkinson's, and many others have been associated with high levels of mercury in the brain caused by dental fillings.

Congressional hearings on the mercury in medicine/dentistry will be held on July 18, 2000. Please know that as a registered voter, I am counting on your representation at those hearings.

Thank you very much,

N. Anne Marquez

Anne Marquez, Ph.D.

McGrath (1)

NEUROLOGICAL PROBLEMS, HIGH BLOOD PRESSURE, TREMORS ETC

July 9, 2000

Congressman Dan Burton
Committee on Government Reform

Dear Congressman Burton:

The following is my personal experience in living with and dealing with the mercury poisoning, that was created by my amalgam dental fillings. I hope that my story will succeed in making the reader aware, just how important the amalgam issue is.

I had my first fillings put in, around the age of 12 or 13. Given the way that mercury affects the brain, I truly believe that it was the cause of me becoming an introvert throughout grade school and my high school years. At one point, I was sent to see the school psychologist, because a concerned teacher thought that I was becoming to withdrawn and too much of a loner. I have remained timid and shy throughout school and throughout my adult life. If the correct knowledge, about amalgam fillings and the affects on the brain and body, had been known at an earlier age, I believe that things would have been different in school and that I would have had a happier childhood and a more productive adult life.

I had absolutely no idea that my dental fillings caused mercury poisoning, until I happened to find out by surfing around on the Internet. I came across a web site that explained how amalgam fillings contain 50% mercury and continue to leach, this poison, into our entire system. As I read the list of symptoms, I felt like I was reading my own medical records, and was relieved knowing that here was an explanation to so many problems that I have been facing. I found out that as I age, my body becomes over burdened with mercury and more symptoms appear. I am now in my 40's, and have experienced many mental, emotional and physical problems. I have had to deal with depression, anger, low self-esteem, emptiness and even suicidal tendencies. I have difficulties finishing projects, I loose interest quickly and creativity rarely comes, for an artist, this is very devastating.

I have neural problems that affect the right side of my face, high blood pressure, low thyroid, tremors in my face and hands, acid reflux, a metallic taste in my mouth, ringing in my ears, double vision, dizziness, pains in my joints and flu like symptoms.

Since I found out about my poisoning, I have contacted a dentist that was willing to follow the correct removal protocol, and have had all 15 of my amalgam fillings replaced with an acrylic composite. He removed them, one quadrant at a time, and I have had amazing results. After the first quarter was removed, the right side of my face became relaxed. My cheek no longer draws up closing my right eye and I talk clearer, because the right side of my mouth now moves normally. I no longer have to grasp my hand to

McGrath (2)

steady it when doing detail painting, because my hands no longer shake. The metallic taste is gone from my mouth and lips and food tastes normal again. I am no longer on prescription medication for my acid reflux and no longer need one of the medications that lower my blood pressure. The dizziness has left, I seem to have more energy, and the pain I was experiencing in my joints, is gone.

I have been on a supplement protocol before, during and after my fillings were removed. Mercury attacks on a cellular level, so I take supplements everyday that build up my immune system and help in removing mercury from my blood, urine and tissues. I will be starting soon on a chelation supplement that will open the blood/brain barrier, and aid in the removal of mercury from my brain. I expect many more improvements as my body and brain are no longer burdened with mercury toxins.

Removing the mercury burden is a very long, expensive and time-consuming process. It is vitally important that people find out about this, early, so it can make a difference in their lives. My parents had no idea that metal fillings could cause such harm, they relied on the dentist's expertise. People need to know and understand now, so they will have the knowledge to protect their children from having this poisonous metal put in their teeth. I can tell you, personally, that it is a scary and confusing experience, to find out that you have been poisoned, and no one understands or believes you. I had to become my own doctor, because the majority of medical doctors, (including my own) nurses and dentists believe what the American Dental Association believes, that there is nothing wrong with amalgam fillings. I am one of so many that can personally say that I have been poisoned, by my amalgam fillings and that these people are wrong.

Carol McGrath
10573 Griffin Rd.
Clymer, New York
14724-9630

ELISSA MEININGER
4316 Windsong Way
Oklahoma City, OK 73120

July 10, 2000

The Honorable Dan Burton, Chairman
U.S. House Government Oversight Committee
U.S. House of Representatives
Washington, DC 20510

RE: Hearing on the use of Mercury in Medicine

Dear Rep. Burton:

Please be aware that I was diagnosed with mercury poisoning from my dental fillings more than 15 years ago. Since then, I have been using the services of homeopaths and other non-allopathic healing arts practitioners exclusively because allopathic (mainstream) doctors, for longstanding political reasons, are not trained to diagnose and/or treat this malady.

Please be aware, also, that preceding the first ***Access to Medical Treatment Act*** hearing in 1994, held by Senator Kennedy's Labor and Human Resources Committee, I was asked to provide a written statement regarding the politics of mercury in medicine from both my personal experience and my interest in the political history of the matter. My written statement can be found on pages 136-137 of the published report of that hearing. (ISBN 0-16—044878-6)

For your convenience, I have attached a copy of my statement with this letter along with additional material (slightly updated) I had also sent Senator Kennedy that was not printed in the report but was noted in the report as available in the Senate archives of that hearing.

The reason I sent this material to you is to show that the controversy over the use of mercury in medicine and/or how to diagnose and treat the illnesses it causes, has been a longstanding political fight in this country since colonial times. I wish to point out, also, that when decisions were made at the beginning of the 20th Century to establish an allopathic medical monopoly, and drive out all competition to silence opposing views to allopathic philosophy, this policy decision has been a disaster to the American public ever since. This ill-advised decision is the specific reason I have suffered a lifetime of ill health.

It is particularly important to note that the dangers of using mercury in medicine, as well as how to diagnose and treat mercury poisoning has been a central flashpoint of argument between allopathy and many other healing arts traditions.

Since members of this committee are no strangers to the politics of vaccination policy and law, thanks to recent hearings, I have no doubt you have a keen interest in getting to the bottom of the mercury issue. In addition, thanks to several hearings over the years on the subject of non-allopathic healing arts traditions (aka "alternative" and/or "complementary"), you and your committee have a solid background understanding of the allopathic/non-allopathic politics. Consequently, I have great hope that you will be able to get to the bottom of the mercury filling mess.

For me, the clearest resolution to this controversy is to establish policy and law to recognize that every citizen has the right to use products and services from ALL healing arts traditions and practitioners of these traditions has the right to have equal legal status and respect currently accorded to allopaths.

Thank you for your interest in holding hearings on mercury in medicine.

Sincerely,

Elissa Meininger

ELISSA MEININGER
4316 Windsong Way
Oklahoma City, OK 73120

Text of my letter as it appears on Pages 136-137 of
Access To Medical Treatment Act Hearing of 1994 (ISBN 0-16-044878-6)

July 22, 1994

Senator Edward Kennedy, Chairman
U.S. Senate Labor and Human Resources Committee
Washington, D.C. 20510

Dear Senator Kennedy:

As you and your colleagues deliberate ***The Access To Medical Treatment Act of 1994 (S. 2140)***, please be aware that for many of us the purpose of this bill is not just to limit the authority of a government agency. It is to put a stop to the systematic suppression of non-mainstream medical practices which many of us rely on for our daily survival.

In my own case, I was plagued for many years with the symptoms of mercury poisoning (memory loss, fatigue, hyperactivity, metabolic and digestive problems) which mainstream physicians had no way of properly diagnosing. At the point when I was no longer able to get out of bed or carry on a coherent conversation, I turned in desperation to the only Homeopathic physician I could find.

He not only diagnosed and cured my illness — he pointed out, among other things, that the symptoms of mercury poisoning had been understood by Homeopaths the world over for many generations, but that the war waged against Homeopathy by mainstream physicians and the proprietary drug industry in this country had been so successful, few Homeopaths remained to diagnose it. Many Americans are not as lucky as I was. Homeopaths are hard to find, their skills are not widely publicized, and they work in constant fear of harassment from state and federal authorities. Yet, the fact remains that after years of mainstream failure, a Homeopath diagnosed and cured my illness.

For me, the bottom line for supporting passage of ***The Access To Medical Treatment Act*** is the fact that we, the public, are still being held hostage to this age-old philosophical fight between mainstream (Allopathic) medicine and Homeopathic medicine. (Around the world, mainstream American medicine is called Allopathy, as opposed to Homeopathy, which is based on a different set of medical principles.) Currently, all government medical policy decisions are being made based on the mainstream Allopathic medical model. So complete is the government's commitment to this single view of medical thought, that anyone who even suggests limitations to this medical model, no matter how learned or respected, is severely

ostracized. Given this climate, few dare risk speaking out, and in this conspiracy of silence, millions of people like me are denied access to appropriate non-Allopathic medical care.

The most vivid example of this systematic denial of other philosophical medical truths involves the dispute over mercury poisoning, which still remains a hot issue. In 1991, the FDA held hearings on the possible dangers of silver-mercury dental fillings. These hearings should have provided a major opportunity for our government to at long last properly address this ongoing dental community fight. (As you may know, there are 180 million Americans with mercury in their teeth, and thousands of reported cases of dental-related mercury poisoning.) But because the FDA relies for advice mainly upon Allopaths, and not Homeopaths, Naturopaths, orrepresentatives of any other alternative medical philosophy now emerging from other parts of the world, the only conclusion they were able to draw was the fairly pitiful and predictable one that the subject needed additional study.

I have included with this letter some startling references dating as far back to 1807, illustrating the fact that for generations, scores of mercury experts have argued with the Allopathic community over the entire issue of the use of mercury in medicine. (You will note that most of these references, starting with a quote from Thomas Jefferson, deal not with the fact that Allopaths were unable to diagnose mercury poisoning, but that they were actually using mercury-based treatment to exacerbate existing illnesses, and in the case of George Washington, probably causing his death.) Amazingly, the Allopathic community has consistently failed to listen and it is very likely that many Americans have died as a result. This material will also give you a flavor of the deeper philosophical argument that exists between Allopaths and non-Allopaths — something we all need to understand as we deliberate all issues surrounding health care reform.

Sincerely,

ELISSA MEININGER
4316 Windsong Way
Oklahoma City, OK 73120

Text of the material I submitted as referenced on page 137 in the report of the Access To Medical Treatment Act Hearing of 1994 (ISBN 0-16-044878-6)
(slightly updated)

1807 - President Thomas Jefferson, Noted Natural Scientist, Rejects Mercury as Legitimate Medical Treatment

"Having been so often a witness to the salutary efforts which nature makes to re-establish the disordered functions, he (the wise physician) should rather trust to their action, than hazard the interruption of that, and a greater derangement of the system, by conjectural experiments on a machine so complicated and so unknown as the human body, and a subject so sacred as human life....From the scanty field of what is known, he (the Allopathic physician), launches into the boundless region of what is unknown. He establishes for his guide some fanciful theory of corpuscular attraction, of chemical agency, of mechanical powers, of stimuli, of irritability accumulated or exhausted, of depletion by the lancet and **mercury,** or some other ingenious dream, which let him into all nature's secrets at short hand. On the principle which he thus assumes, he forms his table of nosology, arrays his diseases into families, and extends his curative treatment, by analogy, to all the cases he has thus arbitrarily marshalled together. I have lived myself to see the disciples of Hoffman, Boerhaave, Stahl, Cullen, Brown, succeed on another like the shifting figures of a magic lantern, and their fancies, like the dresses of the annual doll-babies from Paris, becoming, from their novelty, the vogue of the day, and yielding to the next novelty their ephemeral favor. The patient, treated on the fashionable theory, sometimes gets well in spite of the medicine."

Source: ***The Americans: The Colonial Experience*** **by Daniel J. Boorstin, Librarian of Congress Emeritus**
(The people Jefferson was condemning were the founders of allopathy)

1832 - Leading Physician Claims George Washington Died of Mercury Treatment

"Think of a man being, within the brief space of little more than twelve hours, deprived of 80 to 90 ounces of blood; afterward swallowing two *moderate* American doses of **calomel (mercury),** which were accompanied by an injection; then five grains of **calomel (mercury)** and five or six grains of emeric tartar; vapours of water and vinegar frequently inhaled; blisters applied to his extremities; a cataplasm of bran and vinegar applied to his throat, upon which a blister had already been fixed, is it surprising that when thus treated, the afflicted general, after various ineffectual struggles for utterance, at length articulated a desire that he might be allowed to die without interruption."

Source: ***The Reformed Medical Journal*** **by Dr. Wooster Beach**
(Leader of an organized attempt to reform allopathic medicine, Dr. Beach and his colleagues founded *The Eclectic Institute* and established a distinct medical sect combining allopathy and botanical medicine. Eclectism was the third largest medical profession in America at the turn of the 20th Century but was squeezed out of existence by the 1940's.)

1833 - Samuel Hahnemann, Founder of Homeopathy, Condemns Mercury Treatments

"When it knows not what else to do for the disease which will not yield or which grows worse, the old school of medicine (Allopathy) undertakes to change it into something else, it knows not what, by means of an *alternative,* — for example, **by the life-undermining calomel (mercury), corrosive sublimate and other mercurial preparations in large doses.**

It seems that the unhallowed principle business of the old school of medicine (Allopathy) is to render incurable if not fatal the majority of diseases, those made through ignorance by continually weakening and tormenting the already debilitated patient by further addition of new destructive drug diseases. When this pernicious practice has become a habit and one is rendered insensible to the admonitions of conscience, this becomes a very easy business indeed."

Source: ***Organon Of Medicine (Sixth Edition)*** **by Samuel Hahnemann**
(Hahnemann rejected his allopathic training and its reliance on mercury to found homeopathy, a medical philosophy based on a different set of medical principles. Homeopaths are still taught how to properly diagnose and treat mercury poisoning. Homeopathic products are regulated by the FDA as over-the-counter drugs. Some are specifically designed to treat mercury poisoning including poisoning caused by dental amalgams.)

1849 - Noted Physician Describes Grizzly Effects of Mercury Treatment

"...Read the proofs of the rationality of your **allopathic** cures, the proofs of your recklessness in the haggard countenance of one, the disfigured face of another, the palsied limbs of a third, the rotten teeth, the filthy gums of hundreds; all these trophies of ***calomel*** **(mercury)**: of salivation!* Listen to the complaints, the moans, of your *best* cases; they say, "the doctor salivated me, and I *never have been well since*; my bones ache, my limbs fail, I can't stand still. I am no longer myself."

"....And these innocent children, once pictures of health and happiness, now pale, prostrated, some of them with cheeks and gums eaten away, their teeth rotten, they are made miserable, made simpletons for their lifetime, and laid in a premature grave! And all this by your sheet-anchor **mercury.** Behold! a strong man, has taken cold and is attacked by chills, weakness, etc. It goes the **mercury** in large doses — 12 blue pills a day — he sinks, of course, and this strong healthy man dies in a few days, and when you, the "rational" doctors are asked of what disease; why you put on the most serious faces in the world and say with dignity' "died of sinking chills." Do you say this is not true; such cases do not happen? Do you wish me to state facts". In In cases of rheumatism where **mercury** has been given to salivation the rheumatism seems to yield and for a while the patient is free from pain, but go and see him again in a few weeks or months, pains come at night in the extremities accompanied by sweat; he becomes weaker and weaker; medicines afford no relief except large doses of opium emaciation and debility set in, and finally an organic injury takes place and the scene is soon closed by death; and the doctor's certificate reads, "died of consumption."

(*A common side effect of mercury treatment is the production of large amounts of saliva.)

Source: ***Letter To The Allopathic Doctors of Dayton*** **by Dr. H. Wigand**
(Dr. Wigand abandoned allopathy to specialize in herbal medical treatments. Today he would be considered a naturopath. Naturopathy is based, in part, on the principles of healing the body through detoxification of poisons using natural substances. These principles of treating mercury poisoning actually go back to the 1500's when mercury came into use to treat syphilis and later all manner of other diseases.)

1893 - Chicago Dental Professor Links Chronic Illness to Mercury Fillings

"It is claimed by many physicians of both the leading schools (Allopathy and Homeopathy), but more particularly by those of the Homeopathic school, that the indicated remedy given for any diseased condition of the vital force very often fails in its curative effect, when there is apparently no good reason to view for it so doing. An examination of the mouth reveals the presence of one or more amalgam **(mercury)** fillings in the teeth. The physician at once instructs the patient to go to the dentist and have the fillings removed. The patient obeys in spite of the dentist's assurance that it is all bosh, humbug or nonsense to rely on such advice. What is the result of their removal? Chronic diseases which have hitherto failed to yield to treatment begin at once to respond more quickly and permanently to the medicine; the patient is quick to perceive the improvement of his general health; and the action of each new drug which is prescribed as the character of the symptoms change, advances the patient steadily on to renewed health instead of having but a temporary effect for the better, only to allow the patient to slide back again to where he originally was, as it the case before the amalgams (**mercury fillings**) were removed.

The fact that I have many patients sent to me with instructions from the physician to remove all amalgam fillings found in the mouth, and the rapid improvement which I have noticed has taken place in the condition of every patient who has had such fillings removed at my hands, has made me reflect very seriously, not only upon the injurious effect of amalgam fillings and the almost untold number which I have been guilty of inserting during the first six years of my practice, but has led to the almost total abandonment of amalgams of every kind in my practice."

Source: ***Medical Advance*** **by Charles H. Taft, A.B., M.D. Professor of Dental Surgery and Therapeutics Hering (Homeopathic) Medical College, Chicago.**
(At the time, homeopathy was the second largest medical sect in the U.S. and the principle group which condemned the use of mercury in medicine.)

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CONGRESSIONAL HEARING ON MERCURY IN MEDICINE
Congressional Committee on Government Reform; July 18, 2000.

The Hon. Henry Waxman
Committee on Government Reform
2157 Rayburn House Office Building
Washington, DC 20515

GOVERNMENT REGULATION OF DENTAL AMALGAM

The Issues: Both sides agree that dental amalgam releases mercury over the entire lifetime of the dental restoration. Toxicologists have known the threshold for neurological effects of chronic low-level human mercury exposure for several years.[1] The issue is now whether (A) the risk is such that dentists should be informed of the risk, (B) patients should have an opportunity to give informed consent, and (C) whether dental trade organizations have sufficient will - and dental licensing boards have sufficient toxicological competence - to adequately deal with the matter, or whether outside governmental regulation is required.

The Size and Certainty of the Risk Even though the toxic effects of dental amalgam are neurological and thus "non-specific," i.e. they are difficult to separate from effects caused by other toxic sources, it is well established that:

(A) a large fraction of the general population, including sensitive segments, such as pregnant women and children, are life-long exposed to mercury levels that exceed the threshold at which neurological effects have been determined in occupational populations,

(B) mercury exposure levels from dental amalgam greatly exceed those from any other source of non-consensual mercury exposure

(C) dental amalgam releases mercury 24 hrs/day. Over its entire lifetime, and cannot be avoided during sleep, vacation, illness or any other period.

(D) mercury accumulates in the human brain, and

(E) contrary to earlier belief, mercury has no pharmacological benefit.

Why Self-Regulation Does Not Work: The two primary reason are that

(A) those who are most affected by the dispute, i.e. clinical dentists and their patients, only hear partisan hype, but lack access to scientific facts, because

(1) the toxic effects of mercury are experienced in areas of the body that are outside of the area which dentists treat,

(2) dentists in clinical practice (i.e. those who use the material and those who determine its

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[1] IRIS, Integrated Risk Information System, U.S. Environmental Protection Agency, June 1, 1995. Available on Internetsite: <http://www.epa.gov/ngispgm3/iris/subst/0370.htm>

suitability on regulatory boards) have no toxic training,[2] and are not better qualified to determine the toxicity of mercury than toxicologists are qualified to determine whether dental restorations are well placed, and

(B) Proponents on both side have muddled issues.

(1) The professional trade organization for dentists, and the dental products industry are governed by archaic traditions that perpetuate pre-scientific dental practice. Litigation by the FTC has shown that professional dental organizations are autocratic groups.[3] This leadership jealously limits access to ANSI and other material standardization to dentists.

(2) Some dentists have used the controversy over amalgam to recommend unproven or even dangerous alternative procedures for purely remunerative purposes, and

(3) State licensing boards lack the toxicological competence to determine toxicological issues. Many boards have severely disciplined dentists who have questioned the safety of amalgam for lack of loyalty to tradition; or have lumped them together with quacks and others who practice unproven remunerative procedures.

(4) Dentists and most other health care providers, including the majority of M.D.s, lack even a rudimentary training, knowledge, and understanding of toxicology. Furthermore, the judgment of practitioner is influenced by remunerative considerations (Amalgam is by the cheapest dental material, and is quick and easy to apply).

Toxicological Background Facts:

Exposure levels: A federal interregulatory toxicology panel determined that dental amalgam releases elemental mercury over the entire lifetime of the dental restoration, and that a patient with 7-10 dental amalgam fillings experiences an average daily elemental mercury vapor dose of 1-5 µg/day.[4]

This compares with a value of 0.28 µg/day for what the federal government currently considers the upper limit of the daily human exposure level that is likely to be without an appreciable risk. Accordingly, the daily exposure for such a person is 3 to 20 times higher than the safe mercury level. The primary target organs for mercury are the brain and the kidney. The exposure of dental professionals depends on their practices, but may be even larger than that of patients. Thus, coroners have persistently found accumulations of mercury in the brains of Swedish dentists.

1. Dietary Mercury Exposure:

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[2] The main argument used by the American Dental Association for the continued use is the so-called "test of time," and the claim that no epidemiological study has proved amalgam to be unsafe for general use. See e.g. "Dental Amalgam: 150 years of Safety and Effectiveness," and "Frequently Asked Questions (Internet Site of the American Dental Association, located at http://www.ada.org/ newsrel/1195/nr-02a.html. The Canadian Dental Association shares this view. Foreign dental associations are split. Some State licencing boards have disciplined dentists who have questioned the safety of amalgam. This is the same incorrect argument that had been used for many years to claim that cigarette smoking, formaldehyde and phenol were safe.

[3] See e.g. California Dental Association v. FTC, Pet. No 96-70409 (9th Cir, Oct. 22, 1997; Pet. No 97-1625 (U.S. May 24, 1999) (cite as 1999 WL 320796) in which the U.S. Supreme Court found that the FTC has jurisdiction over the California Dental Association, and remanded the question whether the CDA's Ethical Code provisions against advertisement violated antitrust laws to the 9th Circuit.

[4] 1 g = 1,000 mg (milligrams) = 1,000,000 µg (micrograms) = 1,000,000,000 ng (nanograms). Or: 1 ng = 0.001 µg = 0.000,001 mg

Food and Drug Administration: FDA estimates that the average daily intake for total mercury is between 50 - 100 ng/kg day.[5]

2. Dental Mercury Exposure: Mercury release rate: 1 - 5 µg/day as elemental mercury. Committee to Coordinate Environmental Health and Related Programs. [Peer reviewed value by federal interagency committee] (CCEHRP).[6]

3. **U.S. Regulatory Exposure Limits for Mercury:**

(a) Procedures used by federal agencies: In a nucleus, regulatory agencies appoint expert panels or use the National Academy to appoint expert panels, then review proposed regulation internally, review it through interagency regulatory liaison committees and through outside committees; if formal regulation seems to be warranted, agencies follow the procedures mandated by the Administrative Procedure Act (APA) which provides for publication of an Advanced Notice of Proposed Rule Making (ANPR) in the Federal Register, a public comment period, publication of comments, published response to public comments, revision of proposed rule by implementation of comments, followed by re-iterative public comment - revision cycles which may take 5-10 years. Once a regulation is implemented, it is subject to periodic review under the APA which requires public notice. Federal Regulatory agencies are required to harmonize toxic regulation among the various agencies. Thus, OSHA standards must be consistent with EPA standards, which means that OSHA values which are for 40hr/wk exposure for healthy workers must be consistent with EPA values for 168hr/wk exposure of [virtually] all population segments, including pregnant women and most infirm people.

(b) Status of Regulation:

Food and Drug Administration Early efforts by the FDA to regulate dental amalgam as a dental device have been thwarted by the dental products trade association.[7] The FDA has a maximum contaminant level goal, MCLG = 2 µg/L for bottled water (FDA[8]). This is the same as the EPA level for drinking water.

Agency for Toxic Substances and Disease Registry (ATSDR)[9] Federal law requires the ATSDR

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[5] Gunderson, E.L. FDA total diet study, April 1982- April 1984, Dietary intakes of pesticides, selected elements and other chemicals, J. Ass. Off. Anal. Chemists. 71(6);1200-1209 (1988).

[6] National Institute of Health [NIH], Dental Amalgam: A Scientific Review and Recommended Public Health Service Strategy for Research, Education and Regulation, Final Report of the Subcommittee on Risk Management of the Committee to Coordinate Environmental Health and Related Programs, Public Health Service, January 15, 1993, page III-29. Virtually all authors of this study are dentists, not toxicologists.

[7] FDA, proposed rules, medical devices; classification of dental mercury. 21 CFR Part 872; F.R. 45: 86033 (1980); FDA Rules and Regulations; Dental Devices; 21 CFR Part 872. F. R. 52:30082 (1987)

[8] FDA. Proposed standard for bottled water. 21 CFR 103; Fed. Reg. 58: 381; 1993.

[9] ATSDR, Agency for Toxic Substances and Disease Registry, Toxicological Profile for Mercury (Update May 1994), HHS, PHS, ATSDR, No TP-93-10; NTIS Document No PB95-100194, pages 20, 125, 355, Exh. A6.

to prepare toxicological profiles for hazardous substance and establish priority lists under the Superfund Amendments and Reauthorization Act (SARA); the guidelines under which the profiles are prepared were published in the Federal Register of April 17, 1987. Profiles are periodically updated.

LOAEL,[10], Hand tremors are observed at 0.025 mg/m^3 ; autonomic dysfunction starts at 0.009 mg/m^3 based on impaired performance on neurobehavioral tests, Ngim (1992).[11] (See ftn.1, IRIS, p.3)

MRL (chronic inhalation)[12]: 0.014 µg/m^3 (Fawer 1983). [agency calculation based on data of federal interagency peer review panel] The MRL for chronic inhalation is 0.014 µg/m^3, corresponding to a daily dose of 0.28µg/day; the acute MRL is 0.02µg/m3 which corresponds to a daily dose of 0.4µg/day. The proposed MRL is 0.4 µg/day, based on a rounded inhalation value of 0.02 µg/m^3

OSHA: 8-hr time weighted average (TWA) limit: 50 µg/m^3, based on epidemiological studies (clinical observation of tremors and vasomotor disturbances in the range from 60 to 720 µg/m^3: NIOSH[13]; OSHA[14]). [Final agency regulation resulting from full public review pursuant to Administrative Procedure Act] At an inhalation rate of 10 m^3/work-day and time averaging over a seven day week, the daily mercury intake is:

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[10] LOAEL = Lowest Observed Adverse Effect Level. For an explanation how the procedure by which the U.S. Government evaluates the safety/risk of chemicals see: EPA. Draft report. Principles of neurotoxic risk assessment. Fed.Reg. 58:41556-41599; 1993. EPA. Rfd-uncertainty factors: Fed.Reg. 56:1532; 1991. EPA. Interim Methods for development of inhalation reference concentrations. Office of Research and Development; Office of Health and Environmental Assessment. Triangle Park; NC: Environmental Criteria and Assessment Office Research EPA/600/8-90/066a; 1990. EPA. Methodology for determination of lifetime dose, Rfd. Washington, DC: U.S. EPA 600/8-066F; 1989. EPA. EPA criteria document for water standard; Washington, DC: ECAO-CIN-025; February 1987. EPA. Peer Review Workshop on Mercury Issues, Summary Report; Washington, DC: October 26-27; 1987. EPA. An exposure and risk assessment for mercury; Washington, DC: EPA-440/4-85-011; 1981.

[11] Ngim, C.H., Foo, S.C., Phoon, W.O. Chronic neurobehavioural effects of elemental mercury in dentists Brit. J. Ind. Med. 49(11):782-790 (1992)

[12] MRL (Minimal Risk Level for Mercury: An estimate of daily human exposure to a dose of a chemical that is likely to be without an appreciable risk or adverse non-cancerous effects over a specified duration of exposure. MRLs are derived using a modified version of the risk assessment methodology used by the EPA to derive reference doses (RFDs) for lifetime exposure. To derive an MRL ATSDR selects the end point which, in its best judgment, represents the most sensitive human health effect for a given exposure route and duration)

[13] NIOSH (1973): Criteria for a recommended standard: Occupational exposure to inorganic mercury. HSM 73-11024; GPO No. 017-033-00022; Washington, D.C. U.S. Department of Health, Education, and Welfare; 1973.

[14] OSHA. Safety factors; Fed.Reg. 57:26048; 1992. OSHA; Mercury (aryl and inorganic compounds). 29 CFR 1910.100 Table Z-1-A; Fed. Reg. 54(12):2414; 1989. OSHA; Risk Communication. Material Safety Data Sheets, 29 CFR §1900.1000; Department of Labor. Washington, DC; 1976.

$50\mu g/m^3 \times 10\ m^3$ (5 days/7 days) = 380 µg/day

U.S. EPA: Continuous exposure: R_{fd} [15] = 0.3 $\mu g/m^3$, based on onset of subclinical hand tremor, increase in memory disturbances, and slight evidence of subjective and objective evidence of autonomic dysfunction, observed at 25 $\mu g/m^3$ in the occupational studies of Fawer[16] and Piikivi.[17] Calculated as follows:

$LOEL = 0.025 mg/m^3 (5d/7d)(10\ m^3/20\ m^3 = 9\ \mu g/m^3$

Scale factor of 10 to protect sensitive individuals, not found in the work force, and a factor of 3 for lack of reproductive studies, one obtains the current reference dose = R_{fd} = 0.3 $\mu g/m^3$.

Assuming that an average sedentary person would inhale 20 m^3 air per day, the acceptable daily intake (adi) is 20 x R_{fd} = 6 µg/day.

Drinking Water: R_{fc} (body weight of 70 kg; average water consumption of 2 L/day. The maximum contaminant level goal, MCLG = 2 µg/L (EPA[18]).

Consumer Product Safety Commission (CPSC): Uses "Acceptable Risk" (for neurotoxins = 10^{-6}) estimated by dividing the LOEL by a safety factor of hundred (CPSC[19], see also EPA[20]). Using observed clinical effects (OSHA): a.r. = 5 µg/day; Using observed subclinical LOEL of 25 $\mu g/m^3$ (EPA): a.r. = 2.5 µg/day. [Proposed regulation]

CONCLUSIONS

1. The use of dental amalgam in dental restorations is an unsafe and archaic practice.
2. The use of amalgam restorations in the teeth of patients, contrasts sharply with the progress in the safety of the dental workplace that has been achieved in recent years by OSHA on a federal and state level.
3. The question whether amalgam is safe or not, is in the province of toxicologists, material scientists and chemists. Dentists and their trade associations lack the education, training and skills, i.e. the competence and qualifications to determine the toxicological effects of amalgam on the human kidney, brain and other target organs.
4. Short-term Corrective Action: (a) The FDA should revive proposed regulation of dental

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[15] R_{fd} = Reference Dose; R_{fc} = Inhalation reference concentration = 3-4 mg/m^3 for chronic exposure.

[16] Fawer, R.F.; DeRibaupiere, Y.; Guillemin, M. Measurement of hand tremor induced by industrial exposure to metallic mercury. Brit. J. Ind. Med. 40:204; 1983.

[17] Piikivi, L.; Tolonen, U. EEG findings in chlor-alkali workers subjected to low long term exposure to mercury vapour. Brit. J. Ind. Med. 46:370; 1989, and Liang, Y-X, et al. Psychological effects of lowe exposure to mercury vapor. Application of a computer aided evaluation system of neurological behavior. Environmental Research, 60, 320 (1993).

[18] EPA. Rfd-uncertainty factors: Fed.Reg. 56:1532; 1991; EPA Nat. Primary Drinking Water Regulation. Fed.Reg. 56:3526; 1991.

[19] CPSC (Consumer Product Safety Commission). Regulation concerning artist's materials - supplemental definition of chronic toxicity: 14 CFR 1500.3(c)(2)(ii); Fed.Reg. 57:46656; 1992.

[20] EPA. Final report. Principles of neurotoxic risk assessment. Fed.Reg. 58:41556 (1993), 59:47880 (1994)

amalgam as a dental device, an effort that failed in 1980 (ftn. 7), because the scientific evidence was insufficient at that time.
(b) Congress should initiate an interregulatory, interdisciplinary audit of the safety standards and procedures in the dental industry and profession, and the professional qualifications of those that serve on dental product and device standardization committees.

5. Long Term Action: (a) The development of effective regulation depends on coordination between federal agencies and state licensing agencies. It further depends on interdisciplinary coordination between dentists, material scientists and toxicologists in the triangle between academe, government, and industry.
(b) Medical and dental practitioners should be made aware that they cannot solely rely on FDA and their trade associations to provide them with safe materials. They need to be encouraged to use their right to questions the safety of the products that they use.
(c) State licensing boards and their federation need more interregulatory technical and legal support and guidance, and
(d) the National Institute of Dentistry needs better interdisciplinary ties.

Subj: my story
Date: Sun, 16 Jul 2000 12:39:12 PM Eastern Daylight Time
From: Nastasyal
To: CGRStories
Here Freya, good luck, I send a million positive vibes your way. I also

called cspan last week and left a message.
Nastasya

I will do anything and everything to get Mercury properly banned now.

July'2000

Committee on Government Reform

Dear Senator Burton:

Subj: **My story**
I'm 31, and have had psoriasis since I was quite young. It's not as bad anymore as it has been in the past, but it's still there and on my face a bit. Not enough to scare people though.

Well I belong to a list about psoriasis, and had seen on there that Mercury fillings could be the reason why psoriasis has afflicted me. I thought about it and tried to remember when I first got psoriasis, and the only thing in my life that had changed was that I had gotten a few silver fillings. I was the age that your baby teeth have already fallen out. So this started to make sense to me.

Through my teen years I had gotten three root canals, one which was done badly had to be redone. And when reflecting back, I realized after those were done when I started to have the worst menses ever. Several times I ended up in the hospital screaming in pain and unable to stop vomiting. Of course drs. just would say it was dysmenorrhea and send me home. They tried to put me on the pill, but I would throw up everyday on that. Some were bad some were ok, but never easy.

Recently at my job, I had finally got dental benefits for the first time in my life. I knew I needed dental work done badly as I two of the three root canals had only temp crowns and they both broke. One cracked all the way up in the root. My boss recommended a dentist and I started to go in April of this year. I need gum surgery on the really broken tooth so that the crown will stay. The first visit they put in a couple of white fillings that I needed, and

(2) Natasha

the next they extracted one of my wisdom teeth that was in need of a root canal so they said to chuck it.

Then I had a week where I could get in there like every other day, so they cleaned that broken one out and prepped it for a crown as much as they could. The next visit they filled a wisdom tooth that could stay with white stuff by my request, and two teeth next to it had cracked silver fillings so they went in and replaced them with white fillings. During this process, I began to feel the drill, so they had to numb me up more, which gave me this horrible sensation of heat and a bit of panic. But after five minutes or so I calmed down. So they finished up.

Two days later, I got my period and ended up in the hospital again because I was dehydrated from all the vomiting. When I was released, I didn't feel quite right, but at least the pain was gone and I could keep water down. I hadn't had a period like that in a few years. The day after I felt exhausted and just lay around. The day after that I felt ok. But the next day my whole life went berserk.

I had just come back from lunch at work when my heart started racing and my vision got strange. I felt awful. I couldn't concentrate. I then took a vitamin b complex and felt a hot flash after that. But my symptoms did not go away. I felt like I had to get out of there so I went home and called to make an appt. with my general practioner. It was Monday and I couldn't get in there until Wednsday. I felt awful. First I thought it was withdrawal, because I had been trying to quit smoking with Wellbutrin, and had stop taking the drug a few days before as it wasn't working out. But taking one didn't help. The next day I went somewhere with my sister, still foggy but no hear thing, and while we were out my heart started again and I felt like I had to get out of there.

The day of going to the GP I was miserable and my heart was bonkers. When I got there they thought I was having a heart attack and immediately did some tests, and a blood test. The gp asked if I was under any excessive stress. Well I was, but I have always been. That Monday when it had all started, I had to rat out a coworker, but that normally does not scare me. But the doctor said I had anxiety and gave me Ativan. I believed her and took the stuff and it knocked me out. But I didn't feel any better, the vision thing was horrific. You know how you can just stare into space? I couldn't. I couldn't keep my eyes anywhere longer than a few seconds without feeling panicky.

I used up all my sick days and made myself go to work, but I still had trouble with my eyes. The doctor said I was agorophobic and gave me cellexa (prozac) and that made me sick instantly. She didn't believe me. I only took the ativan if my heart raced but that didn't happen as much after a week. The second week I thought maybe it was the antibiotics I took everytime I went to the dentist cuz I have a heart murmur, so I took some acidophilus, and I felt a little better but the eye thing and concentration
did not improve.

(3) Natasha

The third week (well into May) I took some allergy pills and felt a great deal better, I could stare into space (lucky me) but still the vision/concentration not much better. So I thought it was allergies. Went and got tested, they found nothing. And of course recommended therapy, as did the GP. So I started therapy, she doesn't think I'm depressed or too anxious and told me to switch GP's which I did.

At the end of May, I went back to the dentist to have another tooth prepped for a crown. I didn't get a shot, and only took half the antibiotics and took acidophilus. That weekend I had another attack so to speak. Then I knew it had to be dental related, as they had taken out more mercury.

So I looked it up on the net and found that none of the precautions were taken that dentists should do when removing that stuff. No dental dam, nothing .I fit all the symptoms that I saw on some sites. I went to my new GP that my chiropractor recommended as she said he was east/west and would be more open-minded. He is unfamiliar with Mercury poisoning. I told him I thought it was that. He didn't deny it, but said we should get a hair test, but they couldn't in New York City because they were illegal. He aid he would find somewhere in New Jersey for me. And also recommended that I see this neurologist just in case. That was last week, oh first though he treated me for a sinus infection and gave me some Chinese herbs, just to make sure it wasn't that. It wasn't. My vision/concentration is still screwy. And he hasn't called me back about the test or neurologist (probably gone for the holiday). Since last week I have joined a few lists. I keep getting mail that wants to squeeze me of every dime I don't have.

I'm broke, and owe money. I have been taking C and zinc, then separate from those I take the E and selenium and haven't really seen any improvement, although it's only been six days. I'm starting to get depressed for real now.

My vision is like looking through that thing they put in front of you at the eye doctors when checking your site. Like I'm on the outside looking at another dimension, with a bit of blur around the edges. If I don't try hard I loose focus on anything and this exhausts me.

Music is my life and it isn't the same. I don't feel like me and it's not a mental problem. This whack stuff is 24/7. I feel like I don't really feel. I'd give anything to be back to how I was before.

I still have other mercury fillings in my mouth. I have stopped all appointments with my dentist and really don't know where to go from here.

All the stuff I read about chelation is contradictory, and the one place that I saw that offered it here wants $225.00 just for a consultation. I don't know what to do. I totally feel like my life is on hold, I can't hang with my friends, and it's all revolving around vitamins and doctors and disappointment. I'm slowly losing hope and that's bad. In edition to all the above, I also went to an opthamologist, who found nothing and just had an MRI, no results yet.

Through all this BS with the mercury, my parents have been well supportive, my father is on his death bed (he has mercury fillings but his mouth and body are so mangled a dentist can't even get

(4) Natasha

into his mouth). My mom has never been in the best of health that I can remember either and she has root canals and fillings as well. We talked about all this removal done carelessly and she told me how myGrandpa and his wife got dental work just before he died. I was my Grandpa's favorite, he died a year and a half ago, and I remember everytime he smiled I could see a variety of silver and gold. He had heard of mercury removal and my guess now is his dental work included getting them removed as cheaply as possible which means there were no precautions taken.

Within a week after the dentist he went berserk and went to the neighbor's house and broke their windows. He was taken to the hospital and they decided he needed an operation on his thyroid. At the same time his wife out of nowhere was diagnosed with Alzheimers. They were put in a really nice retirement home/apt complex afterwards. My mom said my Grandpa didn't look good so I went to Florida to say goodbye. He was barely there, he could do nothing but lay in bed flailing around in discomfort. I got him to look me in the eye and I know he recognized me, but that was all that could be done at that point.

If I had only known then what I know now. My step-grandma is still there at the complex, but she is totally out of it. She didn't even know who my grandpa was and she kept saying she was going to escape. He was totally fine for someone in their early 80's until he went to the dentist. It is so awful knowing the state of his mind because I have it now too.

I will do anything and everything to get Mercury properly banned now.

Nastasya

Mary Ann Newell
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Vancouver, WA 98663-1015
Phone Number - 360-694-5770
Fax Number - 360-694-5770
E-mail address - BULLELKMAN@aol.com

November 9, 1999

Congressman Dan Burton
2157 Rayburn HOB
Washington DC 20515

Dear Congressman Burton:

I am one of thousands of citizens of the United States of America that know that amalgam/mercury fillings cause many health issues. I know because I have mercury poisoning and mercury fillings caused my health problems. I know that this information needs to be shared with all Americans. I want to share my medical/health history with all of you to include some of my tests. The tests that I will be presenting with my history are my hair tests and urine test results. I know that this committee is aware that these tests are ATSDR accepted medical tests for mercury toxicity.

I also want to thank U. S. Department of Health and Human Services for the Agency for Toxic Substances and Disease Registry April 1999 fact sheet on Mercury CAS # 7439-97-6. I felt the HIGHLIGHTS of this report to be very IMPORTANT for all Americans. I was thrilled to read the HIGHLIGHTS: "Exposure to mercury occurs from breathing contaminated air, ingesting contaminated water and food and having dental and medical treatment. Mercury, at high levels, may damage the brain, kidneys, and developing fetus. This chemical has been found in at least 714 of 1,467 National Priorities List sites identified by the Environmental Protection Agency."

My favorite question on the ATSDR's Mercury fact sheet is "How might I be exposed to mercury?" Two out of five of the answers are my favorites. One of them is "Release of mercury from dental work and medical treatment." The other one is " Breathing contaminated workplace air or skin contact during use in the workplace (dental, health services, chemical, and other industries that use mercury)."

I look forward to sharing with any or all members of the Committee on my medical history and tests. Please feel free to call.

Thank you,

Mary Ann Newell

Medical History of Mary Ann Newell

NAME: Mary Ann Newell

Age: 47 years old

SEX: Female

RACE: White

ADDRESS: 1400 NW 63rd Street
Vancouver, WA 98663-1015

PHONE/FAX: 360-694-5770

E-mail:BULLELKMAN@aol.com

My symptoms in August 1995:
Excessive saliva
Teeth hurt
Throat hurts, a) itchy throat b) Hard to shallow c) My windpipe feels very small
Gums hurt a) Gums recessed
Bad Breathe
Constant cold sores - painful
My right side of my face hurt when I slept on it
Metallic taste in mouth constantly
Sore tongue always
Mild Rash on chin
Chemical Sensitivity
Restless legs
Dry skin
Chapped lips
Cold feet

My symptoms in November 1999
Cool feet not cold
I am still having problems with my saliva gland but I don't have excessive saliva. That symptom went away after all my mercury fillings were removed

STATEMENT: My tests proved that I had mercury poisoning and most of my symptoms disappeared after I removed my mercury fillings. The other symptoms disappeared after removing the mercury from my body with DMPS which is now allowed by FDA as a chelating agent for removing mercury from the body.

Timeline when my symptoms went away
9/3/96 -after all my mercury fillings were removed - Excessive saliva
9/3/96 after all my mercury fillings were removed - Teeth hurt -
9/3/96 after all my mercury fillings were removed - Throat hurts, a) itchy throat b) Hard to shallow c) My windpipe feels very small
9/3/96 after all my mercury fillings were removed - Gums hurt

9/3/96 after all my mercury fillings were removed - Bad Breathe
Gums recessed - same but not worse
Constant cold sores - painful- stopped on 9/3/96 after all my mercury fillings were removed
On 8/9/96 was the first time in over 8 months that I woke up on my right side. This was the next morning after my first bottom right 2 gold crowns and fillings removed.
9/3/96 after all my mercury fillings were removed. Metallic taste in mouth gone!!- (now I have a wonderful after taste when I eat a Mrs. Field's cookie)
5/15/97 - my constant sore tongue got great relief after right side wisdom teeth removed and total relief after left side wisdom teeth removed on 1/12/98 my tongue stopped hurting. .
Improved over time with chelation - Chemical Sensitivity
Improved over time with chelation - Mild Rash on chin
Improved over time with chelation - Restless legs
Improved over time with chelation Dry skin
Improved over time with chelation Chapped lips
Improved over time with chelation Cold feet
My medical history to include dates/doctors' name & numbers/History

Date	Doctor's Name/Number	History
3/1995	Dr. Dong (family dentist since 1960) 503-283-3519	Got a new gold crown - dentist never used rubber dam (For your information - My new dentist found a huge amalgam on 8/8/96 under my gold crown)
Around June 1996		Strange test in mouth for last month or so. I called Dr. Dong (family dentist since 1960) who informed me to get to a medical doctor
8/31/95	Dr. Baker(GP from Family Physicians Group, Inc.) 360-694-7525	Appt with Dr. Baker for check up and blood test
10/12/95	Dr. Dong (family dentist since 1960) 503-283-3519	Appt with Dr Dong (Dentist) - checked month - everything ok but gum have recessed
10/16/96		Blood test for thyroid - everything OK
10/19/95	Dr. Brady Allergy doctor 360-254-6844	Appt with Dr. Brady for allergy tests for foods
10/25/95		Received letter and report that Food tests results are within acceptable normal range
11/7/95	Dr. Meyers ENT 360-254-7725	Appt with Dr. Meyers, he thought I had night heartburn - he recommended the following: a) No eating or drinking - 4 hours before bed b) Antacid before bed - Maalox c) Avoid fats, chocolate and alcohol (Dr. Brady recommended Dr. Meyers)
11/22/95	Dr. Cooper (GP from Family Physicians	Appt with Dr. Cooper - First day for Pepcid 20mg - results - NO relief - NO comfort - MISERABLE for 8 days.

Medical History from Mary Ann Newell

	Group, Inc.) 360-694-7525	
11/29/95		Call from Dr. Cooper suggested zinc
11/30/95		Appt with Dr. Cooper - Did not take pepacid today but started zinc. Started *Prilosec /given a two week supply/ Medical student with pharmacy degree said the pill should see change 4 to 5 days.
12/1/95		Got mouth guard today
12/5/95	Dr. Daugherty 503-646-0697	Appt with Dr. Daughtey - Portland Naturopathic Clinic - 5:45pm Gave me lymph spleen mammary drops 3x a day
12/19/95		Appt with Dr. Daugherty - Small intenstine drops, inflavonoid and paratid pmg (for recessed gums)
1/2/96		Appt with Dr. D. clinic - Cal-Amo for acid/stopped using toothpaste and now use baking soda
1/3/96		Tooth really hurt - acidy taste
1/4/96		Appt with Dr. D. went to Dr. Dr's Beaverton's office and tested for food, sensitive to tomato, wheat, gluten, filbertnut, milk, cheeses, cloves. New medicine - Crusticum horrse cough - 6 at night and phosfood liquid 3x a day.
1/8/96	Dr. Susan Hansen (Internal Medicince OHSU) 503-494-3948	3:45pm - Appt with Dr. Susan Hansen - examine and tested for strep throat
1/10/96		Last day on naturopathic medicine
1/10/96		Dr. Hansen called and said that I test for strep with a 4+ We'll start to treat throat tomorrow. After Dr. Hansen checks into anti-bodies because of my sensitivity. She was surprised about the 4+ and said so three times. She will try to talk to an Ear Nose and Throat (ENT) Doctor.
1/24/96	Dr. Dale (Dentist at OHSU - Dental School) 503-494-8875	Appt with Dr. Dale - Checked month and gum from 1:30pm to 4:15pm. Gave me Rx for Perigard to take for 4 days
1/29/96		X-rays from student
1/30/96		Dr. Dale called and said everything looks okay. He will call Dr. Hansen
2/6/96	Dr. Kingsmen (GI) from OHSU 503-494-6813	12:45pm - Appt with Dr. Kingsmen, GI, She thought it did not sound like my problem but will do a 24 hour study
2/6/96	Dr. Hansen	Dr. Hansen did a throat culture
2/13/96		9am - 24 hour PH Balance Test - I did not go to work today
2/14/96		Remove tubes
2/18/96		Started Mycelx 7 today
2/23/96		Dr. Hansen - throat culture - she will call with results and 24 PH test results
2/27/96		Dr. Hansen called and I still have strep . She did not hear from Dr.

Medical History from Mary Ann Newell

		Kingsman. She will call an ENT on Monday and forward my medical info to him.
2/28/96		Dr. Hansen left voice mail message that my 24 PH test was normal and okay
2/29/96	Dr. Peter Andersen (ENT at	Appt with Dr. Andersen at 12:45pm, Tubes up my nose and down my throat. Adult size adnoes, no polyps - everything appeared okay and no problem.
2/29/96		Started Veetids - 2x a day
3/6/96 or 3/7/96		Lots of drainage in throat at night
3/9/96		Big wad of something down my throat
3/14/96 3/14/96		CT sinus screen - Dr. Andersen - SAD everything is OKAY and GOOD. Did strep throat test for me. He checked my throat will tubes up my nose again. Dr. Andersen said that I need to go to a Neurologist and He will call Dr. Hansen. Last day for medicince
4/1/96	Dr. Gajanan Nilaver (Neurolgoist at OHSU) 503-494-5035	9am appt with Dr. Nilaver. Did a lot of motor skill tests. Touched face and showed numbness on 2 out of 3 places on my face. He thought possibility of the nerve on face damaged but very rare and he told me not to get to hopeful. It was very rare and hard to find.
4/1/96		MRI -3:30pm about an hour - focused on nerve on face with and without dye.
4/1/96		Lung exam
4/1/96		Dr. Nilaver prescribed Tegretol
4/2/96		Dr. Nilaver called and left voice mail and said everything perfect. Results were good and he was glad everything is fine. I did talk to him and he wanted me to continue medicine in case nerve is damaged. He wants me to call on 4/10 with report.
4/3/96		My tongue starting feeling better today but tooth still hurts
4/6/96		Tongue still feels good but lots of saliva and tooth hurts
4/10/96		Tongue, tooth and gums feel good
4/11/96		Tongue started hurting again and tooth and gum hurts, too
4/12/96		Problems back - sore tongue, tooth and gums hurt
4/23/96		Talked to Dr. Nilaver - continue on medicine.
5/1/96		Left 3 voice mail message for Dr. Hansen - She had to talk to other doctors - she prescribed RIFADIN for 4 days 2x a day. Medicine for TB
5/13/96		Talked to Dr. Nilaver - ween off Tergotold and Start Baclofen - 3x a day (half of pill) ween off Tegretol - (mon, tues, wed, 2x a day) and 1 a day for 3 days.
5/21/96		Increase Baclofen to 2 for 3 days and increase to 3 starting 5/24
5/29/96		Increase Baclofen (5/29,5/30, 5/31) for 3 days and increase to 4 for 4 days
6/6/96		Reduce Baclofen per doctor's instructions - 3 for 2 days, 2 for 2 days and 1/2 for 2 days.
6/17/96		Appt with Dr. Andersen at 10am - Everything looks perfect. Dick informed him that we were going to remove my fillings because my mouth hurt. He went ballistic and said it was to expensive and Dick told

Medical History from Mary Ann Newell

		him it was our money and he commented again and Dick again told him it was our money. He promises to call after talking to Dr. Hansen and Dr. Nilaver to coordinate work on removing teeth and he took throat culture
6/18/96		Dr. Andersen called and said no strep and he told me that Dr. Hansen would be calling me about taking some medicine for compulsive behavior. Dick and I decided for me NOT to take any medicine to mask my symptoms. Dr. Hansen called and I took her that I did not want to take medicine to mask my symptoms because they are REAL. I informed Dr. Hansen that I would go on vacation and relax and see if my symptoms are stress-related.
6/18/96	Dr. Keith Collins DMD 360-574-7477	Appt Dr. Keith Collins at 2pm - He would remove mercury but does not believe in mercury poisoning. He thinks I should see an oral pathologist - He gave names at OHSU. While I was in Alaska - I called Dr. Collins for helping in seeing an Oral pathologist at WSU but he never called me. I called his office at least three times.
7/9/96	Dr Gene George Hung M.D. Acupuncture 503-231-1212	Appt with Dr. Hung at 3pm - He wants to work on my immune system He would like about 5 times to work on my system. First appt about 16 pins
7/11/96		Second appt - about 20 pins
7/15/96		Third Appt - Talked to Dr. Hung about doing the mercury first and then acupuncture - He said to check with Dr. Schaub about the process
7/16/96		Received a call from Dr. Schaub's office that said Dr. Schaub says the mercury needs to be removed before doing acupuncture. With mercury in mouth, I can give only temporary relief.
7/16/96	Dr. Schaub 360-253-4445	Appt with Dr. Schaub at 3pm a) Thinks I have oral galvanism b) Went to St. Joe's for Venous(NOT arterial) blood gas for OXYHEMOGLOBIN Saturation CO-Oximeter is OK. Pulse Oximeter is NOT acceptable.- results in about 48 hours c) Hair test - about 3 weeks for results d) Started Heavy Metal 24 hour urine collection test at 3pm
7/17/96		Took Heavy metal urine test to clinic
7/22/96	Dr. Larry Stryker DDS. PS. (360)254-6411	Appt with Larry at 5pm 1) Meet with Jill Stryker at 4:30 to share/get/give information to her 2) Larry suggested that I see Oral Pathologist - Dr. Dave Downey D.M.D. (Same Oral Pathologist that Dr. Anderson had said the OSHU Oral Pathologist had recommended) Visit to Dr. Downey to check tongue
7/23/96	Dr. Dave Downey D.M.D. (503)629-5300	Appt with Dr. Downey at Noon 1) Examined mouth - everything looked good 2) He thinks I am have Porphyria Diagnosis (Enzyme deficiency) a) You just have to live with it b) Possibility of improvement maybe better days if watch diet and take antioxidants,

		c) Gave me information - hard to read and understand d) Blood test at Mayo Clinic but the test could show enzyme deficiency or not show only 80% to 85% show
7/24/96	Dr Schaub	Took Creatinine Clearence Urine test 7/23 at 8:10am to 7/24 at 8:10am to clinic and got appt to Dr. Schaub today at 4:15pm
7/24/96		Appt with Dr. Schaub at 4:15pm 1) Informed him about Oral Pathologist opinion - Porphyria Diagnosis (Enzyme deficiency) 2) Shared my Blood test 7/16 results - He said low level of OXYHEMOGLOBIN saturation - level- 22 - normal range 80% to 85%- He saids this is a sign of heavy metals 3) He did a meter reading of the teeth for me to share with Larry. This is how Larry will remove my teeth. a) 1st - lower right- mandible b) 2nd - maxilla upper left c) 3rd - mandible - upper left d) 4th - maxilla - bottom right 4) Scheduled to come to clinic tomorrow 7/25 to have a Biocompatibility blood testing for my filling. We decided to use Clifford Labs in Colorado. 5) Scheduled for my first DMPS on 7/30 at 1:30 because hopefully Larry can remove some teeth on 7/30. Will check with Jill tomorrow 6) Purchased Chlorella by Dr. suggested for detoxification - 3 tablets at night until further instructions for Dr. Schaub.
7/26/96		Started new vitamins
7/27/96		Started powder vitamin C - 1500 mg
7/28/96		Vitamin C - 2000 mg
7/29/96		Creatinine Clearance Results are in - faxed Jan permission to release my test results to me. 1) Jan will mail 2) results were normal - everything looked good for me to take chelation - kidneys in good shape and normal range
7/30/96	Dr. Krupa 503-256-9666	Noon appt w/ Dr. Krupa for dental bio-compatibility testing
7/30/96		Appt w/Jill Stryker for pre-planning
8/1/96		4000mg of vitamin C
8/2/96		5000 mg of vitamin C
8/3/96		6000 mg of vitamin C
8/5/96		7000 mg of vitamin C
8/7/96		12:30pm - First DMPS
8/8/96		Appt w/ Larry at 9:30am for first removal of lower right fillings /crowns
8/8/96		1:30pm - Restore vitamins (2 hours) - late that night my tongue started to feel some relief - I think- Started Detoxosode 1/2 tsp in morning & night
8/9/96	NEW BEGINNING	WONDERFUL, GREAT, TERRIFIC, I woke up and my tongue felt GREAT & NO sore throat. I woke up on my right side for the first time in 8 months Throughout day, my battery re-charged and throat really hurts at end of day- EVERY morning

Medical History from Mary Ann Newell

		tongue and throat feels very good. My tongue never hurt as much as it did before my dental work was removed
8/10/96		8000 mg of vitamin C
8/21/96		9000 mg of vitamin C
8/26/96		Appt w/Dr. Paula Bickle for supplement advise: 1) She talked about my vitamins and the supplements 2) Oral Supplements - add different one daily - see attached sheet for supplements
8/28/96		10000 mg of vitamin C
8/29/96		IV - Vitamin - 1:30pm - took only morning and afternoon supplements - plenty for day with IV- Vitamins. Take Chorella and garlic pills.
9/3/96		8am - DMPS -
9/3/96		Appt w/ Stryker - 8:30am ALL my left side - first my top left and then my bottom left. and last god crown on top right side - YEAH!!! -
9/4/96		NO more sore throat
9/5/96		11:30am - Vitamin IV
9/12/96		Vitamim IV
9/17/96		9am - DMPS
9/17/96		Appt w/Stryker at 9:50pm LAST ALL my mercury gone with the removal of last two on top right. THANK GOD for everything!! I had reaction after the last two huge mercury fillings removed - Went to Clinic for a B shot injection
9/20/96		9am - Vitamin IV
9/23/96	Dr. Kreger 360-892-9184	Appt for Panoramic Radiograph at Dr. Kreger at 10am
9/24/96		Appt w/Dr. Krupa at 2:15pm
9/25/96		9:40am appt w/Larry
9/27/96		8:45am - Vitamin IV
10/4/96		9:45am - Vitamin IV
10/8/96		9am - DMPS
10/10/96		10:30am appt w/Larry
10/11/96		8:45am - Vitamin IV
10/18/96		9:15am - Vitamin IV
10/29/96		10:15am - DMPS
10/3096		8am - Larry - new impression of bottom right side
11/01/96		8:45am - Vitamin IV
11/19/96		Venous Blood Gas test - GREAT new results - 41.7% up 19.7% - WONDERFUL - skin is not dry.
11/25/96		9:30am - DMPS Challenge
11/26/96		10am - IV Vitamins
2/10/97		9am - DMPS 9:15am - Dr. Schaub - NT - Dr. Schaub reviewed my dental x-ray and suggested that I send it to Dr. Hussar. Dr. Schaub thinks that I may have cavitation between 31 and 32
2/13/97		1:30pm - IV Vitamins -
2/25/97		9:45am - DMPS
2/28/97		9am - IV Vitamins

Medical History from Mary Ann Newell

3/10/97		DMPS
3/14/97		IV Vitamins
4/02/97		DMPS
4/03/97		IV Vitamins
4/18/97		IV Vitamins
4/21/97		IV Vitamins
4/28/97		IV Vitamins
5/08/97		IV Vitamins
5/12/97		Amino Acids
5/12/97		DMPS
5/14/97	Dr. Christopher Hussar D.D.S. D.O. (702) 826-3001	3:30pm Consultation with Dr. Hussar(NEAT GUY) Reviewed my symptoms Got 3 prescriptions to get before tomorrow a) Probenecid 500mg - 1 tablet 2xday for ten days b) Cipro 500mg - 1 tablet 2xday for ten days c) Hydrocodone for pain if needed
5/15/97	Dr. Christopher Hussar D.D.S. D.O.	1PM - IMPORTANT Surgery Time Right wisdom teeth After surgery - 1) Face was very swollen and 2) My tongue feels normal - DOES NOT HURT or it appears it does not hurt.
5/16/97	Dr. Christopher Hussar D.D.S. D.O.	My tongue feels normal - DOES NOT HURT I took pain pill - threw up again on trip to Dr. Chris' office (NO more pain pills for me) 10:30am - Dr. Hussar's office: To have Dr. Hussar check surgery & stitches 2) To sit with my right side of face on magnetic heat machine for 45 minutes on 2 areas for a total time of 1 and 1/2 hours.
5/19/97		IV Vitamins
		Face swollen for about a week and black and blue for over two weeks - I was black and blue all the way down my throat. I had a bad rash on my chin
around 5/29/97		Received from Dr. Hussar - copies of my Biopsy reports for wisdom teeth.- check out reports
5/27/97	Dr. Larry Stryker DDS. PS. (360)254-6411	12:10pm - Larry removed 4 stitches from top wisdom tooth area and 5 stitches for bottom wisdom tooth area. Larry said areas healed great.
6/3/97	Dr. Chris Hussar	Still experiencing some problems - feels like infection around #31 & #30 Talked to Dr. Hussar 1) He will call in more Cirpro for me to take 10 more days 2) Continue hot pads 3) Continue hot baths
6/30/97		Faxed information to Dr. Hussar describing my weird symptoms.
7/1/97		Dr. Hussar called and left voice mail message for me to get to the clinic so they can help to find out what is wrong
7/2/97	Dr. Rosemarie Otis - Cascade Health	9am - First time to meet - Dr Otis 1) Checked mouth then checked it again 2) My parotid duct inflammation -thrush 3) a) Start Golden Seal - 2 caps 3Xday for 7 days (7/2 to 7/8) then 1 cap 3x day for 7days (7/9 to 7/15) for total of 14 days

Medical History from Mary Ann Newell

		b) Enchinacea - 3x day for 21 days c) Nystatin powder - follow *"Dosing with Nystatin and the Candida Diet"*
7/3/97		Talked to Dr. Hussar He asked how I felt and I said my tongue does not hurt. .
7/14/97		DMPS
7/17/97		IV Vitamins
7/28/97		DMPS
8/1/97		IV Vitamins
8/11/97		DMPS
8/18/97		IV Vitamins
8/27/97	Dr. Bickle	Appt with Dr. Bickle: Reviewed supplements
10/8/97	Dr. Otis & Dr. Bickle	Appt with Dr. Otis: 1) 12 hour fast - urine collection 2) 12 hour fast - TONS of blood given for lab work 3) NT on left side - Bone was soft and I got great relief after my shot and lasted about 3-4 hours
11/11/97		1)Turned in complete paperwork for the new DMPS and Phrase III 2) Reviewed lab results - most looked very good BUT: 3) Lead in blood - one test will show more information. 3) Chemical Screen Parathroid Hormone Lab work DMPS
11/14/97		IV Vitamins
1/12/98		Dr Chris – remove the wisdom teeth on left side Completed the relief for tongue
1/13/98		Dr Chris – oxygen chamber -
1/14/98		Dr Chris – oxygen chamber
2/16/98		DMPS
2/18/98		IV Vitamins
4/27/98		DMPS
5/1/98		IV Vitamins
6/15/98		DMPS
6/19/98		IV Vitamins
7/13/98		DMPS
7/17/99		IV Vitamins
7/27/98		DMPS
7/31/98		IV Vitamins
4/6/99		DMPS
4/12/99		IV Vitamins

I want to thank the Committee on Government Reform for conducting hearings on this issue.

Thank you,

Mary Ann Newell

Medical History from Mary Ann Newell

To: Dan Burton Chairman,
Committee on Government Reform

Here's my story.

I attended Nursing school at Wright State University, Dayton, OH completing 2 years in the early 1980's. At that time I was able to also work part or full-time as a Nurse's Aide. In 1982, I married an orchardist and relocated to central Washington State. I immediately got the flu...had mono for almost a year...easily developed pneumonia if I tried to do things like I used to (ie. work or go to school). In 1992 I got a diagnosis of CFIDS/FM and learned to pace myself so I don't get over stressed...

I started to take lots of supplements....
I had my last "silver" amalgam replaced Feb.'99.

I started DMPS 200mg.IV-Push in May '99. The urine toxic elements lab report by Doctor's Data, Chicago, came back extremely elevated re. mercury 12ug/g creatinine. My June DMPS came
back 9.4. July at 9.2. August down to 4.4. Then my 5th in September included DMPS in a neural therapy around my right jaw and the mercury level came back higher at 6.7ug/g creatinine.

I'm taking Chlorella pills and Cilantro drops, to help move the mercury out. And planning to try PCA (Peptidyl Clathrating Agent) soon.

This has been a financial drain for my family. No miraculous healing as yet. I still fatigue easily, have bouts of depression, ache all over all the time, take 120mg armour thyroid for low thyroid but still have cold hands and feet.

I have to constantly watch what I eat or the systemic Candida will get out of control.
I get some relief with aquacises and yoga...but, basically I feel like a 70 year old in a 40 year old body.

Julie M.Owart
WA homemaker

Personal Account of Stuart Pleima's Experiences with Mercury Amalgam Fillings

MYASTHENIA GRAVIS

Hi! My name is Stuart Pleima. I am 24 years old. This year has been a great year for me and my family, considering that I was diagnosed with possible Myasthenia Gravis four years ago.

I graduated from high school in 1991 and was one of the top weight lifters in my school. I was in perfect health.

My problems began in November of 1994. I had problems swallowing food and I had a fungus on my tongue. The swallowing continued to get worse, so I went to my medical doctor right away. He was puzzled and wanted a Barium Swallow. He said that the fungus was probably from smoking. My mother was not satisfied, so she took me to an ear, nose, and throat specialist and tests were taken. I was worried about throat cancer, but the tests showed nothing wrong and I was given some mouthwash for the fungus that the doctor said was from too much caffeine. Nothing improved, so we went to another throat specialist. He could only tell me to take Maalox for my tongue. He sent me to the hospital to get a Barium Swallow, but it didn't show anything. Everything looked fine.

After awhile I went to my chiropractor, thinking that my problem might be a result of a chain-reaction car accident that I was in on September 19, 1993. I had several treatments, but they didn't help. He referred me to a neurologist and there I was diagnosed with possible Myasthenia Gravis. For the next year and two months I was on Prozac and Prednisone. It seemed to help some at first, but soon I became depressed and fatigued. Finally I decided on my own that the medication wasn't working either, and stopped taking the Prozac and Prednisone without telling my mother or neurologist. The drug treatment was a joke! I managed to keep working, however.

My swallowing problem became worse, like my esophagus was paralyzed and I could hardly swallow bread or meat anymore. My neurologist was concerned and was going to send me to Iowa City for more tests because I wasn't getting any better. He was talking about maybe taking out my thymus gland but wanted more tests done first.

In the meantime my mother's aunt from out of state was at my house on vacation and heard about my symptoms. She called her chiropractor who said it sounded like mercury poisoning. When I thought back, I remembered having some teeth filled on July 17, 1994 and never feeling the same afterward. In fact, two months after I had them filled, I started going downhill. I remembered that when the dentist filled them I wondered whether he was trying something different because he asked his assistant how it was setting up. We called the dentist and asked what was put in the fillings. He stated that it was very rare that anyone had problems with it, but would take it out if we wanted him to.

I went back to my chiropractor and had him send in my hair for a hair analysis. When I got the report we didn't think it showed too much. My mother was very disappointed. Then one Sunday when I could hardly eat my dinner she called a friend who she knew had had health problems and got well after amalgam removal. Her friend stated that the hair analysis would not necessarily show anything and gave us a referral to a mercury-free dentist. The dentist had special devices to keep patients from inhaling mercury during removal and had a mercury-free building. I had an appointment within a few days and drove 143 miles to have it done. We showed him the hair analysis and he looked at my swollen gums and showed me the rust on my fillings. I had all the fillings removed and replaced with composites in one day and headed home. I noticed some improvement almost immediately. The fungus totally disappeared and I had a pretty pink tongue again. My swallowing also began to improve. I had an appointment with my neurologist a week later and we told him what we had done. He was amazed, and when he saw my tongue, he said, "Congratulations!" Then he said I did not have to make any more appointments.

One and a half years have now passed and I continue to improve all the time. I am on no medication. I can now go on with the rest of my life. I have plans to marry a wonderful girl and I have a job I love. We thank the Lord every day for answered prayer and for directing us to the right people to help us find the cause of my problems.

Stuart Pleima
8190 Main St.
Reasnor, Iowa 50232
515-793-2303

July 18th, 2000

Amy J. Pasche
3834 Sacramento Street
San Francisco, CA 94118
(415) 933-8933 (home)
AmyPasche@AOL.com (e-mail)

Congressman Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn House Office Building
Washington DC 20515

Dear Congressman Burton,

I am writing to inform you of my horrible experience with Mercury poisoning in hopes it will influence you to take legislative action to eliminate the use of Mercury in Dentistry, as well as in pharmaceuticals and household goods. I have enclosed my case history as anecdotal evidence that Mercury is harmful to the heath of some people.

What saddens me most is that back in December of 1990, after CBS' 60 Minutes aired a segment on "Mercury, Poison in your mouth?" my mother contacted me to suggest my Multiple Sclerosis came from Mercury. Because, at the time, I had no fillings in my mouth, and then as now, the information about the dangers of Mercury remain unreported and out of the mainstream, I dismissed the possibility outright.

Had I but known how insidious and nefarious the metal can be to a human body, I could have sought help sooner (or chosen never to have used it in the first place), thereby saving myself years of pain and suffering. I find it morally reprehensible that a substance never having been classified, nor approved by the FDA is used freely in Dentistry and that the American Dental Association is allowed to suppress information about its harmful, if not deadly effects on some people.

Given the restrictions already placed on its use in Sweden, Austria, Germany and Australia, and in light of the class action lawsuit in Canada, I am amazed the United States is not also taking steps to control, if not eliminate, the use of Mercury. As an example of how sick Mercury can make a person, it is my sincerest wish my story will help others avoid the same fate.

Sincerely,

Amy Pasche

enclosure

July'2000

To: Committee on Government Reform

From: Amy Pasche

A MIRACULOUS RECOVERY -- a case history of mercury poisoning.

Between the ages of four and six, I had six mercury amalgams placed in my mouth to fill cavities in my baby teeth. Just after placement of the first amalgams, I developed severe allergies to milk, terrible gas pains in my chest, persistent upper respiratory infections, and chronic eczema. These troubles continued until the age of sixteen, when I began to experience severe constipation and amenhorrea. At eighteen, I developed bleeding hemorrhoids, and by twenty, I had acid reflux, and occasions of projectile vomiting.

At 23, I experienced two bouts of optic neuritis, and subsequent testing confirmed a diagnosis of Multiple Sclerosis (MS). At 25, I began to have tonic seizures - a burning, freezing sensation spread down my left side to my waist, my legs grew numb, and I became paralyzed from the waist down. The seizures were infrequent, and lasted only one to two minutes. After eight months, they disappeared. For the next five years, I had the constant sensation my rectum was falling through my pelvic floor, and my problems with constipation and hemorrhoids worsened.

At 30, I started having urgency incontinence and terrible muscle spasms throughout my lower back and pelvic floor, which pinched surrounding nerves and caused terrible pain. My digestive problems worsened, and I began to lose weight. My gastroenterologist told me I had Irritable Bowel Syndrome. Finally, at 31, in constant pain and with swollen abdomen, I started to have severe diarrhea, fever, and rectal bleeding. I was given a fissurectomy, but my condition worsened. Hospitalized, tests revealed I had bleeding ulcers throughout the lower intestines, fistulas forming abscesses in the abdominal cavity, and severe anemia. I was diagnosed with Crohn's Disease, and treated with steroids and antibiotics. Standing 5'5" tall, in just one year my weight had dropped from 125 to 95 pounds.

A month after starting treatment, I developed shingles, and once the sores cleared, I suffered from post-herpetic neuralgia for another two years. Four months into treatment, I had a complete rectal prolapse -- eight inches of my lower intestines fell from my anus and dangled inside out between my legs. Doctors surgically removed twelve inches of diseased colon and explored my abdominal cavity for cancer, but found nothing. While in the hospital, I suffered a grand mal seizure, which doctors were unable to explain.

After surgery, my health continued to deteriorate. My pain intensified, as constant muscle spasms pinched nerves, and neuralgia wracked my body. I had pains in my chest, back, and abdomen, and I became jaundiced. I suffered from chronic insomnia, short-term memory loss, and again, severe constipation. I developed terrible food allergies to dairy, wheat, gluten, eggs, soy, preservatives, spices, sugar, and caffeine, which made the pain I felt after eating, and during digestion, excruciating. I lost even more weight. I also became allergic to my medications and was forced to stop taking them.

Desperate, I turned to alternative therapies, and found an acupuncturist and Doctor of Oriental Medicine (OMD) in Los Angeles, who has developed a sensitive diagnostic

technique to detect hidden pathogens causing illness. I began flying back and forth to Los Angeles from San Francisco for treatment and, for the first time in five years, began to improve. In

(2) Amy

October of 1998, after two months on Chinese herbs, I felt better overall, but I started to experience numbness in my legs and difficulty walking.

A week after the numbness started, I began having violent seizures involving my entire body. I lost all muscle control and thrashed wildly about the floor. My jaws ground back and forth, and I yawned repeatedly. During the third seizure, my jaw dislocated and I was rushed to the emergency room to have it reset. After two days, the seizures were constant and I was hospitalized in an attempt to control them; none of the medications worked. The neurologists had never seen anything like it and could offer no remedy. After three days under heavy sedation, my insurance company denied me further benefits, and I was discharged into the care of a psychiatrist, who tried an experimental antipsychotic drug on me not yet approved by the FDA. The drug's side effects exacerbated my existing symptoms.

I begged that my family return me to the OMD in Los Angeles, and I moved into a hotel near his office where, no longer in any condition to travel or take care of myself, I lived for eight months, the first three under the constant care of a family member. Soon after the move, I became paralyzed from the neck down, retaining only partial use of my right arm. I lost control of my facial features, tongue, and mouth so that speech was nearly impossible. Sometimes, I was unable to even open my eyes or to speak and could move only the pinky on my right hand to indicate I had not lost consciousness. Day and night, I kept a piece of wood between my teeth to prevent my jaw from dislocating again. The pain from neuralgia was exquisite. I felt as if my skin had been burned away, and I were being probed with an electric cattle prod.

After clearing multiple layers of bacterial, viral and fungal infections, high levels of mercury were detected in my brain, spinal cord, and intestinal tract, causing auto-immune reactions. The source of mercury poisoning had come from the dental amalgams placed in my baby teeth, thirty-two years before. Although my last filling had fallen out by the age of eight, the mercury had remained, having entered my system through my lungs, sinuses, and intestinal tract, and permeating throughout my entire body. The MS and Crohn's Disease were caused by my immune system attempting to eliminate both the mercury and the multiple bacterial, viral, and fungal infections.

Blood tests and hair analysis by a Western M.D., specializing in heavy metal poisoning, confirmed I had not only accumulated high levels of mercury from my teeth fillings, but also nickel, another heavy metal used in dental amalgams. Because his treatment for clearing mercury, DMPS IV, increased the risk of seizure, he advised me to continue using Chinese herbs.

As I began to clear mercury, I developed even more symptoms. Mercury activated the Herpes Zoster virus, causing my optic neuritis to flare again, and I developed painful hearing sensitivities and ringing in my ears. I became extremely sensitive to odors of any kind, as the slightest smell made it difficult for me to breathe, and caused a seizure. At other times, in episodes lasting between ten and twenty seconds, my diaphragm froze. I could neither inhale nor exhale, even though I consciously directed myself to. Mercury in my lungs was blocking the nerve impulse transmissions between my brain and diaphragm. Two weeks after a modification to my herbal prescription, the difficulties with my diaphragm disappeared. And gradually, as I cleared more mercury, my problems with vision, hearing, and smell were also resolved.

After two months of taking herbal prescriptions to clear mercury, the paralysis began to recede from my upper torso and I could use my arms to lift myself up out of my wheelchair. I regained some feeling in my legs and could drag myself across a room, or help myself in and out of bed. The constant movements I was having in my limbs, and loss of control of my tongue and facial muscles, were symptoms of Tardive Dyskinesia, a condition of the central nervous system found in

(3) Amy

individuals having taken high dosages of antipyschotic drugs over long periods of time. These drugs chelate manganese; however, in my case, mercury had interfered with the function of both molybdenum and magnesium in my brain. Magnesium regulates neuromuscular contractions and has important anti-seizure effects on the body. I began taking supplements of both, while continuing with herbs to clear mercury, and soon the symptoms of Tardive Dyskinesia disappeared completely, my nerve pain improved, and my seizures became less violent.

The seizures also changed character. Instead of grand sweeping movements, I became either rigid, or twitched incessantly, as my body shook with tremors. My joints swelled and became stiff, throbbing with arthritic pain and my hands and feet curled up into claws. The painful muscle spasms in my back, legs, and pelvic floor returned. Mercury was found blocking both calcium channels and hormone receptors, and mercury antibodies had triggered an autoimmune attack on joint tissue.

Finally, after four months of clearing mercury, the neurological issues began to abate. The paralysis in my hips and legs slowly receded, and after five months, I could walk with a cane, and soon after, with no assistance at all. My seizures and tremors stopped, the numbness and nerve pain diminished, and my joint pain relented. By May of 1999, the neurological issues had cleared, but instead, I began another exacerbation of Crohn's Disease. The debilitating diarrhea with fever returned, as I had 40 to 50 attacks a day, and abdominal cramping left me doubled over in pain. Mercury related microfistulas were found along my entire digestive tract, from my esophagus to my rectum, once again causing pockets of infection in my abdominal cavity.

Though still terribly weak, I moved home to San Francisco in late June of 1999, and again traveled to Los Angeles to continue treatment. Gradually, as I improved, my food allergies abated and my weight came up to 99 pounds. Because the fistulas were slow to heal, in September and October of 1999, under the supervision of my gastroenterologist, I underwent three infusions of Remicaide, a new Crohn's medication that specifically targets treatment-resistant fistulas. The results were positive.

Today, after twenty months of clearing mercury, my intestinal issues are mild, my neurological difficulties, non-existent, my food allergies, gone (although, I continue to avoid all dairy), and, at 115 pounds, my weight has returned to normal. I take a yoga class every other day, and thirty-minute walks, three times a week. I am feeling better than I have in fifteen years. Although I am still clearing residues of mercury, and continue my trips to Los Angeles for treatment, I anticipate once I am completely free of mercury and its related antibodies, I will enjoy a full and permanent recovery.

Amy J. Pasche
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(415) 933-8777 (Fax)
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**The doctor then realized that the mercury was coming from my amalgam fillings!
It was a complete surprise to me to find out that my "silver fillings" were actually 50% or more mercury!**

7/17/00

Mary Robinson, Salem, OR
To: Chairman Dan Burton
Committee on Government Reform
Hearing - "Mercury in Medicine"
2157 Rayburn House Office
Washington, DC 20515

From:
Mary C. Robinson
1595 17th St. NE
Salem, OR 97303 .

Dear Chairman Burton:

I would like to contribute the story of my personal experience of mercury toxicity for your consideration in the Congressional hearings on "Mercury in Medicine".

From childhood I have suffered a variety of health problems (kidney disease, allergies, fatigue, skin afflictions and low immunity). These worsened as I grew older and grew to include hormonal and metabolic disorders and respiratory problems, all of which sharply curtailed my activity level and my potentials. I graduated from a private college "magna cum laude" and had fond hopes of being able to contribute to society in the areas of education, literature and art. More and more, I found that I could, however, barely manage my family and home responsibilities. My broad array of symptoms became devastating about 5 years ago, at age 48. Every system in my body seemed to be breaking down, my broad array of symptoms became very severe, putting me in a debilitated state, unable to continue working and unable even to maintain home life.

After years of not making much progress medically, I had the good fortune to find a naturally-oriented M.D., who through thorough testing was able to find the source of my multiple symptoms to be severe mercury toxicity, high lead toxicity and high nickel toxicity. Reviewing my life, I realized I became mercury toxic while I was a child living in Ambridge, PA within blocks of 4 steel mills, which apparently were dumping wastes into the local creek I played in and from which I collected large amounts of mercury. Of course, we were also daily exposed to the ever present fly ash from the mills, which I have since learned also contains mercury. To make matters worse, we also collected and ate the wild berries growing in the fields surrounding the mills.

Following my diagnosis, my doctor began a year long series of chelation treatments. This brought the lead and nickel levels down to within normal range in about two months and I experienced some relief from my symptoms. My mercury levels, however, even after a year of treatments, remained as high and sometimes were higher than the original test levels. The doctor then realized that the mercury was coming from my amalgam fillings! It was a complete surprise to me to find out that my "silver fillings" were actually 50% or more mercury! My doctor said that my body was in a pre-cancerous state and that I could not get well until I had all my amalgam fillings removed and replaced. He said that mercury wreaks havoc in every cell, system and process in the body and that removing the fillings (the current source of mercury poisoning) and then chelating out the mercury stored in my body offered the only hope of gaining some degree of health and normalcy.

(2) Mary Robinson

Our finances already having been drained by my not being able to be gainfully employed, by the great and largely uncovered medical tests and treatments and vast array of uncovered supplements required to keep me functioning to some degree, we were now facing the huge expenditure of replacing all of my amalgam fillings and crowns which have amalgam underneath them. The insurance company repeatedly refused my appeals to fund this course of action beyond its yearly allowance for dental work, which just scratches the surface. Due to not having the funding and also due (because of mercury toxicity) to being severely reactive to most of the restorative dental materials, the process of removal is going much more slowly than it should be. Nonetheless, both by getting on with the process as best I can and by educating myself on amalgam related illness and how to care for it, I am currently making some progress in gaining my health.

I realize that some of the damage I have suffered may not be repairable; yet, I am hopeful that the quality of my life will improve substantially following total amalgam removal and mercury detoxification. This is not a short journey; but, within the next couple years, I hope I may be able to help repair our very damaged family financial status, restore at least some of the quality and breadth of my earlier life and potential and at least some of the relationships lost or damaged because I had so little of myself left to invest in them.

As I have become aware, and look at the potentials of not only my life, but also of those who, either through me or with me, also suffer the results of mercury toxicity (my children, my husband, my siblings, my extended family), it is not sufficient to say that I am very grieved. I see clearly that those of us, within my extended family, who have suffered the most exposure, and those who were born of such, also suffer the most severe pathologies (M.S., severe depression, bi-polar disorder, respiratory problems, including asthma, severe allergies, severe skin disorders, including eczema, rheumatoid arthritis, heart problems, including heart attacks and arrhythmia; severe fatigue, kidney disorders, endocrine problems, digestive disorders, memory and concentration difficulties and learning disabilities). I am angered at the steel mills, which were so careless and at the American Dental Association, which I have learned, from its inception, has covered up and denied the truth about the toxicity of amalgam to the detriment of millions of people! What both industries have done is unconscionable, reprehensible and inexcusable! What is worst is that the ADA presents itself as an advocate for the public health!
Chairman Burton, I hope that you and your committee will be the force that will begin to put an end to the needless destruction, suffering and irreparable damage that mercury poisoning causes so many in this country, coming, as it does, from without--from manufacturing industries, but also, coming, as it does, an enemy from within, placed by those very health care providers/industries we, the public, all tend to look to with trust: our dentists (using mercury amalgam for filling material) and our doctors (giving children near 30 pre-school vaccines, all containing mercury/thimerosol).

Thank you for allowing me the opportunity to share my experiences and views and for your consideration of them.

Sincerely,

Mary Robinson

July 16, 2000

The Honorable Chairman Dan Burton
Committee on Government Reform
Hearing - "Mercury in Medicine"
2157 Rayburn House Office Building

Washington, DC 20515

Dear Chairman Burton:

Thank you for your service to our country and for the hearing on Mercury your commitee is having. I have responded to several questions pertinent to mercury in dental fillings.

Were you informed that your silver fillings contained mercury. I do not believe I was. I got most of my fillings in the late 60's and early 70's.

Were any of your doctors aware that mercury could be a contributing factor to
your illness. Dr. Bill Deagle, after a blood test done 3-21-2000, indicated that my mental health problems and the positive rhumetoid factor could be from the mercury..

Symptoms and diagnosed illnesses. Toxic level of mercury (27.1, normal <=9) as defined by Great Smokies Diagnostic Lab, Asheville, NC. Depression, Anxiety, Obsessive Compulsive Disorder, Personality Disorder not otherwise specified. Positive rhumetoid factor, some Chronic Fatigue, Fibromyalgia, OsteoArthritis, Chronic Rinitis, Irritable bowel syndrom. Problems with short term memory, confusion when undertaking simple mental tasks, frequent infections, sensitivity to caffine, unable to tolerate stress, irritability. My doctor thinks I have trouble with my adrenal glands.

Length of illness 3 months to 25 years.

Attitude of medical communcity re: mercury toxicity from dental fillings. Grant E. Steffen, MD, Carrier Medical Director, Medicare Part B in Colorado and Wyoming, states in 5-16-2000 letter, "..I do not know of any evidence that shows that mercury-containing dental fillings affect the blood level of mercury."

Were your costs incurred for doctors, tests, hospital stays, and medications
covered by insurance. Dr. Steffen (see above) states "...I would, on individual consideration, allow payment for intervenous chelation if a) a repeat blood level from a local laboratory was abnormal, and b) if your medical record indicates that you have symptoms that relate to this abmormal level. Without both of these conditions, I would deny chelation as 'not reasonable or necessary'." The 3-22-00 blood test was covered by insurance, and the doctor treating me is billing Medicare and Medicaid.

Have you suffered irrepairable damage to your body. I hope not. The question is, will I get well after Oral and/or IV chelation, and possibly having my mercury fillings removed.

How has your illness effected your:

financial status, My in-laws refuse to help me with expenses, but my sister has agreed to help with very limited expenses initially. I cannot aford any of the costs involved. My husband's and my combined monthly income is about $1100.00.

personal life I have been fired 4 times and laid off once. I have not been able to obtain a college degree after 6 years of higher education, though I am said to have a high IQ. I have been on Social Security Disability since 1990.

and relationships. I was divorced in 1979 and the children went to live with their father in 1983. Without proper antidepressant medication, relationships and life in general would be very difficult. When I am not on antidepressants, I am very irritable, and have trouble getting out of the house, even for a short walk.

Thank you and your committee for your concern about this matter, and for considering my problem with mercury.

Sincerely Yours,

Ruth S. Olson
5875 E. Iliff, D-217
Denver, CO 80222

Ferreira

From: <FreKoss@aol.com>
To: <virginia@portone.com>
Sent: Wednesday, March 08, 2000 8:15 PM
Subject: Sara's story (no e-mail at her request)

To: Dan Burton, Chairman
Committee on Government Reform
2157 Rayburn HOB
Washington, D.C. 20515
Re: Mercury Poisoned since Age 8
Dear Senator Burton:

My saga probably began when I began with what became a mouthful of amalgam at age 5, however, the situation came to an acute crisis eight years ago. In 1990, planning to leave our place of work which included free dental care, I arranged to have my crumbling fillings replaced before I would have to cope with paying for it privately. Nearly all my molars ended looking like silver teeth, so little tooth was left. Several were very deep. About 9 months later when I found my self experiencing bouts of depression which I attributed to PMS, I took a friend's advice and began taking the maximum dose of gamma linoleic acid ("Glanolin"). I took if for 3-4 months until I woke up in a severe panic attack one night. For the next half year I rode a psychotic roller coaster that would rise and fall with my hormonal cycle. The LSD-like hallucinations were devastating -- it's a miracle I didn't kill myself or anyone else, (I have never taken mind-altering drugs); I didn't know when or IF that
hell would end. I had no history of schizophrenia nor does it run in my family. The psychosis gradually lessened and ended in 1992. It never recurred since.

During that period I had terrible vision problems, although not double vision. Focusing was nearly impossible, when I walked I felt like the ground was jumping up to meet me -- like my eyes were bouncing in my head. Clinically, the optic nerve was temporarily affected -- I lost peripheral vision in both eyes which I gradually recovered within a couple of years. The extreme dizziness (vertigo?) which plagued me took several months to pass. The horrendous and peculiar odor emitted through my sweat glands gradually passed
together with the psychotic episodes.

Things gradually improved. Although I understood very little of what was causing my problems, I realized candida was probably implicated and went on a strict anti-yeast regimen together with exercise. This helped tremendously. By a year later, my sanity was totally restored, but my general health gradually began to deteriorate. My dentist replaced my cracking teeth with root canals and enamel crowns (most likely nickel based). I simply was wiped out and had no

physical or emotional energy. Then about five years ago, I was diagnosed with FM which I considered a useless diagnosis for explaining my poor health, as the only cause presented for it was "'stress".

Two and a half years ago, the brain fog and sensation of weakness in my legs began to really worry me. Thinking I was having a relapse of candida I took every anti-yeast medication and supplement I knew of. Simultaneously, the GP sent me to the (modern) homeopath for treatment. Shortly after got the test results of B-12 deficiency were received.

At the end of two weeks of intramuscular injections (6 in all), another crisis developed. I broke out in hives all over my body, including some in my throat and developed extreme shortness of breath. An allergic reaction? Perhaps initially, but sensations of throat tingling and swelling persisted for months although nothing could be seen after the initial hives passed. Acute respiratory flare-ups continued for months. (Trauma?) Eventually I was diagnosed with asthma after a metacholine challenge -- a diagnosis I doubt. Still thinking that yeast alone was the culprit, I followed a diet that required a lot of fresh lemon juice and cider vinegar. After several months of this I began to notice I was developing new symptoms that worsened after ingesting these (I wonder about effect of the acid on the metals I had in my mouth): palpitations, tachycardiya, arrhythmia, choking and difficulty swallowing, hoarseness, weakness of voice and body. At that time the few medical tests done revealed only a nickel allergy, high IGM, low complement C. (I think B and T cells were checked and I was told they were OK. ANA was also OK.) The hair test indicated adrenal exhaustion level 3 but did not show toxic levels of mercury (only aluminum). I stopped drinking tap water and eating from metal cookware, which seemed to induce an immediate reaction. When I consulted with a professor of nutrition he told me the culprit was my dental work. The dentist (by no means alternative), also suggested that the cumulative effect of all the amalgam in my mouth might be contributing to my poor health, even though no allergy showed up.

At that point my parents graciously stepped in and made in possible for me to come to them and redo all the dental work. However, my symptoms were so overwhelming I was afraid I wouldn't stay alive long enough to get to them to take advantage of their help. At one point I stopped in a health-food store and asked what could give me to help chelate mercury. I was really desperate, because I am very chemical sensitive and never know when something will backfire, but I felt I had to take a chance. He sold me "Glutamax" by Maxi-Health (glutathione, N-acetyl Cysteine, collodial sulfur,). The change was incredible! But after 3 days I developed such terrible stabbing and pinching in my legs I had to stop.

Blood tests performed after treatment indicate that I have anti-cardiolipin syndrome typified by blood vessel spasms and clotting problems. I doubt this is entirely new since it causes gestational problems and I had 6 miscarriages. I still have high IGM and low complement C. Low-normal counts of WBC,
platelets, HGB, B-12, ferritin and usually iron. Sedimentation rate OK, no RA Latex or CRP, ANA and thyroid in the middle range. According to the ematologist I'm not in bad shape.

If I go off my diet my symptoms will eventually catch up with me and intensify (chronic pins and needles sensations strongest from waist down, breathing problems, depression, infections). About four months finding myself stuck in a depression I took n-acetyl cysteine since it had been helpful in the past. It moved the depression nicely but I ended up with shortness of breath, widespread muscle spasms, and fasciculations that are gradually becoming less pronounced. Normal EMG showing hyper reflexes in my legs (they still feel weak) and fasciculations. I wonder if the 3 months of solgar iron that I took prior to NAC made a difference? Right now I can't even tolerate food
that has sulfur naturally.

I am certainly not cured but my health is generally more reliable; if I start to really feel energetic and do a lot I end up sick. I suspect I still have mercury in my body that is affecting me. I am very interested in finding someway to better my situation although I am very grateful it is as good as it is.

Sara
(Israel)

Subj: story from England
Date: 6/10/00 2:03:26 PM Eastern Daylight Time
To: Chairman Dan Burton
Committee on Government Reform

PERSONAL STORY FROM U.K. - SHIELA

Previous Occupational Health Nurse.

Collapsed at work with abdominal gut pain. Had been feeling ill for some time, but could not pin-point it.

No temperature.- Became more ill, Bilirubin and Protein in Urine, Suggesting Liver or Kidney Problem-no joy, impacted appendix discovered-removed-lost 2 stone in weight afterwards, urine still bad, no known cause. Unable to sleep or eat, started violent shaking.

Pain all through body.

Finally exhausted- admitted to psychiatric Hospital.

Unable to stop vomiting- came out after 5 weeks worse. Heavily sedated with Valium.

Medication could not allay symptoms. Lump appeared on jaw-bone.- unable to tell one pain from another. Leakage finally found of dental amalgam in wisdom teeth-black gums-tattooing on one side. Necrotic bone removed from jaw. Mercury (Amalgam found in jaw-bone on X-ray) and removed.

Vomiting stopped came off all Valium, now 4 years on, it has cost me all my back teeth, as it was a race against time to save them, once I developed a metal allergy

I repeated my hair analysis after removal, to see if there really was anything legit in paying £2000 as I still felt very ill. Mercury levels were down from 0.56 to 0.06 in hair. The first reading was taken when I only had 6 left out of 15, so I dread to think what the reading was, when I was on planet dog under sedation.

Even my General Practitioner seeing my other teeth, thought they would not be saved. Gradually over several months, with white fillings in, they started to turn back white.

Unfortunately, it was too late for my health. I am now diagnosed with Fibromyalgia and ME, and I'm housebound.

I take carbamazepine, an anti-epileptic drug for the spinal pain, & chloral hydrate to sleep.

I now have damaged thyroid cells and I'm on my second immune problem, and due back to immunology in August.

I sincerely hope that this account helps you to achieve your goal, As I feel it would be wrong to continue to allow others to suffer in the way that we have.

Whilst I cannot or would not categorically state it was mercury that entered my Central nervous system, not a virus, resulting in the ME/F'S and chronic fatigue state, I find it impossible to believe that someone can go through that level of leakage and escape it.

The muscles are still rigid down the right hand side of my spine.

I am fully aware of the links between amalgam and immune problems, and the diagnosis I have.- No known cause for my white cells in urine.

My white cell defense against candida was only 593 for 16 years.- now after amalgam removals it is back to 66,000 I am now struggling against pneumococcus, although I have had the vaccine, my system is not responding. I am only 43 years old, and had a promising career.

July 9, 2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Building
Washington DC 20515

Re: Health Recovery After Amalgam Replacement

Dear Congressman Burton:

One week following complete amalgam replacement my far-sightedness reversed and I could read newspapers in the morning again.

The glasses, already ordered, were never needed.

This happened 8 years ago-and no need for glassed yet!

I am a scientist in Sweden and have invented the MELISA TEST for heavy metals

Yours truly,

Dr. Vera Stejskal, vera.melisa@swipnet.se
http://www.melisa.org

September 25, 1999

375 Catalina Blvd #205
San Rafael CA 94901
415-457-8091
martasonn@hotmail.com

Dear advocate for mercury-free dentistry,

After years of fighting to inform the public about the health hazards of mercury we finally see definite signs of change. There is currently a campaign to phase out mercury from medicine. Nearly 170 healthcare organizations are targeting mercury in hospital incineration, thermometers etc. Most notably the Academy of Pediatrics and the US Public Health Service have decided to discontinue the use of thimerosal (a mercury preservative) in vaccines.

The City of San Francisco Board of Supervisors has resolved to eliminate mercury use in every city department. Supervisor Mark Leno deserves much praise for his leadership in this action. An ordinance about the implementation is now being drafted. Supervisor Leno can be contacted at City Hall, 1 Dr. Carlton B. Goodlett Place, Room 244, San Francisco, CA 94102-4689. His Phone number is 415-554-7734; his Fax number is 415-554-5163; or you can e-mail his aide at bob_hartnagel@ci.sf.ca.us.

Unfortunately the use of mercury in dentistry continues unabated. Most dentists use mercury-amalgam fillings and completely ignore the risks they pose to the environment and human health. The waters in San Francisco Bay are heavily polluted with mercury. According to some studies, 50% of it comes from dental mercury. Every person who has amalgam dental fillings continuously excretes mercury, and it eventually ends up in the Bay. Our dentists wash down amalgam scraps when they replace "silver fillings" or make new ones. Amalgam traps installed in the plumbing of all dental offices, would reduce the mercury pollution problem significantly.

What is most horrifying is that dentists who refuse to place amalgam are denied their right and freedom to practice conscientious dentistry. One such dentist is Andy Landerman DDS of Sonoma County. His license was revoked in the late 80s; his only offense being removing mercury fillings. So far his appeals to be reinstated have been denied. At the present time he has engaged former West Virginia Attorney General, Charles Brown Esquire as counsel, and will appeal his case in Sonoma County Superior Court.

We Consumers For Dental Choice want access to mercury-free dentistry, and urge our elected and appointed state officials to support us by upgrading the California Dental Board to include scientists and doctors who realize that toxic metals impact human health adversely. We expect the Dental Board to uphold and set high standards for professional, academic and research excellence, instead of doggedly enforcing the use of an archaic toxic dental material many other nations severely restricted or banned. Letters and petitions supporting Dr. Landerman should be directed to Director Kathleen Hamilton, Attorney General Bill Lockyer and Governor Davis, with a copy to Charles Brown Esq. A letter to your State Senator and Assembly person would also be helpful. Please, act soon.

Sincerely, Marta Sonnenblick RN.

9 November 1999

375 Catalina Blvd #205
San Rafael CA 94901
415-457-8091
martasonn@hotmail.com

Board of Environmental Studies and Toxicology
The Natural Academies of Science
Committee on Toxicological Effects of Methyl mercury
2001 Wisconson ave.N.W.
Washington, DC 20007

Dear Sirs/Madams

In May of 1992 I wrote roughly the following letter to Dr C. who had been my dentist since the end of the 70es thru 1987:

Dear Dr. C:

It was a cruel experiment you conducted in February 1987, when you (without telling me) put new amalgam on top of my gold crowns.

My life has been a nightmare ever since. You were well aware of the severe allergic reaction I had experienced to a previous mercury patch test that had made me decide to replace all my amalgam fillings with composites, a couple of years before. I trusted you since you knew that removing my amalgamfillings had cured the hypoadrenalism that promted me to look into the mercury connection in the first place. And you knew about my extreme mercury sensivity so I could not dream that you would place more of it in my mouth .

For three years I walked around completely oblivious about the fact that I had new mercury out gassing in my mouth. And the amalgam was adhering to the gold alloy which creates serious health consequenses.

A few days after your brutal intervention,I was rushed to El Camino hospital;my heart was beating so fast that my pulse rate could not be counted. I shook violently, was nauseated,and had excruciating pain on top of my head. I know now that my reaction was a textbook example of acute mercury poisoning.

The Emergency room physician dismissed me as hysterical, especially after I disclosed that I was in the middle of divorce.

From then on my health went steadily downhill. I suffered from severe insomnia. Extreme weakness alternated with horrible agitation.I could not make decisions, could not choose between living or dying. I experienced pain and unpleasant symptoms I fear few could have tolerated.I saw numerous physicians, spent lots of money, got lots of incorrect diagnosis,but no relief.

Some diagnosis were--autoimmune deficiency, vasculitis, Hashimotos thyroiditis,neuropathy,malnutrition, malabsorption,maldigestion and muscle attrophy.I also became extremely chemically sensitive. That also meant that I could not take any prescription drugs!

I used to have a strong constitution, had always been cheerful and energetic, but now I felt only helplessness,anxiety and despair.It was a miracle that I did not commit suicide.

In 1989, a mercury-free dentist discovered amalgam on top of the two last teeth on the lower right. An amalgam plug had also been inserted from the cheek side in one of them.

It was Dr. K who discovered the new amalgam.I was overcome with horrible grief and cried there in his chair for a long time. I also recalled a conversation I had with you Dr.C when I came in for a cleaning and check-up six months after your secret mercury insertion. You then pointed out that # 15 appeared dead.. I then said:" Maybe it is because of my, teeth that my health has taken a nosedive?" You replied very emphatically, "Oh, no."

The day after the amalgam was discovered, I called your office and inquired about the fillings that had been placed in February of 87. Your assistant Karen confirmed that you had placed amalgam at that time.

Dr.C I must admit that I heard a sound like when you push amalgam into a cavity when you worked om me that ill-fated day in February 87, but I dismissed my suspision ;i was in good hands I thought. But it turned out that trusting you was the biggest mistake of my life. My health and ability to work has been destroyed and I am financially ruined. I tried going back to nursing, but my chemical sensitivitis made it impossible for me to tolerate the inside of a hospital. I attempted getting a degree in Holistic Health, but the petrochemical fumes from the freeway commute were too overpovering and my sensitivity to news print kept me from studying.

You contended that some other dentist must have placed the amalgam in my mouth, but Dr. C I did not see any other dentists than you before I went to see Dr K who discovered the mercury on the first visit! When my lawyer got my records they showed no trace of the filling placement in #30 and 31 in spite of the fact that your dental assistant readily noticed them when I had called her some months earlier.

The attorney I had turned to dropped my lawsuit and I was too sick to search for a replacement. I have recovered some but my health problems are persisting. Still I am hoping for recovery. Vitamins, minerals and herbs have given me some relief. Networking and activism for environmental causes gives me hope. I also trust that our government soon will follow the lead of Sweden and ban this horrendous public health hazard.
Please do not hesitate to contact me for more information and documentation.

Sincerely,

Marta Sonnenblick RN

July'2000

Committee on Government Reform

Dear Congressman Dan Burton,

I have sent you a copy of my story, a letter that I read to the Pennsylvania State Dental Board on how it relates to the chronic poisoning of modern man, through dental amalgam. I urge you to do research into this issue so that you may be a contributing factor in helping men, woman and
children that are being poisoned by there dental fillings and don't know it!

Sincerely yours,
David G Stahley

This letter was read to the Pennsylvania State Dental Board on July 13, 1998.

Good Morning Ladies and Gentlemen,
Let me start off by thanking you for this opportunity to tell you my story.

My name is David Stahley, I am 42 years old, married to a wonderful woman named Patty, who is here with me today, and we have a four-year-old daughter named Anita. I am currently employed as an electronics technician with a small company and have been with them for 15 years. Prior to my illness, I also operated my own electronic service business, repairing consumer electronics. I closed my service business after my health started to decline.

I grew up in a typical American, Catholic household with two parents, a sister and two dogs. We had good health care due to the fact that my father provided for us well. As part of that health care I had regular visits to the dentist and amalgam placed when needed. By the time I reached high school, I hated going to the dentist, because I was never given anything for the pain. There came a time when I told my parents that enough was enough and I was not going anymore. I took care of my teeth the best I knew how and eventually started to loose fillings, mostly from my molars. After several years of working in the family business, I met Patty and fell in love. At her urging, I began seeing a dentist whom she trusted and convinced me to take care of my teeth. That was in the mid seventies.

I was a healthy male with an extraordinary amount of energy, and an intellect to match. I played racquetball regularly, pumped iron and participated in outdoor activities on a regular basis. Throughout my life I was a fairly healthy person. I would on occasion get colds or the flu but nothing of major concern. In my early thirties I began having sinus problems. It would seem that every year at the beginning of winter, I would develop a sinus infection and constant postnasal drip. My response would be to buy over the counter medicine and treat it my self. As time went on, the infections began to get more severe, requiring a trip to the doctor. The routine would be; sinus x-ray's, then a prescription for antibiotics. This would occur on a yearly basis.

My first sign of trouble began one day while driving. I started to developt he sensation that I was going to pass out. Lucky for me I was close to a friends business, so I pulled off the road and made my way in. I explained to him my situation, then sat down; after about ten minutes the feeling

passed. In retrospect, fours days prior to that incident I had been to the dentist to have my teeth cleaned. This occurred in the spring of 1995 and was about the time that I started with obscure vision problems.

In the fall of 1995, I took a weekend trip to my boss's boat, for the purpose of relaxing. Upon arriving we washed the boat, had a few beers then changed to go out for dinner. While in the restaurant, waiting for our food, I started to develop a spaced out feeling. My facial color changed to all white, I began to feel claustrophobic and all I wanted to do was leave
that restaurant. I lost my appetite and could not eat any food. After
(3)
leaving I began to feel somewhat better. That night I was very restless and had a hard time falling asleep. The next morning I felt somewhat better but decided to make a return trip home. In retrospect again, that week I had been to the dentist to have my teeth cleaned. As winter approached, I developed a serious sinus infection that required me to be on powerful antibiotics for twenty days. It took over a month to clear. That winter I began not feeling well and made a trip to the doctor. My lists of symptoms were; obscure vision problems, sensations of being spaced out, and mild anxiety. Exercising would cause severe blood sugar reactions. He sent me for a complete blood work-up and also an EEG. The tests showed nothing out of range and the EEG was normal. At the time he thought my symptoms to be stress related and told me to take it easy and try to relax. Through the winter I felt OK, but not my normal state of health. In March of 1996 I broke a cusp off a molar that required a trip to the dentist. To repair it she advised me that she could fill it in with amalgam instead of capping it. I agreed and the repair was initiated. After the
first batch of amalgam was used she told her assistant to mix another one. Upon hearing that I asked her if it was okay to be putting all that metal in my mouth. Her response was, "that it was nothing to be worried about". The following month I returned for my sixth month checkup and found that Ihad developed three small cavities. She had asked me if I was eating allot

of sweets and I told her through the winter I was craving foods that were sweet and salty. In the beginning of May, I began waking up at five o'clock in the morning and not being able to go back to sleep. This was quite unusual for me. My norm would be to sleep about seven hours then awaken without an alarm. I started becoming irritable and little things would bother me. I then
decided that I should take a vacation and relax as my doctor had advised. I took my family and headed to Arizona for a visit with my parents. While there I still had the early awakenings, spacey feelings, vision problems and irritability. We spent seventeen days there and my symptoms did not
improve. Upon returning I called my doctor and made an appointment. After explaining to him my vacation didn't help and that I didn't feel I had any extraordinary amount of stress, he sent me for more blood tests and thyroid TSH test. Test results returned and the only thing out of range was the blood glucose. It was on the high side. The problem I found out later was that I did not fast for the test because I was not instructed to do so. He in turn sent me for a glucose tolerance test. During that test I developed the spacey feeling that I told him about and I was happy at that time
because I thought this might lead him in the direction of finding my problem. The test results returned a normal reading. When explaining to him the spacey feeling that occurred during the test, he looked at me with a perplexed expression. He again told me he thought my problems were stress related or the fact I might be depressed and did not

know it. I questioned how that could be, because the only thing I could be depressed about was that he was not finding what was wrong with me. I had given it quite a bit of thought and came to the conclusion that there wasn't anything in my life that could be causing this anxiety or supposed depression. I had a good job, good marriage and a healthy growing child. He in turn told me that sometimes people develop a chemical imbalance in the brain. My rhetorical question was; "Why now after forty years of my life". He didn't have an answer for me.

My sleep problems continued to get worse. I was having trouble falling asleep; insomnia was becoming the norm. I decide to consult a nutritionist that we knew had helped several of our friends. Upon explaining my symptoms to her she told me I had blood sugar problems and that my nervous system was shot. She instructed me to change my diet and begin taking a plethora
of supplements. I called my doctor and he said to go for it. After starting the regimen within days my jaw tension began to disappear and my nerves were feeling a little better. By this time fatigue was starting to set in. Not sleeping was taking its toll on my adrenals. The people I worked with
were beginning to think I was loosing it, everyone except my wife thought I was stressed out. I began begging my doctor for tranquilizers as I thought it was my only hope to calm myself. He reluctantly prescribed a low dse of Zanex. They helped in the beginning but eventually I started taking two and three at a time to get the desired response. Neurological problems were now starting to set in. I was developing numbness in my left hand and foot and tinnitus in my left ear. Fatigue was getting worse and I was down to working about two hours a day.. I would lie down and my brain would not turn off. I would lie still so I could conserve my physical energy but my mind would just race. I would get adrenaline rushes and then tachycardia would set in. For hours I would lay awake, adrenaline surging through my body. I began to develop frequent urination, digestive problems, memory loss, vivid dreams, muscle tremors, depression and irritable bowels. After dragging myself to the doctor once more, I told the nurse I needed to see him immediately. She in turn brought me into a room and I lay down and waited for him. Upon his arrival he sat
down, crossed his legs, and paged through my records, then asked; "Now David, What seems to be the problem"? If I had the energy I might have grabbed him by the neck and choked him. He began to tell me about psychosomatic illness and that the other possibility might be that my wife
and I had been childless for 15 years of our marriage, due to fertility problems, and that the stress of becoming parents was now taking it's toll. I began to break down and he told me that he thought I needed to go talk to a psychiatrist. He then proceeded to give me Zoloft, a medication for depression, and asked me to give it a try. After crawling out of his office, I started to wonder how I was going to tell Patty. I decided to take my family to the seashore for the weekend and figure
outhow I was going to explain to Patty that the doctor thought she was not paying enough attention to me and that was possibly my problem. After a long weekend of crying and soul searching we decided that he was missing something. We knew each other too well for this to be the problem. We had been through enormous amounts of fertility treatments, doctor's visits and
support for our infertility, including psychological testing for the adoption process and nothing out of the ordinary was revealed. Our adoption was a blessing, for it made us the happiest parents on earth. I contacted my nutritionist again and made an appointment.

She in turn referred me to another doctor that she thought would be able to help me. After arriving at his office, the receptionist started to take my personal information. The first questions she asked me was; "Why are you her?" My response was; "My doctor thinks my problems are all in my head!"
After listening to my story, and looking at all of my test results the doctor asked to look in my mouth. Bewildered, but agreeing, I opened my mouth and with a tongue depressor he proceeded. He then made the comment about having allot of metal in my mouth. I replied that I had it since I
was a child. He then proceeded to tell me that he suspected I was suffering from mercury poisoning. After ruling out work related exposure, he told me he suspected it was coming from my dental fillings. My reaction was; "you have got to be kidding me"! By this time my mental state had deteriorated to the point that my comprehension was terrible. He then proceeded tell me
that he was going to do a full metabolic profile and test for mercury. He then gave me a book to read. The title of the book was "It's All In Your Head, The Link Between Mercury Amalgam And Illness" by Dr. Hal A. Huggins. That night I sat down and read the entire book, it wasn't easy. I was elated to think that this might be the answer to my prayers. I then decide to take a look at the dates of my dental visits and found that every time I had a dental visit, I would be at the doctors within a month complaining about symptoms. The tests that the doctor ordered were out of the ordinary, but the lab was familiar with him, and they told me it was not unusual for him to run
them. After twelve vials of blood and containers to collect urine, I was on my way. The protocol was for me to collect my urine for twenty-four hours then return to his office for an injection of DMPS. The DMPS was to draw out the mercury that had been stored in my tissues and dump it into my kidneys for excretion. The test results were as follows; pre DMPS was 3 mcg/L in a 24-hr period and post DMPS was 54 mcg/L. The reference range is 0-20 mcg/L. He also tested for Nickel, Lead, Aluminum and Arsenic. Nickel was 69.9 with a reference range of 1-5 and Arsenic was at the top of the range with 24. Aluminum was within normal range. These levels were the
highest that he had seen in a patient. My TSH level, that is Thyroid Stimulating Hormone, had gone to 11.81 and the normal range is .35-5.50.

Now I understood why my body was in a constant stated of being turned on. The mercury was interfering with my endocrine system. These tests proved to me that my mercury fillings where indeed poisoning my body. After consulting with my new doctor, he told me I had to remove the
sourceof poison in my body. I now had to find a dentist that was familiar with this type of situation. Obviously, my former dentist was not the one. I would not get better as long as mercury remained in my mouth. I did find a dentist that knew the Huggins protocol for removal. I must tell you I had reservations about this and had asked for references to other patients that went through the procedure. After talking to a teacher who had severe asthma attacks, and was taking nine pills a day, had her fillings removed and within five month's was down to one pill a day and no attacks. Her experience had helped convince me this dentist knew what to do. My experience was unbelievable, for the first time in my life I was happy to be sitting in a dentist chair. The first visit involved removing the left lower quadrant that had most of the fresh amalgam placed. That
afternoon I experienced an increase in energy and that night was the first time in months that I had fallen asleep without a tranquilizer. The next few weeks proved to be an experience I will never forget. The dental office was a place were I was going to become healthy again. The compassion and expertise shown by the staff in that office was a great relief from what I had been through. With each visit I knew I was on the road to recovery.

After the poison was removed I had temporary fillings installed until the crowns and bridges could be made. My teeth had been
insulted tremendously. There was some pain but when the last amalgam was removed I was a very happy man.

The day after the last removal I went to the doctor's office for another DMPS push. It was to help clear some more mercury and also to see where my levels were. Test results were: pre DMPS was 5 mcg/L 24hrs and post being 8 mcg/L 24hrs. Arsenic had dropped to 11 mcg/L 24hrs and Nickel was not detected. Upon questioning my doctor as to where the arsenic came from, he said he suspected it was from the amalgam also. Arsenic is used in metals to retard corrosion, how nice that another poison is added to the mix. Within two weeks after the removal I started to have an increase in energy and some relief of the neurological symptoms. The numbness inmy
left hand and foot started to abate and my mental processes became better. I still had endogenous depression, digestive problems, vision problems and ringing in my left ear, but that was minor compared to the other symptoms.

I commented to my dentist that my mouth tasted different, I then found out that it was the fact that I no longer had metal in my mouth. It was a metallic taste that I had always thought to be normal. In Doctor Huggins book he notes that he has seen patients with neurological symptoms associated with the side of the body that amalgam had been placed, I can confirm that finding. The next occurrence was a surprise to me. I woke up early one morning with terrific eye pain, both eyes felt as though someone had punched them. My doctor or dentist was not sure what it was from. I
then made a call to the Huggins Diagnostic Center and was told that yes they had seen patients with this condition. I developed dark circles around the orbital sockets, they were tender to the touch, my sinuses became tender, and my throat was sore but I was sleeping without tranquilizers. My body was now ridding itself of this poison. My next test was for adrenal function, and it proved what I thought, suppressed function. Since the removal of my amalgam I have been detoxifying with the use of vitamins, minerals, homeopathics and some prescription drugs. The list of symptoms that are totally gone are those that follow: anxiety, tachycardia, irritability, muscle tremors, frequent night urination, low body temperature, vivid dreams, irregular heartbeat, insomnia, metallic taste, depression, increased sensitivity to sounds and light and most fatigue
except after strenuous physical activity. Symptoms that have improved are:
concentration, gastrointestinal problems, vision problems, allergy to milk products, sensitivity to certain chemicals and odors, blood pressure and ringing in my left ear. The most notable problem with my sinuses has all but disappeared. I have not had a sinus infection or major cold since my
removal. I have been through two winters now, and not one infection.

My immune system is now working much better without the load of mercury. I often wonder, in retrospect, if the mercury had anything to due with our infertility. In closing I would like to thank the health care professionals that helpedme onto the road of recovery. If it were not for them, particularly my bio-compatible dentist, I know I would have eventually been diagnosed with multiple sclerosis and destined, as so many are, to a life of misery. The facts are there. It is a no brainer when it comes to mercury. Mercury is a poison. There is NO safe form of Mercury in living tissue. Th chronic poisoning of modern man, as Dr. Vimy points out, will go down in history as one of the many mistakes man has made in this century. We are now seeing the effects that the tobacco industry has on society. Hopefully, with persistence, determination and understanding it

will also be said; for that of mercury amalgam. In some cases, the Hippocratic oath that doctors and dentists take, "Though Shall Do No Harm to Thy Patient" seems to have been forgotten. This nation, The United States of America, is first in so many ways; computers, space exploration, technologies of all sorts, but is running way behind in the use of bio-compatible dental materials. Think about it! The dental profession still teaches and uses a technology that is
over 150 years old!

July'2000

Congressman Dan Burton
Committee on Government Reform
Cannon House Office Bldg.
Washington, DC 20514

EDEMA, FIBROCYSTIC BREAST DISEASE
Myasthania Gravis, Polyglandular Auto-Immune and More
HAVE VANISHED

Dear Congressman Burton:

I wanted to share my nightmare from mercury dental amalgams!

IT'S LIJKE A MIRACLE, really. Years of nightmarish atypical **edema** are going away. **Severe fibrocystic breast disease** has virtually vanished. My eyeglass prescription has improved 50%. And I'm an optician!

Still have a lot of the "overt" signs of mercury poisoning, the weird skin flushing, odd lesions, and the list goes on....temperature changes are still dramatic...very little tolerance for heat or sun right now. But my auto-immune problems are so much better that it's truly like seeing a light at the end of a tunnel.

I'm actually able to sleep through the night without getting up literally ten times to Go to the bathroom..my quality of sleep is so much mproved.what a difference that makes in how one feels. I've been plagued with severe problems (chronic fatique, environmental illness-allergic to virtually anything, Myasthania Gravis, Polyglandular Auto-Immune failure (lost my ovaries, thyroid, adrenals, pituitary, part of my thymus, and soon)for over twenty years.....so this improvement is particularly amazing to me.

The smell of perfume still drives me crazy, and I can't promise yet that I won't "kill" someone for using "Bounce" fabric softener.....I swear, I can smell it and get immediately ill from a mile away.

But overall, life is so much better...I used to be on an extreme rotation diet.....can now eat almost everything.....went to Environmental Health in Dallas with William Rae Close to twenty years ago id the shots for years, followed the whole protocol-to no avail....but now things are clearing up. (Still think the world of Dr. Rae though-he did try to help me in a truly honest and forthright fashion)

Vanessa Strange <CASBAHP@aol.com>

July 10, 2000

Dan Burton, Chairman
Committee on Government Reform
102 Cannon House Office Building
Washington DC 20515

Dear Congressman Burton:

NO MORE COLITIS AFTER AMALGAM REMOVAL

How did I feel between '91 and '00? When did I get your life back?

I overcame a horrendous case of colitis within two months after the last quadrant of fillings was removed in May 1991. I had had the colitis for two years. By July 1991 I no longer bled through the colon, no longer woke up with night sweats, no longer felt like I had the flu all the time, and no longer had to clear phlegm from my throat all the time. Other, older symptoms persisted (such as dry eyes, dry skin, and fatigue), but they got better over the next 18 months, and then I hit a plateau. The colitis has never come back.

My health took a huge hit in the fall of 1995 when two root canaled teeth in the lower left jaw became infected and ultimately caused a jaw infection. In the course of looking for he problem, my surgeon opened up the upper left wisdom tooth, and I never recovered from that. I have since had successful surgery on the lower left root canal sites. My last remaining nightmare is the infected upper left wisdom tooth socket and the sinus infection it has caused.

Kip Sullivan
E-mail: Kip@aol.com

251 Kimberly Lane
Lake Forest, IL 60045
April 2, 2000

Congressman Dan Burton,
Chairman of Committee on Government Reform
Attn: Gloria Markus,
2185 Rayburn Office Building
Washington, D.C. 20515

Dear Congressman Burton,

I would like to inform you of a health problem that is unrecognized and uninvestigated in the United States. It is dental amalgam mercury toxicity. These "silver" fillings are 50% mercury, 30% silver, and the remainder is made up of various amounts of copper, tin, and zinc. Mercury is mor toxic than lead, arsenic, and cadmium. There is no known safe threshold according to governmental standards.

Research has shown that mercury vapor is constantly being released from the amlagam fillings. It takes the body 1-2 months to eliminate one-half of one absorbed dose. A person with mercury amalgam fillings are exposed 24 hours a day, 365 days a year, year in and year out. Over time mercury will build up in the body. Biochemical damage will occur long before clinically observable signs and symptoms of mercurialism. This may take many years and may be impossible to connect the two. Mercury is a metabolic poison and can damage any organ in the body. Mercury targets the brain and nervous system along with the heart, joints, kidney, thyroid, adrenals and pancreas. It is a strong suppressor of the immune system. It can damage numerous enzymes and hormones. It has been proven that mercury passes through the plancental membrane and enter the unborn baby. It also passes into the milk of nursing mothers.

I have been sick my entire adult life. Through the years I kept adding symptoms even though I lived a "healthy lifestyle". Prior to having my amalgams out 9 years ago, I was quit ill. I had chronic fatigue, severe allergies, constant headaches, nauseated sick all over feeling, tingling in extremities (pins and needles), numbness in legs, ringing in head, internal trembling, digestive problems, food intolerances, insomnia, chronic sore throat, burning mouth, flu like warmth, fibromyalgia like pains, dizziness, frequent diarrhea, and periods of extreme weakness. After removal, I have and still am detoxing my body from mercury. It has been a long road to recovery but I have gained back over 90% of my health. It makes me angry, that my ill health in adulthood could have been prevented by not having mercury put in my mouth as a child.

I have become a DAMS (Dental Amalgam Mercury Syndrome), Coordinator in Illinois

in order to help others to avoid the health problems I have gone through.

Please Congressman Burton, bring this serious health matter to you committee and start the process to get mercury amalgams banned.

Sincerely,

Karen Truskowski
DAMS, Illinois

John G. & Ruth Van Wyk
2477 Carbon Trl.
Leighton, IA 50143-8035

7/11/00

Dear Sirs (Brown Swanson & Turner)

Please help us with the informed consent issue, of placing Mercury fillings in a patients mouth which is very hazardous. Help us get the message to the public.

Both I & us had our mercury fillings removed and replaced with Compatible fillings with Astounding Results. Health is very much improved.

Please help us get the message out to prevent and protect our nation of people, to be informed on this issue and improve our populations health and performance

Sincerely, (We care)
Mr. & Mrs. John G. Van Wyk
2477 Carbon Trail
Leighton, Iowa 50143

THANK YOU!

January'2000

A Personal Account of Joyce Van Haaften's Experiences with Mercury Amalgams

NEURALGIA-LIKE PAIN, FATIGUE, NUMBNESS, TWITCHING. MEMORY LOSS, UNABLE TO CONCENTRATE

My experiences with amalgams began when I was very young. My teeth seemed to be prone to cavities and my molars came in with hollow centers. They were promptly filled with amalgams. As a result I had more amalgams than most people did and some of them were very large. In hindsight, I think that some symptoms of mercury toxicity began to surface many years ago. I sometimes felt unexplained fatigue and had difficulty concentrating, but I just told myself that it was because I was getting older or because I was too busy.

In 1991, however, when I was 45 years old, I began experiencing severe neuralgia-like pain in the right side of my face and head and then more general head pain, which was always worse on the right side. No matter what remedy I tried, the pain never went away.

During the next three years I went through many tests including a CT scan, an MRI of my head, an MRI of my neck, an EEG, blood tests, and a hormone check, but the only problem that showed up was a disc problem in my neck, which was not thought to be the cause of the head pain. I was treated with nerve blocks, heat therapy, ice therapy, and different kinds of drugs, but nothing helped. Some of the drugs the doctors prescribed during that time made me feel worse, so I took only ibuprofen for the last several months of my ordeal. I also tried rest, supplements, dietary changes, a walking regimen, neck traction, and chiropractic treatments, but they did not help either.

During that period I also spent three weeks in the Mercy Pain Center in Des Moines where a biofeedback machine confirmed what I already knew. The pain was not stress related. The people at Mercy helped me learn to cope with the pain, but were not able to alleviate it. They recommended a new neurologist who specialized in headaches and sent me home.

I continued to feel terrible. I couldn't concentrate, I had trouble with memory loss, and I felt an unexplained restlessness. I also began to notice many other symptoms including fatigue, muscle spasms, muscle twitching, tingling, and partial numbness in my hands, feet, and right side of my face. I tried to keep my life as normal as possible, but it was very difficult. My new neurologist sincerely tried to help me, but she did not have the answer to my problems and I did not know what to.

A breakthrough came in November of 1993, when a very large amalgam broke away from a molar and was replaced by another large amalgam. Several days later, although I didn't

make the connection at the time, I began to experience neuralgia-like pain in my upper legs. It was so severe that I could not rise from a chair without help. At the same time I began to experience tremors, especially in the evenings. It was then that I finally realized that I had a systemic neurological disorder and that all of my symptoms were probably related. I wondered whether I had been exposed to poisonous chemicals on our farm, although I knew it was unlikely because we do not use chemicals during the winter.

Then by the grace of God I remembered hearing something negative about amalgams on the radio. (I had heard just a little bit of a conversation between WHO's Jan Mickelson and members of Dental Amalgam Mercury Syndrome of Des Moines, but that little bit of information was to turn my life around.) After calling the station and getting information from DAMS of Des Moines, I learned that amalgams contain mercury and that my symptoms were consistent with those of mercury toxicity, but it wasn't until I looked into my mouth and saw the amalgam "tattooing" on my gums, that I was certain. The gray discoloration was irrefutable evidence that the mercury and other metals were not "locked in" the amalgams as dentists had apparently claimed.

In January of 1994 I contacted a mercury-free dentist and had all of my amalgams replaced with composites. I was given oral DMSA as a chelator during removal and also had five root canals extracted. Shortly after the amalgam removal my dentist lost his license because of the mercury issue, but I began to slowly improve as a result of his work. Over the next two months I began to feel better generally and all of my symptoms disappeared except for the head pain and the memory loss. Just as I began to doubt that the head pain would go away, it did. For the first time in three years I had no pain and the pressure of my head against a pillow did not hurt! A few months later I was surprised to notice that my eyes were not as sensitive to light and that I did not need nearly as much sleep.

Four years have passed since amalgam removal and I am doing very well except for short-term memory problems and a feeling that my brain is not processing information the way it should. I am again climbing to the top of our grain bins to check the grain and I have won bow saw and one-woman crosscut saw competitions at the Iowa State Fair. I believe that amalgam removal is the only explanation for my getting well. I have been careful not to overlook any other possibility.

I thank everyone who helped me get well and I thank my wonderful husband, family, and friends who supported me all the way. My husband told me later that during the worst period of my illness he considered resigning his position as county sheriff to take care of me. Most of all I thank God who has my life in His hands.

Like most dental patients, I was never told that amalgams contain mercury and that mercury can cause neurological and other problems. With their silence, dentists have unintentionally, but effectively prevented the flow of all information that could connect amalgams with illnesses. Adding to the problem is the chronic nature of the exposure and the number of years it can take for subtle changes to be noticed. As a result the cause and

effect relationship between amalgams and illness has been difficult to establish. Not difficult to establish, however, is proof that mercury from amalgams is released at dangerous levels and that mercury is dangerous to life.

I have become an anti-amalgam activist because I believe that putting mercury in the mouths of human beings has been one of the biggest medical blunders of modern times. I also believe that dental patients have a right to know the facts about amalgams and dentists have an obligation to inform them. Especially urgent is the need to warn pregnant women. Because of continually emerging research, the dental industry is fast losing its ability to plead ignorance about the dangers of amalgams. The issue is very complicated and far-reaching, but it is time for all parties involved in the debate to get together and find a solution that is in the best interest of the public.

Joyce Van Haaften
189 240th Place
Pella, Iowa 50219
515-628-4612

March 25, 2000

The Honorable Stephen Horn
2331 Rayburn HOB
Washington, D.c. 20515

Dear Congressman Horn:

I understand that you are on the committee for Government Reform. In accord with that, I would like to bring to your attention the amalgam filling issue. Silver dental amalgam fillings, with their 50% mercury content, are the source of one of the most under-reported health problems in this country. The mercury in these fillings is not sealed but leaks into the body via breath and saliva. Experiments have shown that mercury from fillings, in pregnant women and animals, is drawn to the placenta and the milk ducts of the mothers, thus affecting the newborn.

Compared with the effects of eating fish, though they contain mercury also, the effects of slow leaching of mercury into the body are very serious. Inside the body, mercury combines with body bacteria to form Methyl Mercury, a deadly compound. DAMS' position is that there is no safe level of mercury in the body. In our experience of dealing with the public's questions about their mercury-related health problems, we have seen far too much suffering to remain silent about this issue. If mercury is so good for people, why do female dental personnel world-wide have 40% less fertility than the normal population? Why do dentists suffer from the highest suicide rate of all white collar professions?

Mercury toxicity symptoms from fillings consist of the following (and this is not a complete list): muscle weakness,

insomnia, memory loss, depression, gum problems, amalgam tattoo (blue staining of gums above fillings), excessive sleepiness, premature rheumatoid symptoms, fits of temper, loosening of teeth, metallic taste, concentration loss, loss of intellectual functioning, frequent infections, tendency to triggering of auto-immune diseases (such as Lupus, MS), possible link to Alzheimer's as a contributing factor, numbness of extremities, incoordination, anxiety.

It is DAMS' position that silver mercury fillings are not good for anyone but they are particularly damaging for that 1 - 15% of the population that has no ability to withstand foreign chemicals in their body. America should be looking to countries like Sweden which have banned amalgam fillings. In that country an insurance study was conducted, showing that workers who had had their amalgam fillings replaced used 40% less sick time than other workers who still had their amalgams. We should be moving in this direction. The use of mercury in fillings deserves a congressional investigation!

Sincerely yours,

Carol J. Ward
Vice President- DAMS,Inc.

August 1987, Health Consciousness — 35

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SPECIAL REPORT NO. 21

MERCURY UPDATE ..... *by Roy Kupsinel, M.D.*

Amalgam Toxicity Case History



Carol Ward

By CAROL WARD

MY HISTORY BEGAN at the age of seven or eight when the first silver/amalgam filling was placed in my mouth. Up to that time, I had been a physically normal child, though quite susceptible to colds. A few months after the first dental work, my mother took me to a doctor to have me checked for a vaginal discharge diagnosed as "Monilia". I noticed at around the same age that I had to get up at least once a night to use the bathroom, after retiring. In the succeeding years I had many cavities due to excessive consumption of sweets. By the age of 12, I developed dark patches on my shoulders after the rest of my suntan went away. My period arrived at the late age of 15. Also at 15, I had an accident on a bike and broke 3 teeth. The dentist installed 3 crowns, containing mixed metals and undergirded by mercury. I developed nervous problems, beginning around this time. Two weeks after the crowns were put in, while playing in a young peoples' concert, I experienced 20 minutes of continuous palpitations. This had never occurred before or since. The following summer I felt very weak, suffered from continuous insomnia and strange headaches. I lost my self-confidence, acquired many fears, and became convinced that something was seriously wrong with me. My family felt my problems were emotional. I felt they were physical.

As a college student, I noticed an acceleration of my nervousness which couldn't be accounted for in any logical way. I was outwardly in fine health, in a beautiful campus environment, having a wonderful experience with courses, fellow students, and teachers. At the age of 19, I developed a tendency to hyperventilate if exhausted or under intense pressure such as exams.

In my early 20s, I went through a stage of eating so many sweets that I was faced with having a raft of new fillings. The dentist I had at that time humorously remarked that

my crowns were the best teeth in my mouth. After getting the fillings, I came down with a virus and did not seem to recover in the normal length of time. Instead I was tremendously sleepy, falling asleep at a moment's notice in cars or buses. This was a dramatic change over a 3-month period, from my former vitality and health.

At the age of 24, I worked in a dry cleaning establishment where the cleaning was done on the premises. The odor from the solvents was very strong. I noticed after a while that I was emotionally very low, tending to cry frequently, and have some suicidal thoughts. While I had some personal reasons for this depression, it seemed out of scale. I quit this job after 10 months and went back to my home in another state to regroup. I didn't expect to fall ill for the next several months of a mysterious problem that robbed me totally of energy and carried with it intense depression. It was as if 1000 weights were dragging me down; I could not even iron a piece of clothing without forcing myself to do it. An immense tiredness filled my days though by early evening, I experienced some improvement. Friends who saw me socially during that period claimed that I appeared to be "drunk". That is how I felt in one respect — stupified. My fingers were often cold and almost numb. My family's solution to my problems was to get me to go to group therapy sessions 3 times a week.

Feeling that I was getting nowhere, I returned to the state where I had begun my graduate studies, prior to working in the laundry. The change proved helpful, removing me from a stressful home environment. I completed my degree, and got a job in a large city. The only unusual health problems I had in those years, by now my middle 20s, were a long-lasting ear infection, low blood pressure, and reactive hypoglycemia. One position I held involved an inordinate amount of overwork and stress; this was when the hypoglycemia developed but it was treated and I did not have to stay on the diet more than 1-2 years. However, the stressful work situation caused arthritic types of joint pains and chest pains. These symptoms disappeared when I transferred. I realized at around that time that I was sensitive to chemicals as the building I worked in was painted; as it was unventilated, the full force of the paint smells was overpowering. I developed asthma after many bouts of bronchitis.

Desiring to build myself up, I began taking an interest in the outdoors. At the age of 30, I joined a hiking club and found that I was a natural hiker. I used to hike at least once a month for 10-12 miles. Being out in beautiful, secluded places and exercising I found to be the best method for alleviating stress and building endurance. At the age of 37, I took up jogging and kept this up for many years, as well as the hiking. My jogging led to my participation in a 5-mile marathon in 1978 in the 85 degree heat.

My health problems recurred at the age of 37 with hepatitis. It took me a full year to recover any degree of energy but exercising seemed to help build my endurance. However, I found that after the hepatitis, I used to wake up from naps with cold arms or legs. Also I could never again drink more that ½ glass of alcoholic beverages without stomach distress and a sensation of discomfort in the liver area the next day.

At the age of 39, I experienced a time of great personal stress but I noticed that the symptoms I experienced seemed so quick and so severe that it didn't make sense. I became much more sensitive to the cold. Out of the blue, my mind seemed to race and to develop obsessions of a melancholy sort. I began a 2½ year battle with depression; finally realizing I needed professional help, I consulted a depression clinic and was put on lithium. The strange part of this depression was that there were other, unaccountable symptoms that went with it. I began to experience minor, but annoying short-term memory loss that took the form, initially, of forgetting whom I was calling if a distraction occurred at work while I was making a telephone call. Sometimes I literally could not remember even on hearing the person's voice and I would have to hang up. These problems were worse if I had slept poorly the night before. I began having a lot of insomnia, with agitation.

My working day at that time involved a heavy commute with frequent waits in traffic. I began to notice that while under stress in traffic, I would feel an inner trembling or nervous weakness of major sort. This nervous reaction tended to happen more when I was tired; I began to sense that my immune system was playing a key role here, most of the time, keeping the symptoms under control. By the spring of '83, I fell while on a hike. This seemed ominous to me as I had never been clumsy in my life. However, most of the time I hiked with my normal strength and my life went on as usual.

By the fall of '83, I was putting additional stress on my system by commuting an hour after work to see a friend regularly, going to class two nights a week and launching several other projects. I experienced weakness when crossing the street after work; it got so bad that there were times I wondered if I would make it across. In conversation with a friend who is knowledgeable on health issues, I happened to mention these symptoms. As she talked about hypersensitivity to amalgam fillings, I felt a dull sensation of horror right down to my toes as if I knew subconsciously that she was right. But I wasn't ready to deal with it.

Paralleling these events, I had begun to have urinary frequency and my waist-line kept expanding. I put on 12 pounds in one year which was totally unlike my naturally thin physique. My expanding waistline and bloated stomach seemed to go with increasing digestive problems. A routine medical check-up revealed nothing unusual except a mild mitral valve prolapse.

In February of 1985 I contracted a flu. It seemed like any other routine flu except that afterward I became so weak I could hardly open a window. When that cleared up, I got the first of a series of four urinary tract infections. The diagnosis was cystitis but the symptoms seemed more serious than that. I had low grade fever and discomfort in the lower back. The antibiotics didn't work and the doctor changed my medication. The infection cleared but in a few days, another would take its place and I grew steadily weaker. By June of '85, I had switched to a urologist and was told to get a kidney x-ray. I could barely walk from my car to the hospital for the x-rays. The urologist told me I had no kidney involvement. The 4th infection found me in a state where I could hardly breathe. I stopped taking the antibiotics, knowing of my tendency to be allergic to them. By early July, I was a complete physical wreck. My mind was buzzing, I could not read even a 1-page newspaper article, I could not remember something I had done two minutes ago. I was confused, distracted, and depressed — the sensation was that of a "devouring depression".

I could no longer work even part-time. I was so weak that eating a meal was an effort and my head had to be supported from behind by a high-backed chair. When I had a massage, the person noticed that my kidneys were outlined in red. I had a metallic taste in my mouth; I had almost constant kidney pain. My legs were cold as ice and strangely enervated. When I woke up in the mornings, my eyes were virtually crossed for the first ten to twenty minutes. I had problems with balance, especially if I had to get up at night. It took 1½ hrs. for me to get myself going in the morning. I found that strong sunlight made me very uncomfortable. I was dizzy a good deal of the time; I could not comfortably ride even as a passenger in a vehicle because I felt I would keel over nor could I drive for more than 5 minutes at a time. It was difficult to walk one city block.

The five doctors I consulted from May through August '85 did not know what to do for me; their diagnoses varied from depression to sympathetic nervous system dystonia. At this point I was no longer able to work or to do housework. I was having migraines and my blood pressure was high. A friend, active in the holistic health movement, heard of my dilemma; she arranged for me to see a nutritionist, renowned in the city for dealing with serious cases. I saw him on August 18, 1985. After filling out a very thorough questionnaire on my medical history, my case was diagnosed as hypersensitivity to mercury in my amalgam fillings and severe candidiasis. I even had candidiasis outbreaks on the outside of my body. Blood tests later showed that I had a score of 195 on the Candida antibody test. I went on a nutritional regime designed to protect my system from the mercury and to counteract the toxins produced by the candida. I was allowed virtually no carbohydrates. I was on several amino acids before the meal and a raft of vitamins and supple-

ments with it. Also, I was on a very high dose of ascorbic acid for my residual urinary symptoms.

Within 3 days I was able to do a few things at home. In 10 more days I was back at work, albeit pale and somewhat weak. The next step was to have my fillings removed; they had already been tested at the dentist's by an Amalgameter. The reading on the worst quadrant of my jaw was a minus 25. My first appointment was Sept. 17; the dentist removed the quadrant of amalgam fillings with the highest reading. Two weeks later the next quadrant was done. My mid-November the 13 fillings were replaced by ceramic fillings (Hercuite), including 3 crowns with mercury underneath. As each group of fillings were replaced, I had more energy and a feeling that I could "see" more clearly. I had had some visual field problems during the summer and these disappeared. I began taking walks with something like enjoyment though I still had occasional leg cramps and unpleasant nerve enervations in the legs. My migraines became infrequent, as did my fits of irritability and temper.

In November I consulted a physician for candida testing and for tests prior to having chelation. I was put on Nystatin for several months, then switched to Nizoral. From the end of January on, I had chelation weekly 'til spring, then bi-weekly since then. After the first treatment, I felt more creative and alive, mentally. After the 2nd treatment, I was able to walk up the large hill below my house without the sensation that my legs were filled with lead. There were times I would feel too weak to go to the chelation treatment but would feel better after it. My blood pressure soon went down to 110 over 70 and has remained there. My memory loss, which had been very severe, reversed itself substantially over the next few months. I began to go on 2 hr. hikes in the Spring of '86 though after I went on Nizoral, I had somewhat less energy. The Nizoral seemed to improve my urinary problems markedly, however.

As the chelation treatments drove the mercury out of my body, I began to recover a measure of my lost self-confidence. In May '86 I made my first long trip for a weekend though my energy was limited and I still had to go to bed by 10 P.M. By Sept. '86 my color had returned to my face. The only new symptom I had was numbness of the toes, technically referred to as "paresthesia". I began taking thyroid in December '86 and my body temperatures went up to nearly normal.

One year and nine months since I began being treated for mercury hypersensitivity, I have made dramatic strides but still have some health handicaps. My energy fluctuates greatly from day to day; I have much greater susceptibility to colds and flus than the average healthy person. My sleeping pattern is fragile and the great effort required by my way of life (strict dietary regime, large numbers of supplements) is at times depressing and is always costly. I have to admit that my recovery on any basis seems miraculous. The very best medical care on the part of experts was responsible, in large part. Also, my utter determination to follow their directions down to the last detail.. and the loyalty of my fiance. It is hoped that in the future, people can learn from the example of someone like me and choose safe dental technology, unprocessed foods, clean water, and whatever else is necessary to insure the health of their children.

This is Tom Warren's story of recovery from Alzheimer's Disease after discovering that the mercury in his silver" dental fillings had caused his illness . He is the author of "Beating Alzheimer's".

To: Dan Burton, Chairman
Committee on Government Reform

Re: **Alzheimer's Disease and Mercury**

Dear Senator Burton and Committee:

My wife, Louise, best tells my Medical Biography. At the time I was diagnosed, June 11th 1983, every physician I went to, told me that I had Alzheimer's disease and the longest anyone expected me to live was seven years. It is very difficult think back in time to recall those events. I understood what I read for about four inches of print, but could not hold on to the thought past that point. I could not carry on a normal conversation more than two minutes, if that long, quite often I had to look up my own telephone number. I even lost the ability to remember close, newer friends names. I felt like I'd been run over by a truck and since I have been run over twice can verify that is an accurate description. More importantly was the fact that my personality changed. I became an overbearing and cantankerous. My irrational behavior devastated our whole family.

That's one thing about Alzheimer's disease; it destroys everyone around you, everything you worked for, everything you wanted to do for your family, it almost turns you into a vegetable. If it had gone any further it would have.

The whole of my medical history will be in the new book. Writing it is more than a little depressing. I do not like thinkimg about that time. It is painful. So for now, I'll let Louise continue this part of the story. But before I turn it over to her I'll tell the reader these two things, first, almost every day I run into people who exhibit sub clinical symptoms of short-term memory loss, or other medical problems their physicians cannot diagnosis and I find a common thread of similar sub clinical symptoms. Secondly, every once in awhile someone tells me, "You saved my life."

Tom Warren

Louise's Story

As the articles about Alzheimer's state, the disease is insidious and hard to recognize at first. The symptoms are vague and you wonder if there is really something wrong and/or what is wrong? All too soon you are certain something is not right and you pray that it is not what you have begun to suspect.

My husband was having memory problems and had started reacting in anger to the slightest provocation. As his memory declined, I was becoming more frustrated. He would repeatedly ask the same question. After the third time within a few minutes, I would ask "Tom, don't you remember you just asked me that." It was at this point I insisted Tom see a doctor who sent him for a CAT scan.

(2) Tom Warren, Alzheimer's Disease

On June 13, 1983, which was also the day that our daughter graduated from high school, we heard the diagnosis-Alzheimer's Disease. Our initial response was utter hopelessness.

The following week there was a Barbara Walters special on television about Alzheimer's Disease we were anxious to see. The program left us more depressed than ever, especially since Tom remembered Rita

Hayworth as a beautiful, talented actress. Understanding how little was known about the disease and that medicine had no idea how to help the patient was devastating.

Then Tom took a tour of the Alzheimer's ward at Western State Hospital near Tacoma, Washington. Whether this was a wise move is debatable. Fortunately, Tom's value system forbids suicide. His first thought was that he would rather die any other way.

A period of deep depression followed. Tom hoped to die quickly. When this did not happen after a period of time, he prayed that through him the cure for Alzheimer's be found.

At the time Tom was 50 years old. I was 39. Tom's mother had spells of mental illness and obvious memory problems. (When Tom's AD first occurred, we did not connect his mother being a dental assistant to her ailments.) She died at 92. The physician told Tom that he might have as long as seven years to live. The prospect was not something that I could dwell on. I refused to think about the probable outcome.

We made a decision not to sit back and wait for the inevitable. The future was too bleak to accept.

Being a pharmacist, I understood the published research papers. Reading every pharmacy article relating to AD didn't give any encouragement. Almost all of the writing was directed toward managing the patient or coping with the stress of being a caregiver. Ironically books on AD still have this same theme. Treatment is "waiting for God."

We frequented health food stores buying books about problems similar to Tom's symptoms. Tom could understand what he read and would mark anything that seemed important because he couldn't remember the ideas more than a few seconds. I reviewed the same material in the evening after I returned from work. By this time Tom had not been able to work for a while. He couldn't think or remember well enough.

If anything suggested possibilities, we investigated carefully. Tom went to physicians who were referred to as being preeminent within their specialties in the books that we read. Some things seemed to help, others were a waste of time and money.

This has been a lengthy learning experience. Our search started with allergies including inhalants and foods. Tom tried acupuncture, chelation, different nutrition ideas and a half dozen other things. A homeopathic MD helped in the beginning. Then in May of 1985, Tom told another doctor to give him a Heidelberg stomach acid test that indicated he had no stomach acid. He began taking betaine HCl and digestive enzymes along with certain vitamins and minerals. In 1986, we learned there is mercury in silver amalgam dental fillings through an article in the Well Mind Association newsletter. Tom tried replacing all of the silver fillings in his mouth, but that

(3) Tom Warren, Alzheimer's Disease

was before Dr. Hal Huggins' materials-biocompatible blood test was ready, and the replacement dental fillings caused severe swelling for weeks. An oral surgeon removed all of his teeth and amalgam fragments within his gums and jawbone. In June of 1987, a 2nd CAT scan was negative. Later we learned about cavitations (jawbone infections), and had over twenty cleaned up, which further improved his health. The journey is basically over but we continue to read and learn and do take nutritional supplements.

The stress of living with and caring for someone with Alzheimer's has been both emotional and financial. Unfortunately, I discovered that I am a stress eater and I gained 80 pounds during this time. Tom was not easy to live with. About 1/3 of people who have Alzheimer's become argumentative, antagonistic and develop dementia. This type of irrational behavior is predictable pathology of the Alzheimer's disease process. Tom's personality change decimated our entire family. As his wife, I had made a commitment "in sickness and in health." And, I remembered how my husband used to be. In June this year, we were able to celebrate our 33rd anniversary. It was a lovely day, Tom is easier going again, almost like his old self, and I'm thankful that we both are aware of each other and enjoy living again.

Tom is reasonably well, but his immune system has been damaged, so he has to be somewhat careful of his lifestyle. He changed careers and has become a writer with zeal to help others. A large research grant for AD was funded, in part, because of his first book, and there are research investigations that back up his discoveries.

It is especially rewarding to hear from other people that have recovered after reading Beating Alzheimer's. These letters make my day. One thank you note left me in tears. It reminded me how fortunate we are. I thank God that he has seen us through this struggle.

Sincerely,

Louise Warren
twarren@speakeasy.org (Tom Warren)

9501 Ave A
B'Klyn, N.Y
11236
02/14/90

Hello Anne,

What's doing? I have received all the info. and I am going through them. It makes me so sad, because I believe that because Mercury is a person it should not be what one would use to put in one's mouth.

I have enclosed the letter from the Ontario health minister when he replied to me. Please send it to my address in Antigua which is M. Williams

Crabbe Hill
St. Mary's
Antigua W.I

When the poem is properly typed, I send you a copy. Presently I have slight tremors in my fingers, please excuse the writing.

I will keep in touch with you. I will be writing to Mr Burton this week.

Presently, I also trying to get to a dentist to work on a tooth that's be worked on twice in Toronto - 6/99. I have quite a bit of pain, since my walking is not steady, I need someone to take me there - and he's far away - and everyone is too busy something I have to contend with all the time. and there are worst situation which I wouldn't go into.

I always thank God to be alive and I know I will be avoiding other people from getting into the same situation that I'm in.

- One mosquito does make a difference in a room.

Please keep in touch. Prayers for you and the wonderful work that God encourages you to do.

Mgt Williams

Ferreira

From: <FreKoss@aol.com>
To: <virginia@portone.com>
Sent: Wednesday, March 08, 2000 7:51 PM
Subject: Ralph Wood Wilson

1/15/00 2:11:42 PM Easter
LETTER SENT TO THE NATIONAL ACADEMY OF SCIENCES:

From: drwilson@quidnunc.net (Ralph Wood Wilson)
To: lhollida@nas.edu
From: Ralph Wood Wilson, N.D., M.S. Acupuncture

To: Laura Holliday, for distribution to the committee on
Toxicological Effects of Mercury Committee on Toxicological Effects of Mercury

I am a practicing naturopathic physician (who was once in M.D. medical school), and I am contributing the enclosed for your consideration. I want you to see that I and many like me are very concerned about the effects of metals on human function. I am sure you will hear a lot from other people. I have learned many sad life histories since I started listening for them after hearing about mental illness being affected by mercury (at a talk by a dentist in 1985). I wish I had time to give you, to make a longer presentation. But I have spent hundreds of hours helping promote awareness of this dental cause of illness, and it is an emotional drain to try once again and then continue to hear that the charlatan ADA is continuing to allow poison to be placed. They are killing people.

But you need more careful presentation of ideas. I put this together for a governor whose state was going to make a gag rule so dentists could not even inform their patients that mercury is in their "silver' fillings and may be a health risk:

I have been in the health care field for 30 years, 15 years of which have been in the alternative medicine field. I attended MD medical school for one year, then withdrew to pursue personal healing (of problems that began within a couple months of receiving several mercury fillings). Now as a naturopathic physician I appreciate both the medical profession and the alternative health care field for what they call to our attention as being of potential benefit for each person. I have observed many patients who were concerned about dental metals as a cause for their problems. Many of them can date physical problems from the placing of mercury fillings. One in particular had her face grotesquely contorted, and had twitching of muscles immediately after having a mercury filling placed above a gold crown in the lower jaw. She experienced near-complete restoration of her appearance after the mercury was replaced with a non-metal restoration.

One of the biggest factors I see is the ELECTRICAL EFFECTS of mercury. The ADA tries to say few people are allergic as if that is the most important problem. There is electricity generated by mercury fillings, higher than what runs the brain. When fillings are removed, the electricity is shut off. That would explain the cases such as the one you probably will see in one of the videos that is widely circulated by anti-amalgam groups--this shows a woman who was in a wheelchair, and she could move her legs after the fillings were removed. Within minutes. That is electrical, not a problem with allergies. It looked like a miracle but there was a reason behind it. I am convinced there would be thousands more miraculous improvements if you allowed mercury to be removed from the people who have this dangerous material in their mouths.

I have met some people who are now dead (one was 25, the other in his 30s) who had learned about the dental connection to health and were trying their best to reclaim their health but could not afford to do all the procedures needed. Others felt their minds became clear again and their energy had increased after removal of amalgams. I believe people need to know there is a potential risk.

My main concern about the incomplete information given to patients is that they will not have a chance to make up their own minds about what is done to their bodies. There is debate, hot debate, about the safety of mercury fillings. I think people have a right to know there is a potential problem now, rather than waiting until the Dental Association decides there is enough proof. We can look to the Tobacco industry to see an example of a dangerous practice that has been defended by non-ethical tactics. Mercury should be banned.

Hopefully, the medical doctors will soon declare mercury to be a medical hazard, and therefore remove the matter from the control of the trade guild Dental Association. MERCURY IS A MEDICAL EMERGENCY, NOT A MATTER OF MERE DENTAL POLITICS.

You probably do not read every word of letters on this issue, so I will close. I hope that you will get the impression that something very important is at stake here.

I will append a document in Microsoft Word 97. This has my comments about what I heard in a presentation about medical school research in Canada about the effects of mercury on the body. The reason there is not work like that in the USA is a result of the behind-the-scenes influence of the ADA on the activities of the AMA. I hope that your organization can help to bring this critically important information to the fore where it can be appropriately studied and the people protected from mercury.

Healthful regards,

, N.D., M.S. Acupuncture
Natural Medicine Services
1223 NE 65th Street
Seattle, WA 98115

7/12/00

Seattle, WA 98115

Written by me in SEATTLE: 2/17/94

News Release: 2/17/94
Dental Amalgams, Ghetto Violence and Mass Murderers

LIMBIC LOBE DESTABILIZATION POSSIBLE--UNIVERSITY OF WASHINGTON RESEARCHER DOWNPLAYS SOON-TO-BE-RELEASED RESEARCH LINKING MERCURY-SILVER FILLINGS AND MENTAL DETERIORATION. Ralph W. Wilson, ND

Today, in a scene reminiscent of clandestine meetings prior to the American Revolution, in a small room deep in the heart of the University of Washington Health Sciences Library complex, a researcher from the medical complex in Calgary, Alberta, revealed studies the medical profession is doing on health effects of an industry once thought of as innocuous--Dentistry. In a calm voice he recounted the research being done, much of it in our nation, that is revealing ways that the heavy metal mercury affects the body. The findings he shared with the group, consisting mostly of researchers and graduate students, with some health professionals, were presented in a detached manner, following careful scientific protocol for analyzing data that has profound social implications. During conversation after the formal presentation, a UW researcher revealed that they are about to release a study linking mercury-silver amalgam fillings with psychological changes.

Medical researcher and fetal physiologist Frtiz L. Lorscheider, Ph.D., of the University of Calgary, detailed research proving that mercury leaches from fillings and has been traced to vital body sites (the brain--especially the amygdala, hippocampus, and nucleus basalis, the kidneys, liver, pancreas, thyroid, the unborn fetus, etc.). Other studies show that nerve cells are damaged by mercury, affecting cytostructural proteins involved with neuronal integrity and allowing for the "neuro-fibrillatory tangles" discovered in brains of Alzheimer's victims, and possibly causing symptoms of MS. Another study showed that mercury is in unusually high concentration in brains of Alzheimer's victims. Another study showed that normal bacteria living in our intestinal tract mutate to become more resistant to mercury after amalgam fillings are placed, and at the same time, possibly through the "jumping gene" phenomenon, these bacteria become resistant to a number of commonly-used antibiotics.

He said now that these findings are being widely published in research circles, other researchers around the world are putting together puzzling findings of their own and painting a picture of wide-spread health effects of amalgams.

A U of W researcher commented that in the next few months they will release a study that may be of value in understanding the effects of mercury on brain function. This study will show "soft" findings relating to emotions, revealing statistically significant relationship of dental amalgams to measurable changes in personality.

Both of these scientists were quick to say that their work is intended to add to the basic understanding of the heavy metal mercury, and not for upsetting the public. Dr. Lorscheider stayed strictly to the scientifically-proven data in his own field of expertise, and refused conjecture about other possible body effects, such as autoantibodies forming against tissues proven to have mercury attached (which could theoretically lead to thyroiditis, diabetes, nephritis). He stated calmly that he wants to stay clear of the politics of the amalgam controversy; he says he has been asked to testify at trials of dentists threatened by the Dental Association for removing amalgam fillings for health benefits, but has declined because he wants to maintain a posture of scientific objectivity.

Written by me in SEATTLE: 2/17/94

There was an air of excitement during Lorscheider's presentation. The listeners realized the implications for the great debate about the safety of amalgams--which one popular writer against amalgams, Hal A. Huggins, D.D.S., has called "The Amalgam Wars". (The Huggins Diagnostic Center hotline is 1-800-31-2303.) There was some reference to the American Dental Association and the Dental Supply industry, and how they are imitating the all-too-familiar deadly legal gamesmanship and maneuverings of the Tobacco lobby--waging a campaign to cloud the air and stall changes that could prevent suffering and death of our citizens. Both the Dental Supply and Tobacco industries have hired scientists to say what they think will help their cause, and release statements that discredit anyone claiming their product is deadly to health.

In a desperate move to protect their financial liability, the American Dental Association has for some time been pushing for widespread governmental participation in placing amalgam fillings in low-income children. They claim that since mercury is "not scientifically proven to be harmful" they are within their legal boundaries to continue to place amalgams. For years now they have targeted the disadvantaged of our country for placement of amalgams, under joint government-industry programs to "help the poor". Now, the evidence is mounting that their selfish actions, just as with the Tobacco industry, are causing great harm to our people. There is the distinct possibility that it is dental amalgams that have been the Unknown Factor in recent societal destabilization, the trigger that sets off unreasonable emotional responses to the stresses of modern life.

IS THERE A POSSIBILITY THAT THERE IS A CONNECTION BETWEEN DENTAL AMALGAMS AND VIOLENCE? A simple study anyone could do (from the media to interested citizens and community organizations) is to make a list of dental conditions in violent youth, and mass murderers (asking mainly about the presence of amalgam fillings, but also metal crowns and braces, root canals, tooth extraction site infections, and use of mercury-based pink coloring in dentures). There is a high likelihood that these individuals have been "pushed over the edge" by the physiological and neurological effects of mercury toxicity and other dental immune challenges. AND--there is help that can be given to such people, through careful sequential removal of amalgams and replacement with high-tech, non-metal "Composite" dental materials, as well as treating infected root canal teeth, and removing non-healing Cavitations which occur often after removal of teeth (such as wisdom teeth).

The success that Dr. Huggins (and the many dentists and health professionals who assist the dentists) are having in dealing with psychological problems is astounding. His book It's All In Your Head, details his successes. It also details the American Dental Association's campaign to discredit his work. When compared to the devious machinations of the Tobacco lobby, the ADA's actions are lock-step...they have learned from the deadly tobacco debate how to mis-use Science and continue a dangerous practice which has obvious potential for injury to people. This news release is an attempt to bring more media interest in his work and the work of the many dentists around the country who have been applying his insights for many years now.

This has become almost a war. There are propaganda, well-orchestrated campaigns, and casualties. But the people will not stay silent. The danger is clear, the evidence exists, people can educate themselves about their choices for dental procedures and the materials placed in their mouths.

Call 1-800-331-2303. And, write your legislators and ask them to work for your freedom of choice in healthcare.

Dr. Watson
My Story

I had suffered from a number of types of heavy metal poisoning from my dental amalgams, namely mercury, tin and nickel.
My Symptoms I suffered since 1991 were numerous. My chief complaint was numerous painful lesions on my scalp, arms and legs. These raised red lesions were full of blood in the beginning but as time passed they became filled with a collection of white blood cells, attempting to fight off the contagion. The dermatologist referred to these oily, red,itchy lesions as "seborrheic dermatitis". He prescribed, as medical doctors often do, an entire list of antibiotics to treat "the infection". Little didthe dermatologist realize, nor did he suspect that my dental amalgams had been leaking for seven years.
I also suffered from hair loss. The roots of the hair shafts were covered with a white follicle. Sometimes, the white discolorations would begin to climb up the follicle. What was so unusual was that I just recently turned 30, and I had white hairs in many areas.

My digestive system was completely in a state of "malabsorbtion" of proteins, carbohydrates and sugars. It had been diagnosed as "toxic bowel syndrome". As a result, I had persistent abdominal discomfort and pain. The application of any pressure on my lower abdomen would be uncomfortable as my lower colon was sensitive to the touch.

Another strange symptom was that both of my kidneys and my lower large intestine would feel cold quite often. I would describe it best as a dull aching coldness and tightness. I required the application of hot water on some occasions because of the coldness.

On several occasions my muscles were beginning to "twitch" involuntarily. This symptom appeared to mimick symptoms similar to seizures or epilepsy. I couldn't stop the twitching, and I often wondered what was happening.

I also must admit that there were some psychological and emotional aberrations which had been present as well. Most notably, there appeared to be a state of persistent and irrational anger. I had no explanation for it, but perhaps it was because of these toxins which had been impairing my vital organs.

Methods of Diagnosis
Mercury poisoning as well as contamination from other methods may be determined through an analysis of the minerals in hair follicles, a blood analysis, and a urine test. My results indicated that I possessed a high level of aluminum in my body (as a result from eating out of aluminum pots and pans, and drinking from aluminum soda cans), but I have no doubt that it was the mercury which had caused my symptoms. Also present was a low level exposure to mercury, tin and nickel.

The Good Dentist I went searching for a bio-compatible dentist with the intent in mind to have my amalgam fillings removed. I located a bio-compatible dentist by approaching a local health food store owner from a health food store which I had patronized for a long time. The dentist was very skilled in recognizing what the symptoms were for mercury leakage from amalgams. The silvery mercury/silver amalgams were black underneath. Furthermore, another symptom of mercury leakage is that my gums were starting to become black in a few areas. Underneath many of my fillings, there were several cavities which were continuing to form. I am convinced that the cavities were somehow connected to the leakage because most

of the fillings which were leaking had cavities underneath. The mercury was leaking directly into the cavities providing a direct path into my bloodstream. The Procedure My dentist followed the protocols for amalgam removal. The protocol requires the application of a rubber dam placed around the tooth with a clamp thereby isolating it from the body. When the fillings are drilled, any debris which falls away falls into the rubber dam and is immediately removed with a vacuum suction apparatus. Of course, the saliva suction apparatus is utilized as well to prevent the patient from drowning on his/her own saliva. I should mention that any mercury tattoos which have accumulated must be removed as well and any bacteria which is located under the filling must be removed with a scraping tool or even with "food grade" hydrogen peroxide.A material which is commonly used to replace the dental fillings is a plastic type of composite, which is squirted out from a tube directly into the tooth cavity. There is no tricturation of metals, as the composite is dried with a heat lamp. After the heat lamp is applied several times, the jaw is closed and moved back and forth so that proper jaw use may be achieved. Any excess, dried composite material is sanded away with another tool. Finally, a sealing chemical named "Seal-It" is applied to the repaired tooth and allowed to dry.
Because these protocols were followed, I was not exposed to any mercury vapors or particles during the removal process. Overall, I had ten mercury-amalgam fillings. More than half of them were severely leaking. My symptoms persisted until the final two fillings were removed.

My Recovery
Just a few days after all of my fillings had been completely removed, my symptoms began to disappear. The first symptom to disappear were the scalp and arm lesions. They have almost completely disappeared. I have not even bugun to take any form of "chelation therapy" yet. Some chelators for mercury and other heavy metals include garlic and the amino acid cysteine. The garlic, because it is a sulfur bearing food, chelates with the heavy metals thus helping to remove them from the body. My digestive distress has begun to repair because I have not felt any more gas bloating or pain. My kidneys have not felt cold since the amalgam removal either. My recovery is far from complete. I am certain that it will take more time to completely recover, and so I must persist at removing the heavy metals which had accumulated up until this time.

My Mission
I believe that it is my mission, now that I have experienced this problem first-first hand, to make certain that other people do not become effected with the same medical afflictions and others. For this reason, I have called for a letter writing campaign to the politicians in the White House, the House of Representatives, and the Senate, to bring the issue into the public arena. If enough people make their voices heard by bombarding these elected officials with public appeals for an investigation and for action, then maybe action will be taken and the ADA could no longer bury the truth from public scrutiny.A "Speak Up on the Issue

March 19, 2000

To: Dan Burton, Chairman
Committee on Government Reform

From: Rosemary Carter
Vancouver, B.C.

Re: **Personal Story of Mercury Poisoning from Dental Amalgams** from Faculty Member of The
University of British Columbia.

About 10 years ago, at the age of 42, my health started to deteriorate rapidly. Until that time had been an athlete, running several every day as well as training horses. And I taught philosophy at The University of British Columbia. I had episodes of severe muscle weakness, episode of very low heart rate (down to about 40 bpm;), episodes of severe fatigue, exercise intolerance, severe lactic acid after doing less than my usual exercise, severe muscle cramps and spasms. These symptoms progressed in severity and length until I had full-blown chronic fatigue and fibromyalgia. The low heart rate episodes where replaced with tachycardia. I had sinusitis; tinitus; stomach and intestinal problems; inability to concentrate; brain fog; depression; rage; severe hormonal imbalances; chronic split lips; burning swollen toes; misshapen and paper thin nails; changes in my voice; and my hair went white. I was so exhausted that I couldn't even sweep my floor. I spend 6 months virtually in bed.

My husband and I spend hours and hours searching on the NET for research that might help me. My brother spend hours and hours in the medical library at UBC. On the basis of what we found, I went on a very extensive supplementation program that relieved many of my symptoms and got me back on my feet, but I was not well. As I continued my search, I found an article on the NET that made the connection between the problems I had and mercury poisoning. I followed this up and was astounded at what I found. There can be no doubt that mercury from amalgam fillings is a severe health hazard, and is responsible for thousands of deaths and millions of peoples' ill health. I also discovered that the supplementation program I had developed for myself is one that helps mitigate some of the effects of mercury poisoning.

I had my amalgams removed and went on a detoxification program. I am now symptom free, though I have not finished removing the mercury from my body and am still on an extensive supplementation program. I am training horses and running or cycling.

I am on the Faculty of the Open University of British Columbia and received my Ph.D. in philosophy from the University of British Columbia. In order to understand the technical scientific article, I had to do a crash course in molecular biology. And now that my brain is working again, I am embarking on a B.Sc. in molecular biology, and am considering doing a second Ph.D.. I am particularly interested, of course, in how toxins like mercury mess up the body.

Rosemary Carter

March 3. I started out walking to a food coop just a half a mile away in a windy, wet weather and "almost died." I came back home feeling very cold and weak, very shaken. I got warmed up at home and had rose hip tea. But I still felt shaken and weak.

March 17 Another health crisis. I left on my bike to go to the bank, about two miles, which is nothing for me on a bike. Despite wearing plenty of warm, wool clothing, after a few blocks I began to feel ill and cold, like I couldn't handle the wind and the cold. I stopped at a church to warm up.

Spring. I had lost most of my sex drive. I am not totally impotent, but I don't orgasm very easily at all. Am I over the hill at age 40. Is this the way it is supposed to be? I can't accept that. I have to figure out what else is going on.
I experienced some unusual (for me) thinking through the issues in my work as an accountant and administrator for a nonprofit organization. I had become more of a plodder, sticking to the familiar mental routines that I knew well, instead of being the creative, the effortless innovator that I had been. But you don't announce to your boss or your peers that you are feeling over the hill... besides, maybe things will change.
Theory: low thyroid function. I came across a book by Dr. Broda Barnes, MD, all about low thyroid function and how that can make you feel cold. But WHY would my thyroid have been impacted...why all of a sudden? I still need to get to the bottom of this.

Then I saw a book for sale while I was standing in line at my local food coop. One of the topics listed on the cover was "Candida, mercury and dental amalgam fillings." I browsed the book for a few seconds. On impulse, I decided to buy it. Later, at home, I began to read the first few sentences and a blot of understanding shot through my mind. MERCURY FROM DENTAL AMALGAM FILLINGS CAN CAUSE HEALTH SYMPTOMS ! That was all I needed. So, the mercury is not safe, after all. All of my strange new problems – waking up at night shivering, sexual dysfunction, fatigue and feeling weak and shaky, and not being able to take the cold, had started soon after having the first amalgam filling placed!! Looking back, now it was obvious! I KNEW! And I was chagrined that I had let a well –meaning dentist poison me!

I went back to the same dentist and asked for the amalgam to be replaced. (I knew nothing back then about mercury free or holistic dentists). After some argument he relented and replaced the amalgam filling with a composite.
Later that day, I remember feeling that my brain had begun to function more normally.
Other things just gradually improved – my energy level, my sexual function, and my creativity.
Some things were worse for a while: I noticed some food intolerances or allergies. I had foot trouble, muscle cramps at times; yeast/candida problems, particularly with persistent indigestion. But I read and researched them and self-treated for systemic candidiasis, a common effect of chronic mercury exposure.

I expected my doctors and my dentist to be very interested in my discovery and my insights and to learn a lot from my whole experience. But they did not; apparently learning from a patient and getting insight from a patient is not part of the typical dental or medical practice.

So, I thought: well, maybe my whole experience with mercury was a fluke. Maybe I have some rare genetic difference that makes me very vulnerable, susceptible, to the mercury that is released from an amalgam. But I thought: I'm going to keep my ears open to any others who may have had a similar bout of ill health due to mercury from amalgam...it was a disaster for me and I shudder to thing what devastation it would have done to me if I'd have lots of amalgams for a long, long time.

Ten years later, the word came: someone I knew had discovered he had been harmed by dental amalgam fillings. He had benefited greatly by having his amalgams replaced. He was forming a Minnesota group for interested people to learn more about the science and health issues. The group also formed to try to defend an outspoken mercury free dentist who was under attack from the state Dental Board. There, in the group meetings, I met a woman who had had MS; she didn't have it anymore. I met a woman who had had severe allergies most of her life and had greatly improved. There were many powerful, moving stories. We all learned from each other. We all learned of the science. We also learned of the repression that pervades the dental profession, with the dental establishment, acting through the dental boards, makes an example out of those few dentists who openly challenge the conventional line about amalgams being safe.

It is not enough for me to have escaped from chronic mercury toxicity. All citizens should have a chance to learn what I have and to find out what the independent scientists are trying to tell us. In order for scientific truth to triumph and save people's lives, our political leaders must take the courage to hear the truth and face the truth in this matter, no matter how appalling the truth may be.
Respectfully,

Leo B. Cashman

Immunization Action
COALITION

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August 3, 1999

Representative Daniel Burton, Chairman
Committee on Government Reform
United States House of Representatives
2157 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Burton:

I respectfully request that this letter be included in the official record for the hearing on vaccine safety and U.S. vaccine policy that is before the Committee on Government Reform today, August 3, 1999.

The Immunization Action Coalition, of which I am the executive director and medical director, believes in vaccinating all people of all ages against all vaccine-preventable diseases. Over 5,000 health professionals actively support our mission. At least twice a year we send an emphatic and clear message through our publications *NEEDLE TIPS* and *VACCINATE ADULTS!* to approximately 500,000 health professionals reminding them to vaccinate all people of all ages against all vaccine-preventable diseases.

I am writing to give input into three important questions concerning vaccines on which the Committee on Government Reform is taking testimony today.

ARE VACCINES SAFE?
Millions of dollars and millions of hours are spent by the Centers for Disease Control and Prevention, the Food and Drug Administration, the American Academy of Pediatrics, the American Medical Association, the American Academy of Family Physicians, the American College of Physicians, the Vaccine Adverse Events Reporting System, the vaccine companies, and countless other agencies and scientific groups to make sure our vaccines are safe. I choose to trust the recommendations of these thousands of experts whose work it is to make sure vaccines are safe.

ARE VACCINES EFFECTIVE?
Vaccines save lives. Consider the following vaccine-preventable disease statistics:

- 15,520 people died of diphtheria in 1921. In 1997, no one died of diphtheria.
- 10,314 people died of measles in 1923. In 1997, 2 people died of measles.
- 9,269 people died of pertussis in 1923. In 1997, 6 people died of pertussis.
- 511 people died of tetanus in 1947. In 1997, 4 people died of tetanus.
- 1,000 people died of Hib disease in 1986. In 1997, 7 people died of Hib disease.

Deaths from vaccine-preventable diseases have decreased dramatically through the use of vaccines. (See attached tables.)

I have also enclosed 19 personal stories and case reports collected by the Immunization Action Coalition of people who suffered or died from vaccine-preventable diseases. Three of the stories are highlighted below:

- **Story #3: Family remembers hepatitis B victim as a girl with promise**
  A. J. is dead. No one knows how A. J. got hepatitis B virus infection. Imagine if there had been a law that she needed to be vaccinated before attending school. She'd be alive today. Ask her family if they wish there had been a hepatitis B vaccination school entry law. After A. J. died, the demand for hepatitis B vaccination by students in her school increased dramatically.

  Hepatitis B virus is a silent disease that anyone from birth through old age can contract. It is not just a disease of adults. Prior to the implementation of routine infant hepatitis B immunization, it was estimated that 35,000 children were infected with hepatitis B virus annually in the United States.

- **Story #11: Measles outbreak associated with an unvaccinated population**
  A measles outbreak occurred in a religious community in St. Paul, Minnesota, in 1996. Shortly after the outbreak, most of the unvaccinated children and young adults in this religious community subsequently chose to receive two doses of MMR vaccine.

- **Story #10: Pertussis claims the lives of two infants**
  Families who make decisions not to vaccinate their children sometimes don't know that their children can infect others including younger siblings who are not old enough to be vaccinated. The two infants who died were too young to be vaccinated. Pertussis (whooping cough) is a disease that can be contracted at any age, but it is particularly dangerous and life threatening for infants because their airways are so tiny.

Commenting on the pertussis outbreak that led to the death of these two infants in Santa Cruz County, California, public health chief Betsy McCarty, RN, MS, said, "People who think they are doing the right thing by not getting their children vaccinated, couldn't be more mistaken. This is as important as putting your kid in the car seat, seeing they have enough to eat, and locking up the poisons."

WHY DO STATES NEED SCHOOL VACCINATION LAWS?

This is a question that arises over and over again. All states have mandatory vaccination requirements for certain vaccines at school entry. Here are some reasons why states have vaccination laws:

- Diseases spread in closed, crowded environments such as schools.
- Unvaccinated schoolchildren are at greater risk of contracting vaccine-preventable diseases which are sometimes deadly.
- Unvaccinated schoolchildren can bring vaccine-preventable diseases home to younger children in their families and neighborhoods who may be too young to be vaccinated.
- Unvaccinated schoolchildren put children who are medically unable to be vaccinated (e.g., children with HIV infection) at risk for these diseases.
- Unvaccinated schoolchildren pose a risk to children whose parents chose to vaccinate them but who are in the category of children who did not respond to the vaccine.
- Unvaccinated schoolchildren can start school outbreaks which disrupt education, increase absenteeism, and lead to loss of income for parents who must stay home with their sick children.

Public health policy concerning the use of vaccines has made it possible for people in the United States and around the world to live longer, healthier lives. There is no doubt in my mind that the work of the Immunization Action Coalition has helped perpetuate the excellent health of this nation by promoting the use of safe and effective vaccines for children and adults.

Sincerely,

Deborah L. Wexler MD

Deborah L. Wexler, MD
Executive Director

Comparison of Maximum and Current Reported Deaths from Vaccine-Preventable Diseases, U.S.

This table compares the maximum number of deaths from vaccine-preventable diseases reported in one year vs. the number of deaths reported in 1997 (the most current year for which vaccine-preventable disease death statistics are available)*

Disease	Maximum Reported Deaths (year reported)	Reported Deaths in 1997	Percent Decrease
Diphtheria	15,520 (1921)	0	100%
Measles	10,314 (1923)	2	99.98%
Mumps	25 (1968)	0	100%
Pertussis	9,269 (1923)	6	99.94%
Polio (wild)	3,145 (1952)	0	100%
Rubella	31 (1947)	0	100%
Tetanus	511 (1947)	4	99.22%
Haemophilus influenzae invasive disease (type B)	1,000 (1986)	7	99.3%

* Data provided by the U.S. Centers for Disease Control and Prevention, Atlanta, GA.

Cases of Vaccine-Preventable Diseases in the United States Reduced Dramatically in 20th Century Thanks to Vaccines!

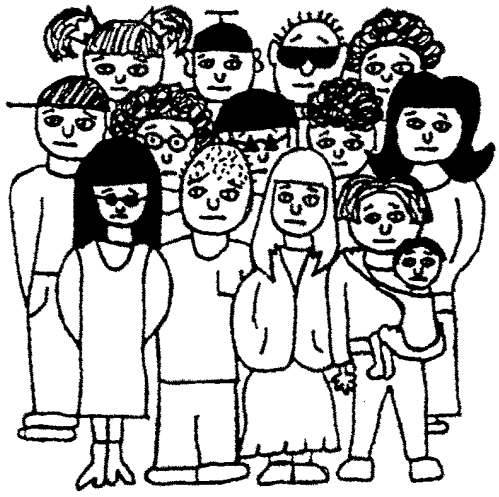
Baseline 20th Century annual morbidity and 1998 provisional morbidity from nine diseases with vaccines recommended before 1990 for universal use in children — United States.

Disease	Baseline 20th Century Annual Morbidity	1998 Provisional Morbidity	% Decrease
Smallpox	48,164[1]	0	100%
Diphtheria	175,885[2]	1	100%[3]
Pertussis	147,271[4]	6,279	95.7%
Tetanus	1,314[5]	34	97.4%
Polio (paralytic)	16,316[6]	0[7]	100%
Measles	503,282[8]	89	100%[3]
Mumps	152,209[9]	606	99.6%
Rubella	47,745[10]	345	99.3%
(Congenital Rubella Syndrome)	823[11]	5	99.4%
Haemophilus influenzae type b	20,000[12]	54[13]	99.7%

[1]Average annual number of cases during 1900-1904.
[2]Average annual number of reported cases during 1920-1922, 3 years before vaccine development.
[3]Rounded to nearest tenth.
[4]Average annual number of reported cases during 1922-1925, 4 years before vaccine development.
[5]Estimated number of cases based on reported number of deaths during 1922-1926, assuming a case-fatality rate of 90%.
[6]Average annual number of reported cases during 1951-1954, 4 years before vaccine licensure.
[7]Excludes one case of vaccine-associated polio reported in 1998.
[8]Average annual number of reported cases during 1958-1962, 5 years before vaccine licensure.
[9]Number of reported cases in 1968, the year reporting began and the first year after vaccine licensure.
[10]Average annual number of reported cases during 1966-1968, 3 years before vaccine licensure.
[11]Estimated number of cases based on seroprevalence data in the population and on the risk that women infected during a childbearing year would have a fetus with congenital rubella syndrome.
[12]Estimated number of cases from population-based surveillance studies before vaccine licensure in 1985.
[13]Excludes 71 cases of *Haemophilus influenzae* disease of unknown serotype.

Adapted from MMWR, Vol. 48, No. 12, April 2, 1999, p. 248

The Immunization Action Coalition presents . . .



Unprotected People

Stories of people who died or suffered from vaccine-preventable diseases

Do you have a story or case to report? Your stories and/or case reports can help save lives! Please e-mail them to us at deborah@immunize.org or fax them to (651) 647-9131.

Sign up for IAC EXPRESS! The Immunization Action Coalition will keep sending these stories and other timely immunization information directly to your e-mail box. To subscribe, send an e-mail to **express@immunize.org** and place the word **SUBSCRIBE** in the Subject field. It's free!

Item #R2057 (3/99)

Immunization Action Coalition • 1573 Selby Avenue, St. Paul, MN 55104 • (651) 647-9009 • www.immunize.org

Unprotected People #1
Haemophilus influenzae type b

A mother's experience with *Haemophilus influenzae* type b

Written by Peggy Archer, RNC, BSN. Reprinted from "Michigan Immunization Update," winter 1998, a publication of the Michigan Department of Community Health.

In 1989, the *Haemophilus influenzae* type b vaccine was relatively new and not yet routine. I was aware of the vaccine's availability, but, busy mom that I was, I had not yet made the trip to the health department to get the immunization for my two-year-old daughter, Sarah. I will always regret that bit of procrastination and the anguish that it caused.

As a registered nurse, I felt confident treating Sarah's colds and sniffles without calling our pediatrician. I did not become alarmed when, late one March evening, Sarah's mild upper respiratory infection progressed to a croupy cough and fever. I gave her a tepid bath and acetaminophen to control her fever, and to relieve her croup I transformed our bathroom into a steam room and sat holding her until I was convinced she was feeling better. Vaporizer at her bedside, I tucked her in with the thought that we would see the pediatrician in the morning. I settled into bed, only to be awakened within the hour by my worried husband. Sarah's breathing was becoming more labored and my concern began to grow. It was clear that Sarah needed immediate medical attention in a hospital emergency room.

As we left the house, my husband, Eric, grumbled a bit about taking a child to the emergency room in the middle of the night, to be seen for a simple cold. It was at that moment that I knew what was wrong with Sarah. It was as if God wanted to override any feelings of doubt instilled by Eric's lack of a sense of urgency. As I prepared our daughter for the ride, I told Eric that she could be suffering from epiglottitis, a condition in which the epiglottis becomes so inflamed that it can completely block the airway. He must have seen the panic in my eyes, because he didn't ask questions. In moments, we were speeding toward the hospital. The 25-minute drive seemed like hours as I watched Sarah's condition deteriorate before my eyes. Even in the dim light of our car I could see her color changing from pink to pale blue and then a dusky blue. Unable to swallow the copious secretions pooling in her mouth, she began to drool. As she struggled to breathe, I began to wonder what implements I had in my purse with which I could perform a tracheotomy.

The emergency physician confirmed my suspicions of epiglottitis. A pediatrician and an ear, nose, and throat specialist were summoned and agreed that Sarah should be taken to surgery immediately for intubation and possible tracheotomy. The pediatrician explained that Sarah was in serious condition most likely due to infection with the *Haemophilus influenzae* type b (Hib) bacteria. Finally, he added that her illness could have been prevented by vaccination. I was overwhelmed at the thought that my negligence caused this to happen.

The anesthesiologist who was to assist the other physicians arrived in the emergency department. I had worked with him on several occasions and knew him to be confident and unexcitable. As he quickly and quietly assessed Sarah, a look of extreme concern came over his face. He became anxious and began to pace as we waited for the staff to prepare Sarah for the operating room. She was in worse condition than I had thought, and I was terrified that I might lose her.

After leaving Sarah's side, I sought support from friends in the familiar Special Care Nursery where I worked as a staff nurse. Just as Eric and I arrived on the unit, a colleague gave us the upsetting news that there were problems in the operating room. Sarah's throat was so swollen that they could not get her intubated. Their last hope before doing a tracheotomy was to try an extra small tube, the size that we used

(continued on next page)

Item #R2057-A (9/98)

in the nursery for the tiniest of premature infants. Overcome with worry, Eric and I headed for the chapel to pray. That is where we were an hour or so later as the surgical team wheeled our little girl past us, on the way to the Intensive Care Unit. My eyes were so full of tears that it took a few moments for me to recognize that she did not have a tracheotomy. The tiny endotracheal tube had been successfully placed, and she was put on a ventilator for respiratory support.

Eric and I sat by Sarah's bedside still fearful for her life. Blood cultures confirmed that *Haemophilus influenzae* type b was the cause of her illness. The pediatrician's admonishment rang in my ears. "This wouldn't have happened if she had gotten the Hib vaccine." I was overcome with guilt as I watched the ventilator pump oxygen into Sarah's tiny lungs. In addition to large doses of antibiotics, the nurses injected her IV with a drug that would temporarily paralyze her, preventing her from becoming restless and dislodging the airway she so desperately needed. I was familiar with the drug, so I knew Sarah could still feel every poke and procedure, but was unable to respond. Knowing that I could have prevented her from going through such torture was almost unbearable.

Thirty-six hours later, the swelling had subsided enough so that the tube could be removed, and Sarah was placed in a humidified oxygen tent. Like most kids, she showed incredible resilience and was discharged on the fifth day. Sarah is 10 years old now and has no memory of the terrible ordeal that her parents will never forget.

I recently began working in a pediatric clinic, and have encountered parents who refuse to immunize their children due to fear of a severe reaction. Perhaps if these same parents are made aware of children like Sarah, who nearly lost her life to a vaccine-preventable illness, they will reconsider their decision not to immunize.

Unprotected People #2 Hepatitis B

Parent of child with HBV testifies about importance of hepatitis B vaccination

A parent whose son is chronically infected with the hepatitis B virus delivered the following testimony in 1997 at a public hearing on the implementation of a hepatitis B school entry law.

The parent spoke on a personal level of the pain her entire family has suffered because of one family member's chronic illness. She concluded by urging parents to learn as much as they can about hepatitis B so that they can make truly informed decisions regarding school immunization and how to best protect their children. The testimony is as follows:

I'm here to talk about my family. I'm not here to add to the list of statistics related to immunization issues. I'm here to personalize them, to bring them to a level that you can relate to from the heart rather than from a business, political, or clinical standpoint. My husband and I have three young children. One is a hepatitis B carrier. Although he is asymptomatic, biopsies at ages 3 and 4 confirmed that he already has cirrhosis. He did not respond to a 7-month course of interferon, a form of chemotherapy, and no other treatment has been available for him.

There is a four-letter "F" word which we try to shield our children from. It's something they shouldn't know anything about at such a young age. The word is Fear. Fear of social repercussions, fear of financial ruin, fear of sickness, death and loss.

You may have noticed that I have not provided our family name. I can't. The first thing hepatitis B families learn, usually after rejection by friends or family, is to go to extreme lengths to protect their child's privacy. We desperately want to reach out for comfort when we learn our child has an incurable illness, but we can't. Local hospitals offer support groups for parents of children with cancer, but no help is available for parents of children who have life-threatening infectious diseases.

We feel an overwhelming need to warn daycare workers, teachers, Sunday school caretakers, babysitters, playmates and their parents that extra care needs to be exercised if our child scrapes his knee, bites or is bitten, has a bloody nose, and so on. We want to tell everyone to get the shots. Yet we agonize over the negative consequences of "telling"....Will our child be treated fairly? Will he be ostracized on the playground? Will we ever find a babysitter? Will they have any friends or will our children be singled out as the kids to avoid? Will information given to the school nurse in confidence wind up as the topic of conversation at a PTA meeting? There are discrimination and disability laws that guarantee our child a public education, but there are no laws to protect my child's heart....

My husband and I attended a school meeting regarding one of our other children. During casual conversation, a mom mentioned that she'd heard that there was a child with hepatitis B in our school district. She went on to tell the other concerned parents that she had visited the school superintendent in an effort to identify the child so that she could better protect her son. We sat paralyzed in silence, waiting for glances to turn in our direction (they didn't!), and all I could think was, get your kid the shots if you want to protect him. We supervise our child's play, we coach his soccer games, we are there as much as possible in order to protect other people's children. But it's obviously impossible to continue this vigilance as the children grow older. A neighbor tried to bandage our child's bleeding cut and I body slammed her away. She thinks I'm overprotective. She has no idea I was protecting her. No one else should have to live with this virus. It's preventable.

We worry about our ability to provide the best care for our child. His interferon treatment cost well

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Item #R2057-B (9/98)

over $20,000 and only a portion was covered by insurance. We are self-employed and we watched our health insurance premiums triple. We can't change carriers because we fear he could become sick or need a transplant during the "pre-existing condition exemption period" with a new policy. If no cure or control is found in the very near future, the likelihood that he will need a transplant is high. We have been warned that transplant and post-transplant care will most likely ruin us financially, and it is only a temporary solution. The virus would eventually attack the new liver as well. We wonder whether we will be able to afford to put our children through college, how we will manage to retire.

I call this virus "IT." Capital I, capital T. Stephen King fans will understand why. IT invades our lives, our thoughts, our spiritual beliefs, no matter what defenses we erect. I watch my happy children playing and IT reminds me that we will soon have to tell my son that he has a serious illness. Whenever he doesn't feel well, I wonder, "Is this IT"? How long will IT allow him to play the sports he loves? How will IT affect his school performance? The quality and length of my son's life are frightening unknowns, but statistics related to the progression and characteristics of this disease make it difficult to be optimistic. You can all look at your young children and fantasize about their senior proms and weddings. I cannot.

My son is a leader. He is clever, creative, charming. He is very protective of our other children and they look up to him. I fear the effect IT will have on his siblings, worry about how they will deal with their brother's illness, or worse. I fear that I will watch my child die, the worst possible thing that can happen to a parent. Doctors and parents have no control over the course this illness chooses within our children's bodies. However, the availability of the hep B vaccine allows us to control the spread of the disease to others. No other family should ever have to experience this pain. Three shots can prevent IT.

Hepatitis B is transmitted primarily through blood and sexual contact with infected persons. There are young, asymptomatic carriers who have not yet been diagnosed. Infected children will be socializing with and dating your children. It is clear to me that those of you who oppose immunizing our state's children are well informed about vaccine composition and side effects. I beg you to learn as much about the hepatitis B virus and disease progression as well. Only then will you be able to make a truly informed decision regarding school immunizations and how to best protect your children.

Signed,
A Parent

Unprotected People #3
Hepatitis B

Family remembers hepatitis B victim as a girl with promise

By Molly Guthrey, Staff Writer, St. Paul Pioneer Press. *Originally printed Saturday, Aug. 6, 1994. Reprinted with permission.*

The family huddled quietly on the eve of their child's funeral in a home cloaked with almost tangible sorrow.

The North Minneapolis house used to be filled with 15-year-olc Arkesha Johnson's easy peals of laughter. But on Thursday, it was painfully silent with grief-stricken relatives.

Terry Johnson, the girl's mother, sat at the kitchen table, her shoulders hunched as she talked about her daughter's sudden death from hepattis B. She spoke softly and her eyes still had a glaze of shock about them, as if her mind was still trying to process her eldest caughter's death six days earlier.

Known to friends and family as Kesha, she was an honors student who excelled at math and science and who would have been a junior this fall at South High School in Minneapolis. She had a boyfriend and a best friend. She loved Janet Jackson and rap music and gospel music, too. She dreamed of becoming a surgeon or a pediatrician and planned to attend college—maybe Temple University—on grants and scholarships.

She was determined to be a success in life. Renee Johnson, one of her aunts, was so sure of her niece's academic talents that she was convinced that someday she would watch as Kesha was awarded the Nobel Prize after discovering a cure for cancer or AIDS.

Now, the family is trying to cope with the death of all those dreams surrounding their Kesha.

"I think any time you lose a child, you feel shock, hurt and pain, everything pretty negative rolled up into one," Renee Johnson said.

Kesha died on July 29 of hepatitis B, family members said, after being diagnosed about two weeks before. Until then, she had been a seemingly healthy and active teenager – but then she started having stomach pains. She was nauseated and throwing up on July 14, the day her mother took her to the Hennepin County Medical Center.

The doctors ran some tests and found her liver badly damaged, family members sa:d. They wouldn't let Kesha go home again, even to pack. She was transferred to the University of Minnesota Hospital, where her illness quickly worsened as family members tried to assimilate what was happening.

She never went home again.

She was removed from life support on July 29 as about 40 family members and close friends filled the room and cried. Only her aunt could bear to watch as Kesha stopped breathing. Some left the room, sobbing.

"I knew Kesha's spirit had already left us," said Renee Johnson.

She was the same Kesha they loved for the first nine days in the hospital, before the disease overtook her body and her mind. She giggled and watched television, visited with friends and family and hoped for the best.

None of them thought she would die. Family members said she was put at the top of a transplant list.

"There was always hope," said Kim Johnson, an aunt from Chicago. "We didn't think it would happen like this. The doctors had hoped it wouldn't. It was just so sudden."

There were so many relatives visiting that they filled up two waiting rooms. The operators at the university received hundreds of calls from well-wishers.

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Family members said they have been told by doctors that it is rare for a person to be overcome so quickly by hepatitis. They're not sure how she caught the disease or why it happened so fast.

Hepatitis B is a highly infectious virus that attacks the liver. Infection can lead to severe illness, liver damage and sometimes death. Nationally, about 300,000 acute cases and 6,500 deaths occur annually, health officials say.

Last year in Minnesota, there were 77 cases of hepatitis B reported in Minnesota, 56 cases involving people aged 15 to 39. The infection has slowly been declining in Minnesota since 1988. Deaths are rare, health officials said.

"It is often a silent disease," said Dr. Deborah Wexler, of the St. Paul-based Hepatitis B Coalition. "This is a perfect example of why every child in the United States needs to be vaccinated against hepatitis B."

Last year, Minnesota became the first state in the nation to recommend that all adolescents be immunized against the hepatitis B virus. State health officials took the step after they discovered the disease was becoming more prevalent among adolescents 15 and older.

At her funeral on Friday at St. John's Missionary Baptist Church on Morgan Avenue, Kesha looked a little bit like an angel in her casket, dressed in a cream dress with sparkly rhinestones sprinkled across her chest, resting in a bed of white velvet.

It was a girlish casket, brown with tiny pink flowers etched onto the sides.

It was a simple service, filled with simple words and songs and prayers. The choir she used to sing with sang for her. Her friend Cornell Washington also sang a song about their friendship, a cappella. He bowed his head to compose himself for minutes before he began.

"You never miss a good friend until she's gone," the boy sang in a shaky voice from the front of the church. "Life goes on, but it's not the same."

And her family and friends bowed their heads and began sobbing openly as the boy's song for Kesha filled the small church.

Unprotected People #4
Varicella (chickenpox)

Three fatal varicella cases in unvaccinated young women

Three fatal varicella (chickenpox) cases in young adult women were reported to the Centers for Disease Control and Prevention by state health departments during January-April 1997. All three women were susceptible to varicella, unvaccinated, and infected by exposure to unvaccinated preschool-aged children who had contracted varicella. These three cases appeared in the Morbidity and Mortality Weekly Report (MMWR), *May 16, 1997, vol. 76, no.19 and are reprinted below.*

NOTE: There are approximately 100 deaths and 10,000 hospitalizations from varicella each year in the United States. The CDC's Advisory Committee on Immunization Practices (ACIP) recommends that all susceptible children (12 months of age and older) and all susceptible adults be vaccinated.

Case 1: Death of a 23-year-old woman

On January 19, 1997, a 23-year-old woman in good health had onset of a classic varicella rash. In early January, her 2- and 5-year-old unvaccinated children had had varicella. On January 22, she had onset of shortness of breath and hemoptysis. When she was admitted to a local hospital on January 23, a chest radiograph indicated diffuse alveolar density consistent with varicella pneumonia, and treatment was initiated with oxygen and intravenous acyclovir. Her condition worsened, and she required intubation several hours after admission. Because of increasing respiratory distress, she was transferred to a referral hospital where treatment continued with oxygen, antibiotics, and intravenous acyclovir. On January 31, her rash became hemorrhagic, and she developed disseminated intravascular coagulation (DIC) and renal failure, followed by progression to multiple system failure; she died on February 2. Varicella zoster virus was cultured from skin lesions and from a tracheal aspirate.

Case 2: Death of a 25-year-old woman

On March 11, 1997, a 25-year-old woman in good health had onset of a classic varicella rash, fever, and headache. Her 4-year-old unvaccinated child had had onset of a varicella rash on February 23. On March 12, the woman had onset of cough, and on March 13, shortness of breath. On March 14, she sought care at a local emergency department (ED) because of increasing respiratory difficulty and confusion. Chest radiograph indicated bilateral infiltrates consistent with varicella pneumonia, and arterial blood gases indicated hypoxemia. Varicella encephalitis and pneumonia were diagnosed; she was admitted to the hospital, and treatment was initiated with oxygen and intravenous acyclovir. Four hours after admission, her respiratory difficulty increased, and she required intubation. On March 15, a computerized tomography of the brain revealed severe, diffuse cerebral edema, and she developed renal failure and coma. On March 16, she was transferred to a referral hospital for renal dialysis; an electroencephalogram indicated absence of electrical brain activity, and repeat chest radiographs indicated diffuse infiltrates. She died on March 17.

Case 3: Death of a 32-year-old woman

On April 3, 1997, a 32-year-old woman with Crohn's disease sought medical evaluation at a local ED because of onset of abdominal and back pain. On March 7, therapy was initiated with 40 mg prednisone daily for an exacerbation of her Crohn's disease. By April 3, her steroid therapy had been tapered to 20 mg prednisone daily. On physical examination, she had mild, generalized abdominal tenderness with no specific signs or abdominal guarding. She was afebrile, and a white blood cell (WBC) count was normal. A benign abdominal syndrome was presumptively diagnosed, and she was discharged.

Her symptoms persisted, and on April 4, she sought medical evaluation at the office of her health-care provider. Findings on physical examination were uncharged. Although an abdominal radiograph, ab-

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Item #R2057-D (11/98)

dominal and pelvic ultrasounds, and a WBC count were normal, because of her underlying medical condition, she was referred for surgical consultation. On April 5, the abdominal pain persisted, and she returned to the ED for evaluation. A WBC count was 15,000/mm3 (normal: 3200-9800/mm3), and she was admitted to the hospital. Diagnoses of colitis and ileitis with possible perforation and intraabdominal abscess were considered, and treatment was initiated with broad-spectrum antibiotics. On physical examination, a maculopapular, vesicular rash with crusted lesions was observed on her trunk, head, and neck. Varicella was presumptively diagnosed, and she was placed in isolation. The patient reported that she had had onset of a mild macular, nonpruritic rash on her back on April 3 and that she had been exposed on March 12 and 13 to her 4-year-old unvaccinated niece with varicella. On April 6, the vesicles became hemorrhagic, and she began bleeding from intravenous sites. She rapidly developed hypotension and DIC, and died from shock the same day. On autopsy, evidence of viral inclusion bodies in multiple organs was consistent with varicella, and varicella was determined to be the cause of death.

Unprotected People #5
Polio

"I awoke one morning unable to walk"

One day, three-year-old Sharon Karber awoke unable to walk. It was 1953. Polio had reached epidemic proportions in the United States, and Sharon had become another polio victim. This is her personal story which originally appeared in "Michigan Immunization Update," spring 1997. It is entitled, "Through a child's eyes: a child's polio experience." As Sharon says, "this is a true story told through the eyes of one child who experienced a crippling vaccine-preventable disease and was rehabilitated. Not everyone was as lucky." Today, Ms. Karber, a registered nurse, is a nurse consultant at the Michigan Department of Community Health. Here is her story:

Through a child's eyes: a child's polio experience
Contributed by Sharon Karber, RN, MSN, Nurse Consultant, Michigan Department of Community Health

For me and my family, the crippling effects of polio will never be forgotten. It was the spring of 1953, and a polio epidemic was occurring in Michigan and the rest of the country. During that year, 2,346 polio cases were diagnosed in Michigan, and, at almost three years of age, I became one of those statistics. I awoke one morning unable to walk and had to be admitted to Mary Free Bed Rehabilitation Hospital in Grand Rapids, where I spent the next seven months.

I recall seeing my parents through a glass door during my stay at the hospital. As I learned later in life, polio patients were quarantined in order to both protect the polio patients from acquiring respiratory infections from visitors and in order to contain the spread of polio to those with whom they might have contact. Eventually it became normal to see my parents only on weekends because they had to travel two hours, one way, to see me. Rehabilitation therapy during those seven months included hot packs to my legs, whirlpool treatments, passive leg exercises and learning to walk with braces and crutches. I was discharged from Mary Free Bed Hospital after seven months of therapy under the condition that my mother would continue to administer my leg exercises. This meant that three times a day she would place me on the kitchen table and massage, stretch and strengthen my leg muscles.

Grade school years were very difficult because of my braces and crutches. It was impossible to run and play like other kids. I required leg surgeries (including four weeks in a cast) every summer until I was 12 years old in order to correct deformities, reposition muscles, and reattach tendons for better leg and foot control. Eventually I graduated from needing braces and crutches, but then came the mis-mate orthopedic saddle shoes. I remember pleading with my mother to buy me regular shoes but the answer was always "no," because the shoes had to be orthopedically built and had to accommodate a two shoe-size difference in foot size.

Junior high school was my first normal school experience. I had at last reached my maximum ability where nothing further could be done to improve the functioning of my legs. I was now able to compete in gym class, wear normal shoes, and cheerlead with the best of my peers. My residual physical limitations were minimal, but what a long road I had traveled with that polio villain!

My experience with this disease was nothing compared to what my parents endured seeing their child go through years of physical limitations and rehabilitation. Until the day my mother died, tears would always come to her eyes when she told her side of this story. To write my story now, as an adult and as a mother, makes my heart ache for my mother, who suffered emotionally because of my disease. Physically losing parenting responsibilities of her youngest child and then having that once-normal child return physically disabled from a disease that a

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Item #R2057-E (11/98)

vaccine could have prevented (had it been discovered earlier) caused terrible guilt for her. I strongly believe my rehabilitation and level of functioning today would not have been possible without her unending devotion in performing my daily leg exercises, compliance with years of physician visits and consents for numerous surgeries.

Today, I have my own family and am a nurse consultant for the Michigan Department of Community Health working with the Immunization Division. My life has come full circle as I now spend much of my time as a strong advocate for immunizations. I believe the work I do to educate health care providers in Michigan about the importance of vaccinating all children on time will help prevent potentially devastating diseases. It is my hope that no child will ever have to suffer any disease that can be prevented by vaccines. This is a true story told through the eyes of one child who experienced a crippling vaccine-preventable disease and was rehabilitated. Not everyone was as lucky.

Unprotected People #6
Hepatitis B

"All of the horrors that I endured could have been avoided"

U.S. Congressman John Joseph Moakley from Massachusetts was gravely ill with hepatitis B virus infection but fortunately received a successful liver transplant. Today, Congressman Moakley is a great advocate for hepatitis B vaccine. As he writes in the following letter, "All of the horrors that I endured could have been avoided if I had had available to me the very safe and effective vaccine against hepatitis B that now exists." Here is Congressman Moakley's story:

Don't Hesitate: Vaccinate!

Contributed by Joe Moakley, Member of Congress of the United States, House of Representatives, 9th District, Massachusetts

In the early 1980s, I was diagnosed with hepatitis B. It has never been determined where or how I contracted the virus. It may have been during a Congressional fact finding trip to China at that time. That is one of the very frightening facts about hepatitis B. While risk factors have been identified that are associated with viral transmission, up to 40% of the cases of hepatitis B in adults have no known risk factors associated with them.

By 1995, I was told by my doctors that I had about two months to live. In my case, the hepatitis B virus had led to cirrhosis of the liver and this vital organ had deteriorated beyond function. I was terribly ill, I had no strength and I had become severely jaundiced. But I was lucky; a liver transplant saved my life. Today I am happy, healthy and so grateful that I have been able to celebrate 25 years in the United States Congress.

Unfortunately, more than 1,250,000 Americans have hepatitis B, and up to 6,000 Americans every year die from the complications associated with the hepatitis B virus. All of the horrors that I endured could have been avoided if I had had available to me the very safe and effective vaccine against hepatitis B that now exists. The three shot series over a period of four to six months can protect most people from the agony of this disease.

I strongly encourage everyone to check with their provider about immunization against hepatitis B for themselves and for those they love. There is no reason for anyone to suffer from this totally preventable disease.

Unprotected People #7
Tetanus

Montana newborn of an unvaccinated mother contracts neonatal tetanus after application of nonsterile clay to the umbilical cord

A case report of neonatal tetanus was published in Morbidity and Mortality Weekly Report (MMWR) *on November 6, 1998, in an article entitled "Neonatal Tetanus – Montana, 1998." The article states that "the findings indicated that tetanus occurred after application of nonsterile clay to the umbilical cord."*

The editorial note includes mention of the Center for Disease Control And Prevention's Advisory Committee on Immunization Practices (ACIP) recommendation to give a booster dose of Td to previously vaccinated pregnant women who have not received a Td vaccination within the preceding 10 years, and unvaccinated or partially vaccinated pregnant women should complete the primary series of three doses of Td.

The article and editorial note are printed below:

Neonatal Tetanus — Montana, 1998

Neonatal tetanus (NT) is a severe, often fatal disease caused by a toxin of Clostridium tetani, a ubiquitous spore-forming bacterium found in high concentrations in soil and animal excrements. NT s associated with nonsterile delivery and umbilical cord-care practices for newborns of mothers with antitoxin levels insufficient to protect the newborn by transplacental transfer of maternal antibody. In 1997, NT accounted for an estimated 277,400 deaths worldwide (1) but is rare in the U.S. During 1995-1997, of 124 tetanus cases reported in the United States, only one occurred in a neonate (2,3). This report summarizes the investigation in March 1998 of an NT case by the Missoula City-County Health Department (MCCHD) and the Montana Department of Health and Human Services (MDHHS). The findings indicated that tetanus in a newborn of an unvaccinated mother occurred after application of nonsterile clay to the umbilical cord.

On March 21, 1998, a 9-day-old newborn, who had no previous medical problems, was taken to a hospital by her parents who reported a 10-hour history of an inability to nurse and difficulty in opening her jaw. Her parents also had noticed a foul-smelling discharge from her umbilical cord during the preceding 1-2 days. No other symptoms were noted by the parents. On admission, the newborn had trismus, increased general muscle tone, and hyperresponsiveness to external stimuli. The umbilical cord was covered with dried clay, which when retracted revealed a foul-smelling yellow-green discharge. Culture from the umbilical cord grew several anaerobic (*C. perfringens, C. sporogenes*) and aerobic (Staphylococcus, Streptococcus, and Bacillus sp.) bacterial species. NT was diagnosed based on the clinical characteristics.

The newborn was treated with tetanus immune globulin (500 units intramuscularly) and penicillin G (300,000 U/kg/day intravenously) for 10 days. On March 24, she required mechanical ventilation and remained ventilated for 12 days. She was discharged on April 10, with no apparent neurologic sequelae and was developing normally on follow-up at age 7 months.

The mother, a 32-year-old non-Hispanic white woman born in the United States, had never been vaccinated because of her family's philosophic beliefs. She had no complications during her pregnancy and was attended throughout her pregnancy by a licensed "direct-entry" midwife* from her community. The newborn was delivered in a local hospital by cesarean section. While in the hospital, she received standard umbilical cord care with isopropyl alcohol. The newborn was discharged at 3 days of age. For home umbilical cord care, the parents applied a "Health and Beauty Clay" powder provided by the midwife. This clay powder was applied to the umbilical cord up to three times daily with a clean cotton-tipped swab. The family lived in a rural area in a house adjacent to a horse pasture. Although the newborn and her mother stayed primarily indoors, the family's dog often ran between the house and the pasture.

The "Health and Beauty Clay" was a bentonite clay from Death Valley, California. According to the manufacturer, it had been sold for 21 years as a cosmetic product without reported adverse health outcomes. The manufacturing process of the clay did not include

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Item #R2057-G (12/98)

sterilization. The clay was shipped in 2-lb. containers, sold by weight in a local store, and dispensed to local midwives in smaller containers. The midwives would further aliquot the clay into 2-oz., presumably clean vials for distribution to their patients. The use of the clay for umbilical cord care was common among local direct-entry midwives because they believed it accelerated drying of the umbilical cord.

On April 9, MCCHD distributed a health-care advisory to more than 60 health-care providers in the area that emphasized the importance of tetanus toxoid vaccination, particularly for pregnant women, and cautioned against using nonsterile products for umbilical cord care. Following this case, use of clay for umbilical cord care was discontinued by midwives in the community. The mother of the case-patient has since been vaccinated with tetanus and diphtheria toxoids (Td), but as of October 1998 has not initiated vaccination for her infant because of concern about potential adverse effects.

Reported by: B Goode, Missoula City-County Health Dept, Missoula; K Caruso, Community Medical Center, Missoula; J Murphy, A Weber, J Burgett, Montana Dept of Health and Human Svcs. Child Vaccine-Preventable Disease Br, Epidemiology and Surveillance Div, National Immunization Program; and an EIS Officer, CDC.

Editorial Note: In the United States, NT is rare. Tetanus-associated deaths among children aged less than one year, an indicator for NT deaths (most tetanus deaths in this age group are caused by NT), declined from 64.0 per 100,000 population in 1900 to 4.5 by the 1940s. By 1967 in the United States, NT incidence was less than 0.01 per 1000 live-born infants.** This decline is associated with improvements in birth practices and increased levels of population immunity following the initiation of routine tetanus toxoid vaccination since the 1940s. Since 1972, 31 cases of NT have been reported to CDC. Of these cases, only five (16%) mothers had a history of ever having received tetanus toxoid, and only one was known to have received more than one dose.

Factors contributing to this case include the lack of maternal vaccination, the anaerobic conditions and *C. tetani* contamination of the umbilical cord resulting from the application of a nonsterile clay, and the potential exposure to *C. tetani* spores from the nearby horse pasture. The case described in this report is the first since 1984 in an infant of a mother born in the United States and with philosophic objections to vaccination. Since 1984, only two other cases of NT have been reported, both in infants of unvaccinated or inadequately vaccinated mothers born outside of the United States (3,4). The case in this report was the first NT case and one of only four tetanus cases reported from Montana since 1965.

Vaccination with tetanus toxoid during pregnancy is safe and effective in preventing NT (5). The ACIP recommends giving a booster dose of Td to previously vaccinated pregnant women who have not received a Td vaccination within the preceding 10 years, and unvaccinated or partially vaccinated pregnant women should complete the primary series of three doses of Td (6,7).

To prevent NT cases in the United States, health-care professionals should review and update the vaccination status of childbearing-aged women and particularly those who are pregnant. In addition, targeted education regarding the importance and safety of tetanus vaccination is needed among parents and direct-entry midwifery groups, and parents and health-care providers should avoid applying nonsterile products to the umbilical cord of newborns, including products that create anaerobic conditions. Unless all women giving birth are vaccinated appropriately with tetanus toxoid, even hospital-born infants in the United States are at risk for developing NT, especially if unconventional practices of umbilical cord care are followed.

* Direct-entry midwives are a group distinct from certified nurse midwives; in Montana, they are licensed to attend women during uncomplicated pregnancies, labor, and postpartum periods.

**Data on NT incidence per 1000 live-born infants were not available until the 1960s.

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Unprotected People #8
Varicella (chickenpox)

Story #8: Five varicella deaths that could have been prevented

The following five stories of varicella-related deaths appeared in the fall/winter 1998-99 issue of NEEDLE TIPS.

Editors' note: *We hear many stories from parents about physicians who are not encouraging varicella vaccination. We hope that the following reports of deaths secondary to varicella infection will motivate clinicians to recommend this vaccine for all their susceptible patients. There are approximately 100 deaths (half of these in children) and 10,000 hospitalizations each year in the U.S. from varicella. These deaths and hospitalizations are preventable. Please recommend varicella vaccine to your susceptible patients of ALL ages.*

Cases 1, 2, and 3 below were reprinted from the MMWR, *May 15, 1998, vol. 47, no. 18. Cases 4 and 5 were reprinted from* Michigan Immunization Update, *winter 98, vol. 5, no. 1.*

Case 1: Death of a 21-month-old

On February 28, 1997, a previously healthy, unvaccinated 21-month-old boy developed a typical varicella rash. He had no reported exposure to varicella. On March 1, he was taken to a local emergency department (ED) with a high fever and was started on oral acetaminophen and diphenhydramine. On March 3, his primary-care physician prescribed oral acyclovir. On March 4, his mother noted a new petechial-like rash. The next morning, his primary-care physician noted lethargy, a purpuric rash, and poor perfusion. He was transferred to a local ED. Fluid resuscitation and intravenous ceftriaxone were initiated, but the child continued to deteriorate rapidly, requiring intubation, mechanical ventilation, and inotropic support with dopamine. Blood cultures were negative for bacterial pathogens. Laboratory tests indicated disseminated intravascular coagulation and severe dehydration. Approximately 1.5 hours after arrival at the ED, he was transported to a tertiary-care center. Within 10 minutes of arrival, he suffered cardiac arrest and died. The death was attributed to varicella with hemorrhagic complications.

Case 2: Death of a 5-year-old

On December 21, 1997, a 5-year-old unvaccinated boy with a history of asthma was taken to a local ED with a fever of 104.5 F (40.3 C) and a typical varicella rash in multiple stages of healing. The child was treated with antipyretic and antipruritic medications and discharged.

That evening, the boy developed mild dyspnea and was treated at home for a presumed asthma attack with metered-dose inhalers and one dose of oral prednisone. He returned to the ED on December 22 with shortness of breath and a 4-hour history of abdominal and leg pain. On presentation to the ED, one of the patient's siblings had active varicella and another had recently recovered from varicella. Physical examination revealed numerous chickenpox lesions, one of which appeared infected. He was tachypneic, and his extremities were mottled consistent with peripheral septic emboli. Chest and abdominal radiographs revealed a right pleural effusion, pneumonia, and mild ileus. Thoracostomy produced pleural fluid containing gram-positive cocci, confirmed 8 hours later to be group A Streptococcus (GAS). A peripheral blood sample revealed gram-positive cocci. He was admitted to the hospital and treated with intravenous ceftriaxone, nafcillin, and acyclovir.

After admission, his breathing became labored and his extremities increasingly mottled. He rapidly developed hypotension, obtundation, and bradycardia. Despite efforts at cardiopulmonary resuscitation, the child died five hours after arriving at the ED. A postmortem examination attributed the death to GAS septicemia, pneumonia, and pleural effusion, complicating varicella infection.

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Case 3: Death of a 23-month-old

On December 14, 1996, a previously healthy, unvaccinated 23-month-old boy developed fever and a typical varicella rash. Approximately 1-2 weeks earlier, his unvaccinated 4-year-old sibling had contracted varicella. He was taken to his physician on December 17 because of persistent fever and cellulitis of the left foot, and he was hospitalized on December 19 for failure to improve on an unspecified outpatient antibiotic regimen. Because his condition deteriorated despite intravenous methicillin and ceftriaxone, he was transferred to a regional hospital on December 21. Sepsis, possible viral meningoencephalitis, and mild pleural effusion were diagnosed. A cerebrospinal fluid examination revealed lymphocytic pleocytosis, and blood and urine cultures grew penicillin-resistant Staphylococcus aureus. Antibiotics were changed to nafcillin and gentamycin, and intravenous acyclovir was added on December 23. On December 24, the child developed an aortic insufficiency murmur, and an echocardiogram revealed a 9x9 mm vegetation on the aortic valve, consistent with bacterial endocarditis. Serial echocardiograms displayed growth of the vegetation and development of a pericardial effusion. He was transferred to a cardiac surgery center on December 26. While awaiting surgery, he developed refractive heart failure secondary to staphylococcal endocarditis. He became incoherent, probably secondary to a major embolic neurologic event, and died on January 8, 1997.

Case 4: Death of a 35-month-old

In March 1997, a 35-month-old unvaccinated, previously-well male child presented to the local hospital emergency room with gastrointestinal bleeding and onset of shock. He was transferred to a larger hospital and admitted to its pediatric intensive care unit (PICU). On admission to the PICU the child had a seizure, followed by rapidly progressive multisystem failure. The child died 2.5 hours after admission. Autopsy determined that the cause of death was chickenpox and associated complications (causes of death noted in the hospital medical record were cardiac arrest secondary to profound hypotension, possible myocarditis, massive gastrointestinal hemorrhage, and varicella infection). This child had onset of varicella eight days prior to admission (an unvaccinated older sibling had onset of varicella three weeks prior) and was seen by a physician at that time.

Case 5: Death of a 42-year-old

In early 1997, a 42-year-old male presented to a hospital emergency room complaining of epigastric pain. A physical exam noted rash consistent with chickenpox. The patient stated all three of his children had been diagnosed with chickenpox in the previous three weeks. His previous medical history included severe chronic emphysema and chronic bronchitis, which was being managed with steroids under a physician's care. During the course of his hospitalization he developed varicella-related pneumonia and septic shock. The patient died three days after admission. According to a sibling, the patient was thought to have had chickenpox in childhood, but this could not be documented.

Unprotected People #9
Hepatitis B

"I was at no risk for ever having hepatitis B!"

The following letter is written by a 35-year-old woman who contracted hepatitis B virus (HBV) infection. This mother of three children, like at least one third of people who contract hepatitis B, had no known risk factors for HBV infection. We are printing her story because, as she says, "I hope my story helps convince people to get their children and themselves immunized. No one should have to go through what I went through."

The letter is as follows:

I am a married 35-year-old woman and a stay-at-home mother of three young daughters — ages 4, 7, and 10. I live in a small town on the New Hampshire seacoast. I've always been extremely healthy and active.

Last November 12th, I woke up and my joints were aching, especially my hips, knees, and ankles. I had just started an intense walking program, so my first thought was that I had "overdone" it. Each day, I felt progressively worse, and I finally made a doctor's appointment after suffering for about a week.

At the doctor's, I described my symptoms. He said that he thought my symptoms indicated "stress." He took some blood work to rule out rheumatoid arthritis and sent me home with a prescription for ibuprofen and the advice that I should consider going on antidepressants to eliminate the symptoms of "fibromyalgia." I felt devastated because I was sure something was wrong with me.

I continued to feel worse and worse every day. I began to feel more nauseated and exhausted than I can describe. Worse yet, my doctor had made me feel that it was "in my head" even though I told him that I did not feel depressed and was under very little stress!

After getting sicker and sicker, I finally made another appointment ten days later. The nurse practitioner took one look at me and noticed how jaundiced I looked. Also, my stools had become pasty looking and my urine quite dark. I thought I was just dehydrated from not eating for so long. She took blood work to determine if I had hepatitis and what type. I knew absolutely nothing about hepatitis at this point. I was just relieved that I had a diagnosis for what was wrong with me. She then described the ABC's of hepatitis.

I immediately assumed that I had hep A because I am in a category not considered "at risk" for the other types. Two days later, she called back with the results that I had hepatitis B. I felt as if my whole world had caved in.

My husband had to be tested. During the two days that we had to wait for the results, I felt that everything I believed about my marriage had to be a lie. When the results came back negative on my husband, he had to receive immunoglobulin because I had potentially infected him. I then had my two older daughters begin the vaccination series (my youngest had completed the series).

During the approximately six weeks that I felt so sick with this infection, I was so ill that I couldn't even take care of my kids. This whole experience was so incredibly demoralizing and humiliating. I believe that most people know nothing about hepatitis — I know I didn't. If I had known that I had even the minutest chance of becoming infected with hep B, I would have run to my doctor's to get immunized. I've never felt so ill.

I can't describe how it felt to have to wait for six months to finally have the blood work done to rule out the chance that I had become a chronic carrier. No amount of reassurance from the nurse practitioner could convince me that my chance was minimal that I would be chronic. After all, I was considered at no risk for ever having hep B at all!

In June, I received my blood work results and the knowledge that I am completely recovered from

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Item #R2057-I (11/99)

hep B. I thank God for that. But I'm still dealing with the after effects of what I went through. My husband and went to a counselor to deal with the stress that this whole situation placed on our marriage and how angry my husband felt because I hadn't trusted him. I feel sick at the thought that during the time of my acute infection, I could have infected my children or my husband.

This virus has such a stigma attached to it! I stopped telling anyone that I had been infected with hepatitis B.

If my story makes even one person reconsider and have their child or themselves immunized, then it will make me feel better.

Over one third of all people who are infected each year with hepatitis B are in the "no risk" category for infection. I'm one of them, and even a year later, I'm trying to put my horrible experience behind me. No one should ever have to suffer through being infected with this virus — it is totally preventable with a series of three shots. "No risk" living is a meaningless term. If you go to a dentist, borrow a toothbrush, get your ears pierced, get a manicure, or engage in countless other mundane activities, you could become infected.

I hope my story helps convince people to get their children and themselves immunized. No one should have to go through what I went through.

Unprotected People #10 Pertussis

Pertussis claims the lives of two infants

The deaths of two infants from pertussis were reported in the "San Francisco Chronicle" on July 2, 1998. The article reports that the pertussis victims were a 2-month-old boy who died on April 4, 1998, and a 2-month-old girl who died one month later.

The newspaper article entitled, "Bay Area Rash of Whooping Cough Cases: Unvaccinated children help spread the disease," leads off by saying, "Whooping cough, the childhood scourge that just won't go away, has increased in worrisome numbers in the San Francisco Bay Area."

At the time of the article's publication (July 2, 1998) there were, according to state epidemiologist Cynthia O'Malley, PhD, 198 cases of whooping cough in California, most of them concentrated in the Bay Area.

The article ends with this powerful statement from Santa Cruz County public health chief Betsy McCarty, RN, MS: "People who think they are doing the right thing are not getting their children vaccinated. They couldn't be more mistaken. This is as important as putting your kid in the car seat, seeing they have enough to eat, and locking up the poisons."

To read the entire article from the San Francisco Chronicle's website, go to: **www.sfgate.com/cgi-bin/article.cgi?file=/c/a/1998/07/02/MN20754.DTL**

Item #R2057-J (1/99)

Unprotected People #11 Measles

Measles outbreak associated with an unvaccinated population

Although the information in the article entitled, "An Outbreak of Measles Associated with an Unvaccinated Population," is two years old, it highlights the timeless fact that members of unvaccinated communities, such as the religious community in which this outbreak occurred, continue to be victims of vaccine-preventable diseases.

This Minnesota story on a measles outbreak appeared in the February/March 1996 issue of the Minnesota Department of Health's Disease Control Newsletter. *Shortly after the outbreak, most of the unvaccinated children and young adults in this religious community consequently chose to receive two doses of MMR vaccine.*

The "Outbreak Summary" section of the article is reprinted here in its entirety:

"In early 1996, two measles cases were reported to the Minnesota Department of Health (MDH). After a major resurgence of measles both nationally and in Minnesota during 1988-1991, Minnesota had been measles-free since July 1992. During the course of the 1996 case investigations, additional cases that had gone undetected by the medical community were identified with rash onsets dating back to December 6, 1995. During this outbreak, 14 laboratory-confirmed cases and 13 probable cases were reported to MDH. Of the 27 cases, two were Wisconsin residents. The last known rash onset was January 29, 1996. The majority of cases (17; 63%) occurred in persons 20-29 years of age, three were over 30 years of age, six were 10-19 years of age, and one case was an 18-month-old child. All but one of the cases were associated with a religious community whose members live in the St. Paul area and operate a community school. It is not clear how the virus entered this community. Of the 25 Minnesota residents, 22 had not received vaccination against measles. One (an 18-month-old infant) had a documented history of receiving measles-mumps-rubella (MMR) vaccine; one (a 25-year-old) had a probable vaccination history; and for one (a 35-year-old), the vaccination history remains unknown.

"Many of the children and young adults (70%) in the religious community had not been immunized before onset of this outbreak; most have since received two doses of MMR. Two of the laboratory-confirmed cases occurred outside the religious community in a 35-year-old receptionist at a medical clinic where one of the cases had been treated, and in a 44-year-old woman residing in Hennepin County. This second case had no apparent association or exposure to the religious community."

Item #R2057-K (1/99)

Unprotected People #12
Varicella (chickenpox)

Child dies of varicella encephalitis

IAC EXPRESS received the following case report via e-mail from a Canadian physician describing the death of a 3½-year-old boy from varicella encephalitis. At the time of his death, a vaccine against varicella was not yet available in Canada.

The physician's e-mail is reprinted as follows:

A 3½-year-old boy developed chickenpox April 5, 1998. His 7-year-old brother had it at the same time. The younger child had a mild case with relatively few lesions.

Four days before admission the 3½-year old became sleepy and developed a headache. Two days later he developed increasing lethargy, vomiting, drowsiness and disorientation. He was taken to our community hospital on April 11. He had a lowered level of consciousness, responding slightly to pain. The next morning he had shaking movements, probably due to acute herniation of the brain due to swelling. He became comatose, was transferred to a major medical center, and pronounced brain dead on April 13. Life support was discontinued, and he died. The autopsy confirms a diagnosis of varicella encephalitis.

At the time of his illness, varicella vaccine was not available in British Columbia.

A footnote: the mother of this child was devastated by his death. She has refused to set foot in our hospital again because of the unbearable memories, and plans to deliver the child she is now carrying in another city.

Dr. Kirsten Emmott
Comox, British Columbia
Canada

Item #R2057-L (1/99)

Unprotected People #13 Hepatitis A

Virus saps grad in her peak weeks

The following article appeared in the daily newspaper, The Spokesman-Review, *on June 7, 1998. It is reproduced with permission from* The Spokesman-Review, *(Spokane, WA) Copyright 1998. By Cynthia Taggart, staff writer.*

Just thinking about how she got sick nauseates Allison Jester all over again.

"To know how I got it is just disgusting," the Lake City High senior says, cringing.

She's thin, hardly a presence inside jeans not designed to be baggy. She tires so quickly that her days are a series of naps. That's what hepatitis A does. It's cleaned Allison out and broken her down, scared everyone around her and changed her life. And she did nothing to cause it.

Sometime in March, food or water she ingested was contaminated with infected feces.

It could have happened in Seattle or Bellingham, where she was checking out colleges. It could have happened after golf team practices at any burger joint that offers immediate relief to gnawing stomachs.

It could have happened at a grocery store or even a friend's house. Allison will never know. By the time she was diagnosed three weeks ago, the virus had incubated inside her for two months. Tracking its origin was impossible.

When the virus reached maturity, it devoured Allison's liver like a starving lion.

As her senior year began to culminate in stage productions, golf championships, debate tournaments, academic projects and pre-graduation bonding parties, Allison fell ill.

It began with nausea, fever and aches, which Allison interpreted as the flu. She had a major role in the school production of "Noises Off" and willed herself to make it through rehearsals.

"I didn't want to give that part up," she says.

She forced herself through school, although she fell asleep in the auditorium during a special activity. She was so sick that she had to quit a high school golf tournament after the fourth hole.

By the weekend, her stomach refused to hold anything. Her mother, Patti, began to suspect hepatitis after she noticed Allison's urine was unnaturally dark.

Doctors didn't agree with Patti and gave Allison an anti-nausea shot. But Allison continued to vomit the rest of the day until dehydration became a worry.

"I felt like I was going to die," she says. "I had never felt so sick."

Her parents took her to Kootenai Medical Center's emergency room that night. Patti sensed her diagnosis was right when blood test results sent nurses scurrying to warn everyone about Allison's infected body fluids. Hepatitis A zeroes in on the liver, weakening it so much that it can't process medications.

There's no treatment. The virus has to run its course, which varies from weeks to months. Most people fully recover.

Ingesting fecal-contaminated food or water is the only way to catch the A virus, unlike the more dangerous but slightly less common hepatitis B virus. Hepatitis B most often is transmitted through sexual contact.

Food servers who don't wash their hands after using the bathroom spread hepatitis A. Unwashed shellfish from contaminated water can carry the virus. Drinking water contaminated with sewage is another way to catch it.

Hepatitis A is so common that 152,000 cases are reported in this country each year. Forty cases already have been reported to Panhandle Health District

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through May this year, which equals the total number of cases in North Idaho in 1997.

The number of hepatitis A victims is rising so fast that public health agencies have launched a national campaign promoting good hygiene–the best prevention.

Allison's parents, younger sister and uneasy friends got immune globulin shots to boost their immune systems. Some friends panicked and stayed away from Allison. She tried to explain that the virus isn't spread through casual contact.

Doctors prescribed rest. Allison quit the play and her two jobs. School moved to her home. More than anything else, she wanted to compete in a national debate tournament in St. Louis, Mo., on June 14. She was one of four students from Spokane and North Idaho to qualify.

"I was willing to give up everything to do that," she says.

Changing her senior project to accommodate her illness broke Allison's heart. She'd planned to photograph herself on a difficult rock climb in Post Falls. But she was in the hospital the weekend she scheduled the climb.

"I'll do that climb this summer for sure," she says.

Her appetite and energy are growing. She still wilts quickly beyond her house, but mustered the strength to march in Saturday's graduation ceremony.

"We've lamented that she's not been able to enjoy the last few weeks of her senior year," says Patti, who, like Allison, doesn't waste energy stewing over the unfairness of it all. "This is a special time of her life."

Allison will go to the national debate tournament, perhaps a touch more philosophical than she was before her illness.

"The hardest part was realizing I couldn't do everything I wanted," she says. "But it's made me step back a little. The little things don't matter. Things come your way you don't expect. You just deal with it."

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Unprotected People #14 Rabies

Man without history of a bat bite dies of rabies

An article entitled "Human Rabies — Virginia, 1998" was published in the February 12, 1999, issue of the MMWR. *The article is a case report of a 29-year-old incarcerated man who did not have a definitive history of an animal bite was eventually diagnosed with rabies and subsequently died.*

The "Editorial Note" states: "Since 1990, 27 human rabies cases have occurred in the United States (an average of three cases per year). Although 20 (74%) have been attributed to bat-associated variants of the rabies virus, a definitive history of a bat bite was established for only one of these cases."

The "Editorial Note" further states that "medical personnel should consider rabies as a diagnosis in any case presenting with the acute onset and rapid progression of compatible neurologic signs, regardless of whether the patient reports a history of an animal bite. Although early diagnosis cannot save the patient, it may help minimize the number of potential exposures and the need for postexposure prophylaxis.

The entire article is reprinted below:

Human Rabies — Virginia, 1998

On December 31, 1998, a 29-year-old man in Richmond, Virginia, died from rabies encephalitis caused by a rabies virus variant associated with insectivorous bats. This report summarizes the clinical and epidemiologic investigations by the Virginia Department of Health and CDC.

On December 14, 1998, an inmate at the Nottoway Correctional Center in Nottoway County, Virginia, developed malaise and back pain while working on a roadside clean-up crew. He sought medical care at the prison on December 15, compiaining of muscle pains, vomiting, and abdominal cramps, and was treated with acetaminophen. His clinical signs progressed to include persistent right wrist pain, muscle tremors in his right arm, and difficulty walking. On December 18, the patient was sent to a Richmond emergency department, where he had a temperature of 103°F (39.4°C). He initially was alert and oriented but had visual hallucinations. During the next 12 hours, he became increasingly agitated and less oriented. Physical examination revealed anisocoria, increased tone in the right forearm, and hyperesthesia over the entire right side of the body. Intoxication with anticholinergic agents such as pesticides or Jimson weed was considered; however, toxicology studies were negative.

The patient's condition worsened, with hypersalivation, priapism, and wide fluctuations in body temperature and blood pressure. He was intubated and heavily sedated on December 20. Laboratory findings included a white blood cell count of 20,800/uL (normal: 3700-9400/uL), myoglobinuria, and a compensated metabolic anion gap acidosis with renal insufficiency. Peak creatine phosphokinase levels were 130,900 U/L (normal: 50-450 U/L), indicating rhabdomyolysis. Analysis of cerebrospinal fluid (CSF) showed a white blood cell count of 57/uL (normal: 0-5/uL), protein levels of 128 mg/dL (normal: 12-60 mg/dL), and glucose levels of 46 mg/dL (normal: at least two thirds of a concurrent serum glucose value, which was approximately 136 mg/dL). A computed tomography scan of the patient's head revealed no abnormal findings.

A diagnosis of rabies was first considered by the patient's physician on December 20. Samples sent to CDC for testing on December 21 included a nuchal skin biopsy, which tested positive for rabies virus by direct fluorescent antibody test on December 22, and saliva and skin, which were positive by reverse-transcriptase polymerase chain reaction (RT-PCR) assay on December 23. The sequence of the amplified RT-PCR product showed greater than 99.7% DNA homology to a rabies virus variant associated with eastern pipistrelle bats (Pipistrellus subflavus) and silver-haired bats (Lasionycteris noctivagans). Serum and CSF samples obtained December 21 contained rabies virus neutralizing antibody titers of 1:50 and 1:36, respectively, by rapid fluorescent focus inhibition test (RFFIT). A serum sample obtained December 28 showed a ra-

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bies virus neutralizing antibody titer of 1:1200 by RFFIT. After the removal of all sedatives, the patient showed no purposeful movement and loss of brainstem reflexes. He died December 31.

Postexposure prophylaxis (PEP) was administered to 48 persons who possibly had contact with the patient's saliva between December 4 (10 days preceding the first clinical signs of illness) and death. Of the 48, 29 were prison inmates who reported possible contact with the patient's saliva, either while caring for him during his illness or through shared cigarettes or drinking and eating utensils. Three family members who visited the patient at the prison on December 6, 15 health-care providers, and the pathologist who conducted the autopsy also received PEP.

Family members, friends, and prison staff reported the patient had not indicated any contact with or bite from an animal in recent months, and prison medical records did not document evidence of a bite or scratch. The patient lived at a work center that housed up to 160 inmates in two separate dormitories. He had worked around the prison on a farm repairing fence lines and feeding cattle, in a paper recycling facility, and along roadsides cleaning up trash and debris. No evidence of bats was found within the prison or on prison grounds, although inmates reported occasionally seeing bats flying near the outdoor lights in the summer. Several stray cats were reported to occasionally approach inmates at the facility; however, the patient was not known to have handled them.

The patient had been incarcerated at Nottoway for approximately 6 weeks after transfer from another correctional unit. At the other correctional facility, the patient worked inside the prison and on a road crew cutting brush and picking up trash along highways. No evidence of bats was found in the prison, and inmates reported that they had never seen bats inside the facility. Prison staff and inmates reported that they did not recall the patient ever being bitten by an animal while working, and that he usually did not handle small animals found by the road crews.

Editorial Note: This report describes the only case of human rabies diagnosed in the United States during 1998 and the first case in Virginia since 1953. A definitive history of an animal bite could not be established for this patient, and the most likely explanation is an unrecognized bat bite occurring either at the farm or recycling facility or while the patient was working on a road crew. Because the incubation period for rabies varies from several weeks to several months, he may have contracted rabies before his transfer to Nottoway.

Since 1990, 27 human rabies cases have occurred in the United States (an average of three cases per year). Although 20 (74%) have been attributed to bat-associated variants of the rabies virus, a definitive history of a bat bite was established for only one of these cases. Of the 20 attributed to bat-associated variants, 15 (75%) have been caused by the same eastern pipistrelle/silver-haired bat variant responsible for the death described in this report. Although bat-associated rabies virus variants theoretically can be secondarily transmitted from terrestrial mammals, an unrecognized bat bite is the most likely explanation for these cases.

The reasons for the preponderance of human rabies cases associated with the eastern pipistrelle/silver-haired bat virus variant remain speculative. Epidemiologic findings suggest that it can be transmitted following minor, undetected exposures. Insectivorous bats, such as those implicated in the human rabies deaths in the United States, have small teeth that may not cause an obvious wound in human skin. Accordingly, it is important to treat persons for rabies exposure when the possibility of a bat bite cannot be reasonably excluded. In all cases where bat-human contact has occurred, the bat should be collected and tested for rabies if possible. If the bat is not available for rabies testing, the need for PEP should be assessed by public health officials familiar with recent recommendations.

The total of 48 persons who received PEP after contact with the patient described in this report is similar to the mean of 49.8 persons who received PEP after exposures to human rabies cases during 1990-1997. Consideration of rabies before the patient's death may have minimized the number of hospital staff that received PEP in this case.

Although this patient did not exhibit classic hydrophobia, other typical clinical signs, such as hypersalivation, hallucinations, priapism, paresthesias, muscle spasms, and autonomic instability occurred. The use of sedatives may have masked hydrophobia in this patient. Medical personnel should consider rabies as a diagnosis in any case presenting with the acute onset and rapid progression of compatible neurologic signs, regardless of whether the patient reports a history of an animal bite. Although early diagnosis cannot save the patient, it may help minimize the number of potential exposures and the need for PEP.

Unprotected People #15
Hepatitis B

Mother's death from hepatitis B moves daughter to action

In May 1998, IAC EXPRESS received an e-mail from a first-year Asian American medical student in which she shares the details of her mother's sudden death from hepatitis B. The tragedy has motivated this student to educate herself and her family and other Asian Americans about the risks of this vaccine-preventable disease.

The student's e-mail, printed with her permission, is as follows:

I recently suffered an immense loss. In the middle of January of this year, my mother experienced a sudden onset of peripheral edema and ascites. She tested negative for hepatitis B, but the doctors said that she had either liver cancer or severe cirrhosis. In the middle of February, a liver biopsy definitively diagnosed my mother as having hepatocellular carcinoma. This time, her hepatitis B serology came back positive, but her virus levels were low and nonreplicative. By the beginning of April, to the dismay of my family and all those who knew her, my mother fell into hepatorenal syndrome. She died while I was holding her days afterward, only two months after the diagnosis and one month after her intended early retirement.

Being a medical student, I could not help but feel helpless as I watched my mother slip away. What disturbed me even more was how unknowledgeable my cousins and I, all of whom are most likely infected with the same virus, were on the topic. I am writing to you today because I would like to stop feeling helpless. I would like to help educate my cousins, and other Asian Americans like us, of the risk that we face. Therefore, I would greatly appreciate it if you could inform me of the services that you provide, of the resources that you offer, and of the projects you plan. Please let me know how I can best join your effort, and how I can become actively involved with your organization. Thank you.

A First-Year Medical Student

Editorial Note: The Coalition sent this student a packet of our hepatitis B educational materials and referred her to other national organizations that are involved in hepatitis B activities in Asian Pacific Islander American communities. The Coalition's hepatitis B educational materials for providers and patients (some available in 16 languages) can be downloaded from our website at www.immunize.org.

Item #R2057-P (1/99)

Unprotected People #16
Tetanus

Tetanus is far more than a "rusty nail" disease

When I lost my mother to the disease of tetanus, I took it personally. I spent a year grieving about what I should have done differently so that she wouldn't have died. My thoughts were futile, but I had to reconcile myself somehow to her death.

In August 1996, my mother developed an infection in her big toe. The location was at the base of her toenail in the corner. This area was probably the site where tetanus got into her body. I learned later that a site could be as tiny as a thorn prick in the skin. Nevertheless, my mother often wore open-toed shoes, and the infected area must have become contaminated as she worked in her garden.

Tetanus thrives in compost and manure. My mother made compost from fruit and vegetable peelings, egg shells, etc. My husband and I raised farm animals and shared the resulting manure with Mom a couple of times. Hence, I feel some guilt because the manure that was to enrich her garden may have harmed her. Furthermore, she was the kind of person who used sterilized soil for her tomato seeds so they would have a disease-free start.

My mother told me that she was worried about the infected toe because it was deep purple. She said she washed it well after being in the garden, but wondered if she should get a shot. I explained that just the year before, I had cut my finger on a rusty piece of corrugated metal lodged at the end of a railroad tie. Ten years had passed since I had a tetanus shot, and I should have gone for a booster. The doctor was a half hour away, so I didn't go. Instead I looked up "tetanus" in an old 1950 medical book. The information indicated that once tetanus was contracted, symptoms would appear in 2 or 3 days to 2 or 3 weeks. I really worried during this period, was very vigilant for symptoms, but figured I probably wouldn't get tetanus. I knew I had taken a risk, and I tried to tell my mother it wasn't worth the worry I had gone through. As it turned out, she got busy and didn't go either.

Mom's infected toe healed perfectly, and she forgot about tetanus. When she began to feel poorly, she noticed a feeling in her throat. She described it as being like a sore throat, but different. She went to her neighborhood doctor whom she saw regularly and often. Her doctor did five tests. The results would be back in two days. Meanwhile, Mom went back home. That night she could barely swallow her blood pressure medicine. In the morning she called the doctor who then pushed for the test results. They were negative. The doctor questioned my mother further and told her to get an emergency appointment with a neurologist. The neurologist diagnosed the disease as tetanus and hospitalized her.

The next 10 days were a downward spiral. Mom developed double vision as the damaged nerves began to affect her voluntary muscles. At times her chest heaved in spasmodic waves as the muscles locked. The pain was worse than anything she ever experienced, even childbirth. When the pain medicines weren't adequate, the doctor paralyzed her to release her from the pain. Her kidneys failed. She suffered a heart attack and died.

The neighborhood doctor came to my mother's funeral. At communion time she stopped at our pew, held my father's hands in hers, and apologized. She said she never put 2 and 2 together until now. She never connected my mother's many gifts of garden vegetables with the potential for tetanus.

In looking back, I shudder to think of the years I went unprotected. No doctor offered me a booster for a period of 40 years. If people understood the horrific nature of the disease, many of them would ask a doctor to update them, as my family did within a month of my mother's death.

Signed,
A Loving Daughter

Item #R2057-Q (1/99)

Unprotected People #17 Pneumococcal

Two deaths in a nursing home ignite pneumococcal vaccine campaign

Editorial note: *Pneumococcal disease causes approximately 40,000 deaths, 500,000 cases of pneumonia, and 50,000 cases of bacteremia each year in the United States. A 1997 CDC survey indicated that only 45% of adults 65 years of age and older have received their recommended dose of pneumococcal vaccine (MMWR, October 2, 1998, vol. 47, no.38).*

*The following article originally appeared in the Texas Department of Health's newsletter, "*Accent on Health,*" on March 10, 1997, and was reprinted with permission in the spring/summer 1999 issue of* NEEDLE TIPS.

According to Devora Goodnight, it wasn't just luck that only two people died in a recent outbreak of deadly pneumococcal disease where she works at the Houston County Nursing Home in Crockett. What undoubtedly saved lives when the outbreak began was a combination of the nursing home staff's recognizing the seriousness of the outbreak and their getting an immediate response from experts at the Texas Department of Health (TDH). But perhaps the most decisive single factor was the quick immunization of all potential patients with a vaccine which often is overlooked by physicians and patients alike.

After two patients died of streptococcal pneumonia infections and one other was stricken, Goodnight said, "We knew we had a situation that might cost many of our residents' lives if it got further out of hand. We had never had anything like this happen before and didn't even know what to expect if we called TDH for help. But we knew we would most likely lose more of our 'family' if we didn't."

At TDH's Infectious Disease Control and Surveillance Division, epidemiologist Beverly Ray said that Goodnight and the home's nursing director Debbie Hargrove showed "the highest standard of concern for their residents."

Ray explained that although outbreaks of pneumococcal disease caused by the *Streptococcus pneumoniae* bacteria are rare, the bacteria spread rapidly among unimmunized people whose health may already be compromised. People in good health with normal immune systems are not as likely to develop infections, but ill people, such as elderly nursing home residents with existing problems, are especially at risk of developing pneumonia after exposure to the bacteria.

According to Ray, *Streptococcus pneumoniae* causes about half a million individual cases of pneumonia, some 3,000 cases of meningitis and about seven million ear infections in the United States every year. The most susceptible people are the elderly and ill, such as those at the Crockett nursing home, infants and toddlers, people with chronic health conditions such as diabetes or emphysema, and people without spleens or with weakened immune systems. Outbreaks of the disease occur most commonly during the winter months, among nursing home patients, jail or prison inmates, and other groups who share close living quarters and often breathe the same air.

The U.S. Centers for Disease Control and Prevention recommends that all people 65 years of age or older receive one dose of pneumococcal vaccine. Those at greatest risk for serious complications from pneumococcal disease need to receive a second dose five years later. The vaccine is effective against at least 23 different strains of streptococcal bacteria and is fast acting. However, Ray said that in a recent survey of Texans 65 and older, only 42 percent said they had been vaccinated against bacterial pneumonia.

Ray said, "This vaccine is one of the most effective, fastest-acting vaccines we have for averting outbreaks among such groups as nursing home resi-

(continued on next page)

dents, yet it is unbelievably underused. We hope that physicians will offer the vaccine more often to their own patients who may be at risk, and that more patients or family members will remember to ask for the vaccine if they have not already had it."

After TDH received the Crockett nursing home's call for help on Jan. 23, Ray and a team of other epidemiology staff drove directly to Crockett to begin taking blood samples from about 90 nursing home residents and staff and obtaining permission to begin vaccinating as many of the residents as possible. Only 14 of 88 residents had previously been immunized. Vaccinations began the following morning, Jan. 24.

According to Hargrove, she and others on the nursing home staff "were amazed at how quickly TDH brought the outbreak under control."

Although two patients out of the first three diagnosed with pneumococcal disease died, the remaining victim of the outbreak survived and has recovered. The vaccines which the other residents received have begun protecting the home's residents from further infections. For a few days after the residents were vaccinated, some of their visiting friends and family members were advised to take antibiotics as an additional precaution against more pneumococcal infections, but no other cases occurred.

Goodnight said that the loss of the two residents who died from pneumococcal disease has been hard on the other residents and the staff alike. "They were part of our family. We always try to operate as one big family here, and a death is personal to all of us. We are just very, very grateful that help was there when we needed it to prevent even more tragedies," she said.

Unprotected People #18 Hepatitis B

Lack of prenatal screening for hepatitis B causes multiple tragedies for one family

The following case report of a mother who had a previous history of hepatitis B, but received no prenatal screening, serves to illustrate the importance of following the recommendation of the Advisory Committee on Immunization Practices to screen every pregnant woman during each pregnancy. Not only did this woman's baby die of fulminant hepatitis B infection, but when hepatitis B screening was done for the surviving family members, it was found that mother, father, and the other two young children were all positive for HBV.

This case report is excerpted from an Immunization Action Coalition (IAC) educational piece entitled "Universal prenatal screening for hepatitis B," *a piece that reviews neonatal transmission and screening rationale for health professionals. It was written for IAC by Deborah K. Freese, MD, pediatric gastroenterologist and member of the transplant unit at Mayo Clinic. She is also a member of the IAC Advisory Board. Written in 1993, this educational piece continues to be distributed because there are still health professionals who do not screen every pregnant woman for HBsAg during each pregnancy.*

The excerpt of Dr. Freese's article follows:

An infant with fulminant hepatitis B

The medical and economic costs of failing to screen for HBV can be illustrated on a more personal level by the case of a single infant recently cared for in the Twin Cities. This patient was the child of a middle class couple from a farming community in a neighboring state.

During her initial prenatal visit, the mother gave a history of having had hepatitis of some sort 20 years previously. She was told at that time that she had recovered from the disease and would subsequently be immune to further hepatitis infections. Despite the fact that a previous history of hepatitis would place her in the "high-risk" category, no prenatal HBV screening was done. Pregnancy and delivery were uncomplicated, and the baby did well for the first two months of life.

At that time, the parents began noting feeding difficulties, irritability, and jaundice. Evaluation revealed severe coagulopathy, markedly elevated liver tests, and hypoglycemia. The infant was eventually referred for liver transplantation with the diagnosis of fulminant hepatitis B. The infant was admitted to the intensive care unit, received very aggressive medical management, and an urgent search for donor was initiated. No suitable donor coulc be located, the child continued to deteriorate and died after two weeks from hepatic encephalopathy and herniation.

Hepatitis B screening was then done for the surviving family members. It was found that mother, father, and the other two young children were all positive for HBV. Mother and one child had significantly elevated liver tests and are undergoing further evaluation. It seems clear that had HBV screening been carried out, none of the children would have been infected and the death of the youngest could have been prevented.

The economic impact on the health care system from this one family alone is significant. It includes the costs of hospitalizations at two hospitals of the infant who died (approximately $100,000), the immediate costs of evaluation and possibly therapy for the surviving child with evidence of chronic hepatitis, and the long-term costs of monitoring and observation in both chronically infected children. Had successful liver transplantation been possible for the infant, the costs of that procedure and lifetime immunosuppression would have further increased the costs.

If you would like to read the complete article by Dr. Freese in camera-ready format, go to: www.immunize.org/catg.d/p2120uni.pdf

Item #R2057-S (1/99)

Unprotected People #19
Varicella (chickenpox)

How many varicella deaths will it take?

In 1998, six people in Florida died of varicella. The case reports of their deaths were published in the May 14, 1999, issue of the MMWR *as part of an article entitled "Varicella-Related Deaths Florida, 1998."*

The May 14th issue of IAC EXPRESS (#77) included these case reports. We are reprinting them here as an UNPROTECTED PEOPLE story because we believe these tragic deaths will convince those health professionals who still believe varicella is a harmless disease to begin vaccinating their susceptible patients.

Case 1: Death of a 6-year-old
On February 19, a healthy, unvaccinated 6-year-old boy developed a varicella rash, abdominal pain, malaise, and loss of appetite following exposure to a classmate with varicella. The child had asthma and intermittently had been on inhaled steroid therapy but had not received steroids within the previous month. On February 22, he was hospitalized with hemorrhagic skin lesions, tachycardia, tachypnea, and a platelet count of 89,000 (normal range: 150,000-350,000). Several hours after admission he developed pulmonary edema and respiratory insufficiency and required mechanical ventilation. He died on February 23. Tissue samples of multiple organs had a positive polymerase chain reaction for varicella zoster virus (VZV).

Case 2: Death of a 58-year-old
On March 27, a healthy, unvaccinated 58-year-old woman developed a varicella rash. She was born in Cuba and had moved to the United States in 1995. She did not have a history of or known exposure to varicella. On April 3, she was hospitalized with a 5-day history of increasing shortness of breath and productive cough and was diagnosed with varicella pneumonitis. She was treated with intravenous acyclovir and ceftriaxone, but developed adult respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy, renal failure, and coma. She died on April 20.

Case 3: Death of a 29-year-old
On April 27, a healthy, unvaccinated 29-year-old man developed a varicella rash. In early April, his children had contracted varicella. On April 29, he sought care at a local emergency department for chest pain and respiratory distress. Chest radiographs showed bilateral pulmonary interstitial infiltrates. On April 30, he began coughing up blood, was intubated because of increasing respiratory insufficiency, and was treated with intravenous acyclovir and antibiotics. He developed sepsis, ARDS, and multiorgan failure, and died May 12.

Case 4: Death of a 21-year-old
On May 5, a 21-year-old unvaccinated female employee at a family child care center developed a varicella rash after exposure to a child with varicella. The employee had a history of asthma and was treated with 5 mg prednisolone per day. She was hospitalized on May 7 with varicella pneumonitis and received intravenous acyclovir on May 8, but she died the same day.

Case 5: Death of an 8-year-old
On July 11, an 8-year-old unvaccinated boy developed a maculopapular rash diagnosed clinically as varicella and confirmed by direct flourescent antibody test on July 23. He had acute lymphocytic leukemia (ALL) and had been on immunosuppressive therapy since receiving a bone marrow transplant on May 15. He had not had varicella and had no known varicella exposure. He was treated with varicella zoster immunoglobulin on July 16 and acyclovir on July 23. He died on July 25 after recurrence of leukemia with a graft-versus-host reaction complicated by disseminated varicella, cellulitis, ileus, and hypertension.

Case 6: Death of a 45-year-old
On October 3, an unvaccinated 45-year-old man with diabetes mellitus, asthma, and cirrhosis of the liver developed a varicella rash. He was born in Cuba

Item #R2057-T (1/99)

and had resided in the United States for 35 years. He had no history of varicella and no known exposure. He was not receiving steroids or immunosuppressive drugs. He was admitted to the hospital with varicella on October 5 and on October 6, treatment was initiated with oral acyclovir. He died on October 8; pathologic evidence from the postmortem examination revealed VZV in all major organs.

Five of the six case-patients who died because of varicella were eligible for vaccination. The sixth, a child with active ALL (case 5), was ineligible for vaccination. Under a special protocol, children with ALL who meet inclusion criteria may be vaccinated. Although one case-patient was receiving systemic steroids when she contracted varicella, the dose was not large enough to be a contraindication; varicella vaccine can be administered to adults receiving less than 20 mg prednisone per day or its equivalent, and to children receiving less than 2 mg per kg body weight per day or a total of less than 20 mg per day.

Two case-patients (2 and 6) were aged greater than 30 years and were born and raised in Cuba. The epidemiology of varicella in tropical regions differs from that in temperate regions. VZV is heat labile and may not survive and transmit well in warm climates. In the tropics, age distribution of cases and VZV seroprevalence data have indicated a higher proportion of cases occurring among adults. Clinicians should be aware of the greater susceptibility of adults to varicella when evaluating persons from tropical countries.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC 8

OFFICE OF CONGRESSIONAL AND
INTERGOVERNMENTAL RELATIONS

The Honorable Dan Burton
Chairman
Committee on Government Reform
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

Attached are EPA's responses to your follow-up questions from the July 18 Government Reform Committee hearing on mercury in vaccines. Please have your staff contact Reynold Meni of my office at 202-564-3669 if you have any questions.

Sincerely,

Diane E. Thompson
Associate Administrator

Attachment

Follow-up Questions and Answers from July 18 House Government Reform Committee Hearing on Mercury in Vaccines

1. **The National Research Council report is about methylmercury in fish. What is the existing research in thimerosal and/or ethylmercury?**

We are assuming your question relates to EPA's research activities. Significant research on ethylmercury is being done by other organizations, but EPA is not conducting any research in thimerosal and/or ethylmercury. To date, EPA has focused its efforts on methylmercury, because methylmercury is the most common form of environmental contamination by mercury. Ethylmercury is not found in the environment.

EPA is eager to continue working with the Food and Drug Administration (FDA), the Centers for Disease Control (CDC), and Congress to better understand these chemicals to ensure that public health is adequately protected.

2. **Do you consider it safe for a child to get 41 times the EPA limit in one day for mercury?**

EPA considers that exceeding a child's daily limit, or reference dose (RfD), for mercury by 41 times is of serious concern. The literature on ethylmercury and our research on methylmercury suggest that exposure at such levels of ethylmercury or methylmercury may potentially cause neurological and/or developmental damage, such as tremors, altered visual function, and impaired hearing. Although EPA's RfD for methylmercury (the daily dose at which an individual could be exposed without adverse health effects) is designed to provide a range of protection, EPA is generally concerned when a RfD is exceeded.

3. **What would be the expected results of such an exposure?**

Please note that we can only speak to the effects of exposure to methylmercury. The expected results of high exposure to methylmercury would depend on the stage of development of the nervous system, as well as the magnitude of the methylmercury exposure. We would expect the predominant effects of exposure to be developmental delays and/or deficits in motor and sensory processes. These delays/deficits are associated with poorer results on diverse tests of intellectual functioning.

4. **Is there a difference between acute doses every few months and low dose exposure daily?**

Yes, there is a difference between these two types of exposure. Doses that exceed the daily allowable limit every few months may adversely effect the developing nervous system, and effect motor and sensory processes, depending on the dose level. Daily low dose exposure,

as long as those exposures are at or below the daily allowable dose, is expected to not be of concern. The RfD is designed to provide a range of protection when exposures occur on a low dose chronic basis.

5. Why are vaccines not listed on the EPA's website as a source of mercury?

EPA does not have authority to regulate vaccines and does not have information on the effect of vaccines to the environment. Although EPA has focused on methylmercury as an environmental contaminant, EPA also addresses the uses of mercury in health care products and facilities, and the disposal of mercury from health care facilities. Information about this is available on the EPA website (e.g., EPA regulates medical waste incinerators and promotes the substitution of mercury-free products to help keep them out of the waste stream).

6. Do you think it would be prudent to remove mercury from vaccines?

EPA has no formal policy regarding the removal of mercury from vaccines, as we do not have the authority to regulate vaccines.

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CHRISTOPHER SHAYS, CONNECTICUT
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ONE HUNDRED SIXTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON GOVERNMENT REFORM

2157 RAYBURN HOUSE OFFICE BUILDING

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INDEPENDENT

July 25, 2000

Delivered via fax: (202) 260-3573

Ramona Trovato, Ph.D.
Director
Office of Children's Health Protection
Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Mail Stop (7203)
Washington, D.C. 20460

Dear Dr. Trovato:

On behalf of the Committee on Government Reform, I want to thank you for testifying at our recent hearing entitled: "Mercury in Medicine – Are We Taking Unnecessary Risks?" Your testimony will assist us in continuing our further investigations into mercury levels in vaccinations and the threat it poses to our children's health and safety.

At the conclusion of the hearing, I asked you to respond to written questions submitted by the committee for the record. I informed you that the answers to these questions would be made public and reminded you that you are still considered under oath for the purposes of answering these questions. Attached, you will find these questions. I hope you will answer them to their fullest extent possible.

Please return the responses to my professional staff member, S. Elizabeth Clay by August 1. Please contact Ms. Clay at 202-225-5074 should you have any questions. Again, thank you for your cooperation and keep the Committee informed of your research results.

Sincerely,

Dan Burton
Chairman

Enclosures

Questions to Dr. Ramona Trovato, Environmental Protection Agency

For the Record for July 18, 2000
Hearing Before the Government Reform Committee

1. **The National Research Council report is about methylmercury in fish. What is the existing research in thimerosal and/or ethylmercury?**
2. **Do you consider it safe for a child to get 41 times the EPA limit in one day for mercury?**
3. **What would be the expected results of such an exposure?**
4. **Is there a difference between acute doses every few months and low dose exposure daily?**
5. **Why are vaccines not listed on the EPA's website as a source of mercury?**
6. **Do you think it would be prudent to remove vaccine from medicines?**

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BERNARD SANDERS, VERMONT,
INDEPENDENT

July 25, 2000

Roger H. Bernier, Ph.D., M.D.
National Immunization Program
Centers for Disease Control and Prevention
1600 Clifton Road
Mail Stop E05
Atlanta, Georgia 30333

Dear Dr. Bernier:

On behalf of the Committee on Government Reform, I want to thank you for testifying at our recent hearing entitled: "Mercury in Medicine – Are We Taking Unnecessary Risks?" Your testimony will assist us in continuing our further investigations into mercury levels in vaccinations and the threat it poses to our children's health and safety.

At the conclusion of the hearing, I asked you to respond to written questions submitted by the committee for the record. I informed you that the answers to these questions would be made public and reminded you that you are still considered under oath for the purposes of answering these questions. Attached, you will find these questions. I hope you will answer them to their fullest extent possible. I would also ask that you review the report, "Autism: A Unique Type of Mercury Poisoning" and the National Research Council's report on Methylmercury and comment back to the Committee regarding the information provided and how the Food and Drug Administration will address the concerns raised.

Please return the responses to my professional staff member, S. Elizabeth Clay by August 1. Please contact Ms. Clay at 202-225-5074 should you have any questions. Again, thank you for your cooperation and keep the Committee informed of your research results.

Sincerely,

Dan Burton
Chairman

Enclosures

Questions to Dr. Roger Bernier, Centers for Disease Control and Prevention

For the Record for July 18, 2000 Hearing Before the Government Reform Committee

1. **The Advisory Committee on Vaccine Practices (ACIP) has a vacancy. Will the CDC be adding a consumer representative in this slot?**
2. **Why aren't vaccines identified in the ATSDR and CDC web sites as sources of mercury?**
3. **The ACIP recently met and acknowledged that there was a statistically significant positive correlation between mercury exposure and the following conditions: unspecified developmental delay, tics, ADD, speech delay, and neurodevelopmental delay. The investigation team determined that a possible association between neurological developmental disorders and mercury exposure through vaccines existed before the age of six months. How then is it that the ACIP stated that the evidence was insufficient to support a causal relationship between vaccines and the above mentioned disorders?**
4. **What documentation has CDC sent to physicians to notify them of the potential for mercury poisoning through vaccines?**
5. **You stated that the CDC had been given a "vote of confidence" for its management of the ACIP. What were you referring to?**
6. **Please provide to the Committee the conflict of interest waivers relative to the current membership of the ACIP and for the most recent meeting at which thimerosal was discussed.**
7. **What is the liability to the CDC and the Federal Government for selling the states health agencies mercury-containing vaccines?**
8. **Is the CDC concerned about the potential for harm for children in Third world countries who are given vaccines by the United States that contain mercury?**
9. **Please provide a list of the vaccines that are in consideration by the CDC and ACIP for consideration to be added to the Childhood Immunization Schedule.**
10. **You referenced a fire in a manufacturing facility that hindered the delivery of a mercury-free vaccine. Please provide the details of this manufacturer, the specific incidence you refer to and contingency plans that CDC has developed in the incidence that the MMR vaccine, which comes from a sole source, would be delivered if Merck's facilities were damaged by fire?**
11. **Are all the new thimerosal-free vaccines truly mercury free?**
12. **As the largest purchaser of vaccines, what is the CDC doing to assure that only mercury-free vaccines are purchased?**
13. **You mentioned that during questioning that too swift a change to thimerosal-free vaccines could be harmful. Please explain what that harm would be.**

14. **Please provide any and all information relating to the demography of the samples (i.e. age, sex, race, etc.) used in studies relating to thimerasol that CDC or HHS has utilized.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention

August 7, 2000

The Honorable Dan Burton
Chairman
Committee on Government Reform
House of Representatives
Washington, DC 20515-6143

Dear Chairman Burton:

Enclosed are responses to the questions that you sent as a follow up to the July 18, 2000 House Committee on Government Reform and Oversight Hearing, "Mercury in Medicine: Are We Taking Unnecessary Risks?"

Your letter on July 25, 2000 also requested that I review and comment on the report, "Autism: A Unique Type of Mercury Poisoning" and the National Research Council's report on methylmercury. CDC is finalizing its review of the report on autism and will provide comments both to you and the authors when the review is complete. As for the National Research Council's report, we defer to ASTDR or the FDA who have responsibility for issuing guidance values regarding exposure to mercury.

Thank you for your continued interest in this important public health issue.

Sincerely,

Roger H. Bernier

Roger H. Bernier, Ph.D., MPH
Associate Director for Science
National Immunization Program

Enclosure

QUESTIONS TO DR. ROGER BERNIER, CENTERS FOR DISEASE CONTROL AND PREVENTION

For the Record for July 18, 2000 Hearing Before the Government Reform Committee

1. **The Advisory Committee on Vaccine [sic] Practices (ACIP) has a vacancy. Will the CDC be adding a consumer representative in this slot?**

Nominations have moved forward to replace the members of the ACIP who are rotating off of the Committee. However, the ACIP Charter is being amended to add three additional members, including a consumer representative. We anticipate the Charter amendment will be signed by November 1, and with that change a consumer representative will be selected for Committee membership.

2. **Why aren't vaccines identified in the ATSDR and CDC web sites as sources of mercury?**

CDC, with the support of ASTDR and other federal agencies, has pursued an extensive communication effort to clearly convey the position of the Public Health Service on this issue. CDC's Web site has several sections that provide the latest available scientific information about thimerosal in vaccines. Some of these site locations are listed below.

<http://www.cdc.gov/nip/vacsafe/concerns/thimerosal/thimerosal.htm>

<http://www.cdc.gov/nip/vacsafe/concerns/thimerosal/joint_statement_00.htm>

<http://www.cdc.gov/od/nvpo/fs_tableVI_doc2.htm>

3. **The ACIP recently met and acknowledged that there was a statistically significant positive correlation between mercury exposure and the following conditions: unspecified developmental delay, tics, ADD, speech delay, and neurodevelopmental delay. The investigation team determined that a possible association between neurological developmental disorders and mercury exposure through vaccines existed before the age of six months. How then is it that the ACIP stated that the evidence was insufficient to support a causal relationship between vaccines and the above mentioned disorders?**

Not all correlations equate to causal relationships. ACIP considered the strengths and weaknesses of the evidence from the Vaccine Safety Datalink study and evidence from at least two other studies. In regard to the VSD study, the ACIP heard a description of the study from the principal investigator and heard the report from consultants who spent two days reviewing the

methods and results from that study. These experts concluded that the evidence is very weak and insufficient to support a causal relationship. In addition, the ACIP heard the results from another managed care organization which did not confirm the earlier findings from the VSD study, and they heard results from NIH scientists who found that blood levels of mercury after vaccination were no higher than what would be expected as background levels. For these reasons, the ACIP concurred with the joint statement issued by the American Academy of Pediatrics, the American Academy of Family Physicians, and the Public Health Service agencies that there is no convincing evidence of harm caused by low levels of thimerosal in vaccines.

4. **What documentation has CDC sent to physicians to notify them of the potential for mercury poisoning through vaccine?**

The risk of harm from thimerosal in vaccines remains a theoretical risk. There is no convincing scientific evidence of any harm caused by low levels of thimerosal in vaccines. However, the CDC has done much to inform physicians about thimerosal in vaccines, including:

- The U.S. Public Health Service (including CDC) issued two joint statements with the American Academy of Pediatrics and the American Academy of Family Physicians on thimerosal;

- Publishing a joint statement and a summary in the CDC's Morbidity and Mortality Weekly Report, a publication for health professionals that typically generates much mass media and specialized media coverage;

- Posting the joint statements, along with a number of informational materials, on the CDC's National Immunization Website (http://www.cdc.gov/nip)

- Working with the American Academy of Pediatrics and American Academy of Family Physicians to disseminate the joint statements and other information about thimerosal to their members via their newsletters, professional publications, and websites;

- Having non-governmental immunization organizations, including the Immunization Action Coalition, post the joint statements on their websites, along with links to the information found on the CDC's National Immunization Program website; and

- Sending thimerosal updates, the joint statements, and guidelines for transitioning to thimerosal preservative-free vaccines (July 1999) to state immunization program managers who, in turn, provide the information to public sector physicians.

5. **You stated that the CDC has been given a "vote of confidence" for its management of the ACIP. What were you referring to?**

At the hearing "FACA: Conflicts of Interest and Vaccine Development" held by the House Government Reform Committee on June 15, 2000, Ms. Marilyn Glynn from the Office of Government Ethics stated "(a)s to the CDC, we found that they had a sound, what we call a sound ethics program..."

6. **Please provide to the Committee the conflict of interest waivers relative to the current membership of the ACIP and for the most recent meeting at which thimerosal was discussed.**

See additional documentation attached.

7. **What is the liability to the CDC and the Federal Government for selling the states' health agencies mercury-containing vaccines?**

The CDC negotiates vaccine purchase contracts through which the States order vaccine for use in the Vaccines for Children (VFC) program. Also, the CDC contracts are made available to the States to purchase additional vaccine using their 317 grant funds and other State funds. These contracts generally include all childhood vaccines that are licensed in the United States and recommended by the ACIP for use, including those containing thimerosal and those that are preservative-free. Selection of particular brands of vaccines to use in the VFC program, or to purchase using 317 or other State funds, is left to each State, which may in turn shift such choice to the medical provider. Given State/provider choice and the current standard of care regarding these vaccines, purchases through CDC contracts presumably do not present significant potential liability for the Federal government.

8. **Is the CDC concerned about the potential for harm for children in Third world countries who are given vaccines by the United States that contain mercury?**

CDC shares the same concern about reducing risks of vaccination among children in Third world countries as for U.S. children. CDC has assured that the World Health Organization and representatives of the European Agency for the Evaluation of Medicinal Products have been aware of and participated in the deliberations regarding thimerosal in vaccines in the United States. These groups are currently considering proposals to reduce the exposure to thimerosal in vaccines worldwide.

The vaccination of children in much of the world continues to require the use of multi-dose vials for reasons of cost, production, shipping and storage capacity. Multi-dose vials require a preservative to prevent microbial contamination after the vial is opened. Thimerosal continues to be the most widely used preservative in inactivated vaccines such as DTP, hepatitis B and

Haemophilus influenzae type b throughout the world; most countries do not have access to vaccines with no or reduced thimerosal.

Children in developing countries are at highest risk for serious illness, disability and death from vaccine-preventable diseases, while the potential risk of harm for children who receive vaccines containing ethylmercury has not been established. Therefore the benefit-risk ratio is strongly in favor of vaccination with available vaccines in countries where vaccine-preventable diseases are still widely prevalent.

9. Please provide a list of the vaccines that are in consideration by the CDC and ACIP for consideration to be added to the Childhood Immunization Schedule.

CDC and ACIP are always reviewing and discussing information related to new vaccines which are being developed or may be licensed which could eliminate vaccine-preventable diseases, but ACIP is not currently engaged in the development of recommendations for adding any vaccine to the childhood immunization schedule. Some vaccines which may be considered over the next several years might include influenza vaccine, hepatitis A vaccine (already recommended for routine use in certain geographic areas), and meningococcal conjugate vaccine.

10. You referenced a fire in a manufacturing facility that hindered the delivery of a mercury-free vaccine. Please provide the details of this manufacturer, the specific incidence you refer to and contingency plans that CDC has developed in the incidence that the MMR vaccine, which comes from a sole source, would be delivered if Merck facilities were damaged by fire?

CDC maintains a stockpile of single source vaccines (MMR, E-IPV) to provide protection in case of an emergency supply problem. In the early 1980's the Merck manufacturing facility had a fire in their lyophilization cabinets used to process MMR vaccine. They were unable to produce the vaccine for a period of time and "borrowed " the existing CDC stockpile to meet their public and private orders until they could rebuild their plant.

11. Are all the new thimerosal-free vaccines truly mercury free?

We defer this question to the FDA, as they are the appropriate agency to answer this question.

12. As the largest purchaser of vaccines, what is the CDC doing to assure that only mercury-free vaccines are purchased?

CDC has spoken with all vaccine manufacturers and made it clear to them that we wish to rapidly move toward a thimerosal free vaccine supply. As each new product receives licensure from the FDA, CDC will establish contracts to allow immunization programs to select these products.

Additionally, CDC indicates which vaccines contain thimerosal so that providers may select those vaccines if they prefer.

13. You mentioned that during questioning that too swift a change to thimerosal-free vaccines could be harmful. Please explain what the harm would be.

Our recent experience with changing recommendations for hepatitis B and for making preferences for some children to continue receiving vaccines and for others to postpone vaccination revealed that a selective policy does not work smoothly. Some children fall between the cracks and disease occurs when it could have been entirely prevented.

If a recommendation is made to preferentially use certain vaccines rather than others before an adequate inventory of preferred vaccines is available to all providers, some children are likely to not receive vaccines because providers and parents will be reluctant to use the vaccines that are not preferred. The result will be children remaining susceptible to vaccine-preventable diseases who otherwise could be protected.

14. Please provide any and all information relating to the demography of the samples (i.e. age, sex, race, etc.) Used in studies relating to thimerasol that CDC or HHS has utilized.

The demography of the cohort used in the Vaccine Safety Datalink analysis is as follows:
Gender:
Male 50.5%
Female 49.5%

Age distribution at the end of follow-up:
1-2 years old: 22.8%
2-3 years old: 19.6%
3-4 years old: 17.3%
4-5 years old: 15.8%
5-6 years old: 14.5%
6-7 years old: 10.0%

Data on race was available from one of the two HMOs. It represents 66% of that sample.
White: 83%
Black: 3.7%
Asian: 6.5%
Hispanic: 6.8%

The demography of the cohort used in the Harvard Pilgrim study is as follows:
Gender:
Male 50.1 %

Female: 40.9%

At the end of the follow-up the distribution was:
1-2 years: 18.1%
2-3 years: 17.0%
3-4 years: 16.8%
4-5 years: 15.6 %
5-6 years: 13.2%
6-7 years: 12.2%

No race data were collected.

We do not have demographic data for the NIH study that was reviewed.

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BERNARD SANDERS, VERMONT
INDEPENDENT

July 25, 2000

Ms. Lyn Redwood
254 Trickum Creek Rd.
Tyrone, Georgia 30290

Dear Ms. Redwood:

On behalf of the Committee on Government Reform, I want to thank you for testifying at our recent hearing entitled: "Mercury in Medicine – Are We Taking Unnecessary Risks?" Your testimony will assist us in continuing our further investigations into mercury levels in vaccinations and the threat it poses to our children's health and safety.

At the conclusion of the hearing, I asked you to respond to written questions submitted by the committee for the record. I informed you that the answers to these questions would be made public and reminded you that you are still considered under oath for the purposes of answering these questions. Attached, you will find these questions. I hope you will answer them to their fullest extent possible.

Please return the responses to my professional staff member, S. Elizabeth Clay by August 1. Please contact Ms. Clay at 202-225-5074 should you have any questions. Again, thank you for your cooperation and keep the Committee informed of your research results.

Sincerely,

Dan Burton
Chairman

Enclosure

Questions to Lyn Redwood

For the Record for July 18, 2000
Hearing Before the Government Reform Committee

1. As a Nurse practitioner what is your opinion on the role of immunizations in public health.
2. Has your view changed given your family experience with mercury poisoning?
3. When your child was vaccinated, did the information provided to you indicate that your child was being given a vaccine that contained mercury?
4. What is your opinion of the Centers for Disease Control and Prevention's Facts Sheets on Immunization?
5. What should the Federal Government be doing about the massive rate increases in ADD and autism?
6. What is the role of the health care practitioner in informing parents about newly raised concerns about vaccine safety?
7. During the hearing Dr. Marie Bristol-Power stated that 80 percent of children display some symptoms of autism from birth? Do you agree with that statistic?
8. When did your child first display symptoms of autism?

Congress of the United States
House of Representatives
Committee on Government Reform
2157 Rayburn House Office Building
Washington, D.C. 20515-6143

July 30, 2000

Dear Ms. Clay,

Below please find my response to additional questions submitted by the committee.

Sincerely,

Lyn Redwood

1. As a Nurse Practitioner what is your opinion on the role of immunizations in public health?

   Vaccines have obviously been of value from a public health perspective, but I'm concerned that the value has been over inflated and reports of harm have been carelessly dismissed. I am now aware that many of the diseases that the vaccine program takes credit for having eradicated were already on the decline prior to the introduction of the vaccine. I also have concerns that the vaccine program has become over zealous in its efforts to vaccinate for relatively minor diseases, like chicken pox and rotovirus, and that profit motives from vaccine manufacturers may be exceeding basic science. Having actually attended an Advisory Committee for Immunization Practices meeting it was obvious from the lack of discussion prior to voting, that the decisions had already been made behind closed doors prior to the meeting.

2. Has your view changed given your families experience with mercury poisoning?

   Yes, most definitely. Prior to the announcement by FDA that some infants had been exposed to mercury from thimerosal in vaccines in excess of Federal Safety Guidelines, I had total confidence in the safety of the Nations Vaccine Programs. Today, as a result of my further investigations into this occurrence, I have grave concerns regarding the science behind our current vaccine recommendations. Most astonishing to me was the fact that the FDA, CDC or ACIP had never thought to look at the cumulative exposure to mercury when new vaccines were added to the early immunization schedule. The addition of 3 Hemophilus influenza B injections and 3 Hepatitis B injections the first 6 months of life, which took place in the early 1990's, essentially tripled an infant's exposure to mercury. I think it is not a chance occurrence that it has been during this same time period that we have seem such a tremendous increase in learning and behavioral disabilities, pervasive developmental

disabilities and autism. I also have concerns that other additives to vaccines, like aluminum and formaldehyde, have not been investigated as well for their cumulative toxicity. As with the case of thimerosal, there appears to have been no additional safety studies required for this product after the 1930's, when it was first introduced as a preservative. Each time a new vaccine was evaluated, the safety of thimerosal was assumed from its long tract record of use. It is deplorable to think studies from the 1930's would be recognized as adequate and utilized in the 1990's.

3 When your child was vaccinated, did the information provided to you indicate that your child was being given a vaccine that contained mercury?

No

4. What is you opinion of the Center for Disease Control and Prevention's Fact Sheets on Immunization?

The information provided is not only false, but misleading as well. First of all they state that the amount of mercury in vaccines is "tiny" and that the levels are still within the safety margins established by Federal Agencies and that everyone is exposed to mercury in their lifetime. This paints a picture of mercury being a harmless non-toxic substance. They go on to state that there is "no evidence" that children have been harmed by the amount of mercury found in vaccines. From my investigations and personal experiences, I have found that the FDA and CDC admit that they do not review nearly 12,000 vaccine adverse events collected yearly. The FDA also acknowledges that less than 10% of physicians actually report vaccine adverse reactions. Therefore, taking into account the gross under reporting of vaccine adverse events coupled with inadequate investigations of those reported events, I am not surprised that the FDA and CDC say there is "no evidence" of harm. According to Dr. Neal Halsey of the Johns Hopkins Institute for Vaccine Safety the truth is that they can say there is no evidence of harm from thimerosal in vaccines, but the truth is they have not looked.

5. What should the Federal Government be doing about the massive rate increases in ADD and Autism?

As stated by Chairman Burton in his opening statement, Vaccines are the only drugs that Americans are required by a government agency to take. This requirement has even extended in some states where parents have been threatened that their children will be taken away for non-compliance with state laws which require vaccinations. Therefore, I feel that the responsibility falls back on the Federal Government to demand answers to the questions that were raised during the recent hearing July 18, 2000. It appears that there are striking similarities between the neurotoxicity of mercury and those of ADD, PDD and autism. This association had also been reported in recent Vaccine Safety Datalink observations. The dramatic increase in the prevalence of these disease entities coincides with the increased exposure to mercury via thimerosal in vaccines. This concern is also supported by parental reports of regression after

vaccines and documented levels of mercury in infants for which no other source could be found that would account for those levels. The Federal Government should also ask for the immediate withdraw of all remaining thimerosal preserved vaccines to prevent further neurological damage to young infants who may receive these remaining vaccines for years to come.

6. What is the role of the health care practitioner in informing parents about newly raised concerns about vaccine safety?

   Parents need to be given factual information from which they can make informed decisions concerning which vaccines would most benefit their child. There are too many variables to consider to make this a "One size fits all" program which it has become. Unfortunately, I do not believe that pediatricians are being given this type of information from the Federal Regulatory Agencies. Therefore, both parents and health care providers are being kept in the dark as to the real risk-benefit ratio of immunizations. A case in point is found in the Summer 1999 issue of the Hepatitis Control Report article on thimerosal where the American Academy of Pediatrics requested that their members needed more information about thimerosal. As reported in the article the AAP "feared that pediatricians who continued to administer thimerosal containing vaccines could face a flurry of lawsuits, perhaps claiming that children had acquired learning disabilities from mercury exposure". Even within agencies there is disagreement. One arm of the FDA, which regulates food, recommends that pregnant women limit their exposure of certain seafood known to contain mercury to no more than one meal per month in an effort to keep exposures minimal. For example, the average can of tuna contains 17 mcg of mercury. On the other hand, the FDA has continued to approve vaccines that cumulatively result in 62.5 mcg mercury exposures at bi-monthly intervals, with cumulative exposures of 187.5 mcg mercury the first 6 months of life for infants. This dichotomy within the same agency defies logic.

7. During the hearing Dr. Marie Bristol-Power stated that 80 percent of children display some symptoms of autism from birth? Do you agree with that statistic?

   Based on my personal experience as a parent and as a consultant to parents with autistic children I have not found this to be the case. Our son's first year of life was textbook, where he easily attained all his early developmental milestones. There was no evidence of any developmental or neurological problems. He was a very social, playful baby, who began regression around 13 to 15 months of age with bouts of infections and then loss of speech. In my work as a consultant this past year, I have found this to almost always be the case. Data collected by Autism Research International since the 1960's reveals that the onset of autism around 18 months to be a recent development. Parent reports from the 1960's through the early1980's identify that children with symptoms of autism from birth outnumbered by 2 to 1 those with onset at 18 months. Over the past decade we have seen a dramatic reversal in the demographics where now onset around 18 months far outnumbering those with onset at birth.

8. When did your child first display symptoms of autism?

   In reality our son did not exhibit the "classical" symptoms that we all associate with autism like social withdraw, rocking and self-injurious behaviors. Looking back at my son's symptoms, they more closely paralleled that of chronic mercury toxicity than autism. This included evidence of immune dysfunction, a regression and ultimately loss of speech, slow waves on EEG and abnormality on auditory evoked responses. He also developed difficulty chewing and swallowing food, a very selective diet, evidence of gluten intolerance and sensory disturbances, all of which are documented to occur in association with mercury toxicity. This presentation was coupled with documented levels of mercury in his baby hair at 20 months of age, which far exceeded safe levels of exposure. Therefore, I find a diagnosis of neurotoxicity from heavy metal poisoning to be more accurate than the descriptive diagnosis of Pervasive Developmental Disorder, not otherwise specified. Especially now, since we know the specifics.

espectfully submitted,

yn Redwood

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BERNARD SANDERS, VERMONT
INDEPENDENT

July 25, 2000

Ms. Elizabeth Birt
723 Ashland
Wilmette, Illinois 60091

Dear Ms. Birt:

On behalf of the Committee on Government Reform, I want to thank you for testifying at our recent hearing entitled: "Mercury in Medicine – Are We Taking Unnecessary Risks?" Your testimony will assist us in continuing our further investigations into mercury levels in vaccinations and the threat it poses to our children's health and safety.

At the conclusion of the hearing, I asked you to respond to written questions submitted by the committee for the record. I informed you that the answers to these questions would be made public and reminded you that you are still considered under oath for the purposes of answering these questions. Attached, you will find these questions. I hope you will answer them to their fullest extent possible. Please also provide to the Committee a copy of the FDA petition when it is filed.

Please return the responses to my professional staff member, S. Elizabeth Clay by August 1. Please contact Ms. Clay at 202-225-5074 should you have any questions. Again, thank you for your cooperation and keep the Committee informed of your research results.

Sincerely,

Dan Burton

Dan Burton
Chairman

Questions to Elizabeth Birt

For the Record for July 18, 2000 Hearing
Before the Government Reform Committee

1. **During our April Autism hearing, we referred to your son's trip to England to be treated for bowel obstruction. What happened in the United States that led you to seek medical care in England?**
2. **During the hearing Dr. Marie Bristol-Power stated that 80 percent of children display some symptoms of autism from birth? Do you agree with that statistic?**
3. **When did your child first display symptoms of autism?**
4. **Please explain the type of petition that is being filed with the FDA regarding a request to recall thimerosal-containing vaccines? (Please provide a copy of the petition to the Committee when it is filed.)**
5. **What treatments have improved your child's condition?**

Elizabeth Birt's Response to the Government Reform Committee for Record of July 18, 2000 Hearing

1. *During our April hearing, we referred to your son's trip to England to be treated for bowel obstruction. What happened in the United States that led you to seek medical care in England?*

I took Matthew to see two pediatric gastroenterologists, one at University of Chicago in January of 1998 and the other at Rush Presbyterian-St. Luke's Medical Center in December of 1998. Both physicians told me that Matthew was growing normally so that they did not feel as though anything from a gastrointestinal perspective was wrong even though I told both physicians that Matthew had chronic diarrhea since April of 1995. Neither of these physicians performed any medical tests other than a stool analysis and blood test. I specifically asked the physician at Rush-Presbyterian about Dr. Wakefield's work on autistic enterocolitis which was published in 1998 in The Lancet. He told me that he did not think much of it and that it was very controversial. At this point I feel as thought I had taken Matthew's gastrointestinal issues as far as I could in the United States. Matthew had also stopped sleeping through the night in January of 1997 and no physician could help us resolve either the diarrhea or the sleeping issue. I met Dr. Andrew Wakefield at a medical conference in Chicago in September of 1999; it was at this time I asked him if I could bring Matthew to London to be evaluated based upon Matthew's physical symptoms. If it were not for Dr. Wakefield's compassionate care for Matthew he would not be able to sleep and would be in constant pain.

2. *During the hearing Dr. Marie Bristol-Power stated that 80% of children display some symptoms of autism from birth? Do you agree with that statistic?*

I do not agree with the statement nor does it make any sense. The two major reasons parents take their child to a developmental specialist regarding autism is lack of speech and socialization. These skills develop much later in children. I do not know of any symptoms which are present at birth that can be observed to indicate that a child has autism.

3. *When did your child first display symptoms of autism?*

I became concerned about Matthew's behavior in the fall of 1995 when he started to lose speech, began hand-flapping and acting "deaf". Matthew was approximately 21 months old at that time.

4. *Please explain the type of petition that is being filed with the FDA regarding a request to remove thimerosal containing vaccines.*

I am attaching to this testimony a copy of two letters which have been sent to Dr. Jane Henney, Commissioner of the FDA. The first letter is simply a citizen's petition asking the FDA to remove thimerosal containing vaccines from the market. The second letter is asking the FDA to initiate a Class 1 recall of all vaccines containing thimerosal. The next step will be to initiate a legal petition for an injunction if the FDA does not take action.

5. *What treatments have improved your child's condition?*

Matthew responded immediately to having his bowel obstruction removed. He started sleeping through the night. He no longer has to take as many laxatives since being on Pentasa (an antiinflammatory medication used for ulcerative colitis) because his colon is not as inflammed. Additionally he no longer suffers from gastric reflux. Since starting him on oral immunoglobulin therapy in April of this year, he has started to put words and signs together to indicate his wants and needs. He also is toilet trained. I recently started chelation therapy on Matthew and have pulled out mercury, lead, arsenic, nickel and aluminum from his body. The combination of all of these therapies have allowed Matthew to sleep, be socially engaged with his family and peers, be less self stimulatory as far as jumping, screaming and hand-flapping, increased his receptive speech dramatically, become more verbal and in general lead a happier life. I would never have gotten this far with his medical care if I had left it up to his pediatrician.

FROM : STEPHANIE_CAVE,MD FAX NO. : 225 767 4641 Jun. 25 2001 11:06AM P2

Questions to Dr. Stephanie Cave

For the Record for July 18, 2000 Hearing Before the Government Reform Committee

1. In previous hearings, we have discussed the MMR vaccine being linked to autism. Please explain the theory regarding the MMR vaccine and the mercury-containing vaccines and the onset of acquired autism.
2. Once a child receives a toxic dose of mercury either through the food supply, environmental exposure, or through injections of vaccines, are they harmed beyond repair? Can children (or adults) recover from mercury poisoning?
3. What can be done to detoxify from mercury poisoning?
4. If mothers ingest or are injected with mercury during pregnancy, can that affect the fetus?
5. What actions should expectant mothers take to protect their babies from mercury poisoning?

QUESTIONS FOR THE RECORD OF JULY18, 2000 HEARING BEFORE THE GOVERNMENT REFORM COMMITTEE
Stephanie F. Cave, M.D., F.A.A.F.P.

1. In the previous hearings, we have discussed the MMR vaccine being linked to autism. Please explain the theory regarding the MMR vaccine and the mercury-containing vaccines and the onset of acquired autism.

The children receive a total of 187.5 mcg. of mercury through vaccines before they receive the MMR vaccine. Mercury has an effect on the immune system. It causes a shift in the CD4 lymphocytes from TH1 to TH2 predominate. The TH1 lymphocytes are the ones that fight viruses, parasites, and yeast/fungi in the body.When there is a shift to the TH2 lymphocytes, the body can no longer fight viruses effectively. The MMR is a live viral vaccine containing three live viruses. The measles virus, Rubeola, goes to the GI tract of the child receiving the vaccine. The immune system is altered because of the mercury from prior vaccines and the virus multiplies in the GI tract of the child receiving the MMR. A persistent viral infection is set up in the GI tract of the child (Dr. Wakefield's theory). The infection causes the walls of the GI tract to become inflamed—affecting the release of cytokines that cause the GI tract to become permeable to substances that should not cross this barrier to the blood stream.
The autistic children attach casein and gluten to morphine in the GI tract. These substances go through the gut wall into the blood stream and are carried to the brain across the blood brain barrier that has become permeable also in the presence of cytokines (Dr. Reichelt's theory). The opiod substances affect the children, causing bizzare behavioral consequences. The enzyme that breaks down the morphine peptides in normal people, Dipeptidyl Peptidase IV, is inhibited by mercury and the morphine substances cannot be broken down to forms that the child can eliminate. These morphines circulate and increase in concentration, continually affecting the child's behavior. The children are high on morphine and are addicted to casein (dairy) and gluten (wheat, oats, barley, rye) containing foods through the morphine. We are testing these morphine peptides in the autistic children's urine. They are much higher than they are in the control group studied.
IN SUMMARY:
The mercury, therefore, affects the child's system at several levels.

1. Shift of TH1 lymphocytes to TH2 lymphocytes cutting down on viral killing ability of the immune system leading to a persistent measles infection.
2. Affects the production of cytokines leading to a permeable GI tract and blood brain barrier.
3. Inhibits the Dipeptidyl Peptidase IV that breaks down the morphine peptides so that these substances circulate to the child's brain—affecting behavior.

2. Once a child receives a toxic dose of mercury either through the food supply, environmental exposure, or through injections of vaccines, are they harmed beyond repair? Can children (or adults) recover from mercury poisoning?

This is difficult to assess at this time. If the neurons and supporting cells in the brain are permanently damaged, complete reversal may not be possible. There is not enough data yet to make any conclusions.
There are suggestions that autism may be cured if we can remove all of the mercury. There have been cases in which adults have had a complete reversal of neurologic symptoms upon mercury removal. The difference is that the adults have fully developed brains before the metal poisoning. In children the metal is introduced prior to brain maturation and in some instances, during fetal development. Children, however, have superior healing ability, so that their capacity for normalizing may be greater than adults. The data that we have from our experience in our clinic is that the prognosis is dependent on the age of the child at the time of treatment. Three age groups have been identified:

1. Birth to 7 years-----complete recovery possible
2. Age 7 to puberty-----language and social gains are possible along with the elimination of problem behaviors (aggression, self-injurious behavior, etc.) Complete recovery probably not possible.
3. After puberty-----probably no language or social gains, but possible elimination of problem behaviors.

Hopefully we can more fully define prognosis as more data becomes available.

3. What can be done to detoxify from mercury poisoning?

There are a number of medications and supplements that will help with detoxification. In our clinic, we use DMSA, a substance approved by the FDA for treatment of lead poisoning in children. It does a good job of removing the mercury, but the kidney and liver function need to be assessed during the treatment. It also removes some of the beneficial minerals, so we have a protocol to replace minerals and vitamins during treatment.
DMPS is another drug that will take mercury out of the body, but it is not approved for use in children. It is used in adults who are toxic with heavy metals like mercury.
EDTA is a chelator which should not be used for mercury detoxification because it does not aid the release of mercury from the body as well as the other agents.
While we are treating, we encourage the patients to take fish out of the diet to eliminate food sources of mercury. We also discourage the use of dental amalgam fillings in anyone—especially the children because of the chance for contamination from this source.

4. If mothers ingest or are injected with mercury during pregnancy, can that affect the fetus?

Yes. The mercury ingested or injected during pregnancy can definitely affect the fetus. At times the fetus will have a greater concentration of mercury in the blood stream than the mother because of transplacental transport. The presence of mercury in RhoGam and the influenza vaccines concerns me greatly because these are given to pregnant women during fetal development. I do not think that the thimerosal removal will extend to these products. Even mercury from a woman's diet can go to the fetus who cannot dispose of it because he does not produce bile, necessary for mercury to leave the body.The mercury coming off the amalgam dental fillings is a significant source for the fetus. The World Health Organization has determined that the mercury from fillings makes up a significant source of the metal in humans.

5. What actions should expectant mothers take to protect their babies from mercury poisoning?

1. If possible, do not have dental work done during gestation or insist on the use of non-mercury containing materials.
2. Do not ingest mercury through fish---particularly tuna, shark, or swordfish.
3. Use only single-dose vials of RhoGam if they have no thimerosal.
4. Do not take the influenza vaccine unless it is mercury free.
5. Do not use ultrasonic toothbrushes if they have mercury amalgam fillings .
6. Assess mercury toxicity prior to getting pregnant and remove sources of the metal if toxic levels are demonstrated.
7. Be sure to take the pre-natal vitamins and minerals during pregnancy.
8. Use safe water sources for drinking.

The FDA and CDC should mandate that all thimerosal be removed from vaccines, including RhoGam and influenza NOW. Children continue to be harmed daily, and I am afraid that the numbers include many beyond autism.

Stephanie F. Cave, M.D., F.A.A.F.P.

Questions to Dr. William Egan, Food and Drug Administration

For the Record for July 18, 2000 Hearing
Before the Government Reform Committee

1. When did the FDA first learn that mercury could cause harm?

The toxicity of mercury has been known since antiquity. In the late 1920s, chemists developed organic mercury compounds with antibacterial properties such as thimerosal, phenyl mercuric acetate, borate and nitrate, mercurochrome, mercurophen, and metaphen. Toxicity studies of thimerosal performed in animals and humans during the 1920's, prior to licensure of products containing thimerosal as a preservative, provided evidence of its safety at the low levels found in vaccines and other biologics. These toxicity studies showed kidney and intestinal lesions in animals associated with high levels of mercury exposure from thimerosal. FDA also may have been aware information regarding mercury from other sources, prior to the development of thimerosal (in the late 1920s and 1930s).

2. When did the FDA first realize that thimerosal contained mercury?

The fact that thimerosal contains about 50 percent mercury by weight was known at the time thimerosal was first used as a preservative in vaccines in the 1930's. Data available at the time of licensure of products containing thimerosal as a preservative indicated its safety and effectiveness at the levels found in these products.

3. What studies were submitted to the FDA to prove that thimerosal was safe? Please provide copies of the studies submitted for licensing.

Human studies of experimental drugs and biologicals including vaccines are subject to the provisions of 21 CFR Part 312 and should be performed under an investigational new drug application (IND). In these studies, the sponsor seeks licensure of the complete product as it is formulated for use. Safety and efficacy data of a product are submitted for FDA review during the IND process. Such safety data would generally indicate any acute toxicity, whether from one ingredient or a combination of ingredients. Therefore, if thimerosal caused acute toxicity, the pre-market safety data would indicate acute toxicity, even if the association could not be confirmed. To date, the pre-market data have not shown acute toxicity in vaccines containing thimerosal. Because pre-market data typically do not include long-term safety data, FDA monitors post-marketing adverse event reports and subsequent clinical studies for long-term safety problems involving the product. There are no post-marketing long-term data that provide convincing evidence of significant safety problems with the long-term use of vaccines containing thimerosal.

As part of the over-the-counter (OTC) rule making, mercurials, particularly thimerosal and phenylmercuric nitrate have been recommended by The Advisory Review Panel on OTC Ophthalmic Drug Products, as useful preservative for commercial ophthalmic solutions. The panel recommended that thimerosal when used with maximum

concentration of 0.01% is safe. (45 FR 30002 at 30018, May 6, 1980) Allergic reactions to mercurials may occur. The panel recommended that an allergy warning statement should be stated in the labeling. Thus, when the Ophthalmic Drug Products for OTC use monograph (21 CFR 349.50) published on March 4, 1988, the monograph permits the use of mercury-compounds as inactive ingredients (preservative). A general allergy warning is required on the labeling (21 CFR 349.50 (c) (3)).

By contrast, mercury compounds used as active ingredients in OTC drug products have been found not to be generally recognized as safe (GRAS) and effective and are classified as new drugs.

In general, the Agency does not ask for safety data specific to an inactive ingredient unless there is evidence of a safety concern. However, one sponsor provided FDA with safety data regarding the use of thimerosal as a preservative in its product. In a study submitted to a new drug application (NDA), to assess the preclinical safety of diclofenac sodium (the active ingredient), data on chronic toxicity was provided for 0.001% thimerosal used as preservative in this aqueous solution. (Summary of the study is enclosed as TAB A(1)).

4. How effective is thimerosal as a preservative? What studies have been published to show this?

Thimerosal is an effective preservative. Thimerosal meets the requirements for a preservative as set forth by the United States Pharmacopoeia; that is, it kills the specified challenge organism and is able to prevent the growth of the challenge fungi. Prior to its introduction in the 1930's, data were available in several animal species and humans providing evidence for its safety and effectiveness as a preservative. Since then, thimerosal has a long record of safe and effective use preventing bacterial and fungal contamination of vaccines, with no ill effects established other than minor local reactions at the site of injection.

Thimerosal in concentrations of 0.001% to 0.01% has been shown to be effective in clearing a broad spectrum of pathogens.

1. Havener, W. H., "Ocular Pharmacology" fifth Edition, 1983. P 125. (TAB A(2))

Studies: Tab A(3)

1. Batts, A. H., Narriott, C., Martin, G. P., et al., "The Effect of Some Preservatives used in Nasal Preparations on Mucociliary Clearance," *Journal of Pharmacy and Pharmacology*, 41 (3): 156-159, 1989.
2. Batty, I., Harris, E. and Gasson A., "Preservatives and Biological Reagents," *Developments in Biological Standardization*, 24 : 131-42, 1974.
3. Beyer-Boon, M. E., Arntz, P. W. and R. S. Kirk, "A Comparison of Thimerosal and 50% Alcohol as Preservatives in Urinary Cytology," *Journal of Clinical Pathology*, 32(2) : 168-70, 1979.

4. Cox, C. B., Feeley, F. C. and Pittman, M., "Sterility Testing: Detection Of Fungi And Yeasts In The Presence Of Preservatives," *Journal of Biological Standardization*, 1 (1) : 11-19, 1972.
5. Goldman, K. N., Centifanta, Y., Kaufman, H. F., et al., "Prevention of Surface Bacterial Contamination of Donor Corneas," *Archives of Ophthalmology*, 96 (12) :2277-80, 12/78.
6. Keeven, J., Wrobel, S., Portoles, M., et al., "Evaluating the Preservative Effectiveness of RGP Lens Care Solutions," *Contact Lens Association of Ophthalmologists Journal*, 21 (4) :238-41, 1995.
7. Naito, R., Itoh, T., Hasegawa, E., et al., "Bronopol As A Substitute For Thimerosal," *Developments in Biological Standardization*, 24 :39 - 48, 1974.
8. Wozniak-Parnowska, W. and Krowczynski, L., "New Approach to Preserving Eye Drops," *Pharmacy International*, 2(4) : 91-4, 1981.

5. Who is the manufacturer? What information has been provided to the FDA to insure that thimerosal is safe?

There are a number of suppliers of thimerosal; we do not have information on the number of manufacturers of thimerosal. Vaccine manufacturers who use thimerosal provide safety data for the final formulated vaccine, not the individual components that go into the vaccine. Vaccine manufacturers are not required to provide information on the source of thimerosal used in vaccines. They do, however, provide certificates of analysis of reagents that are used in the vaccines. These certificates of analysis indicate the purity of the reagents. The source of thimerosal does not necessarily remain constant. Manufacturers often obtain chemical reagents from a variety of sources.

6. When vaccine manufacturers submit newly formulated vaccines, that no longer have thimerosal, what research studies are required to insure the safety and efficacy of the new vaccine?

When vaccine manufacturers submit license supplements for products reformulated without thimerosal as a preservative, evidence for safety and effective must be provided to FDA. The type of information required depends upon the role of thimerosal in that product, e.g., whether it is added as a preservative during the final formulation of the vaccine, or whether it is used during the manufacturing process as an inactivating agent. For newly reformulated products with thimerosal removed as a preservative, manufacturers have formulated the vaccines in single dose containers. Single dose containers do not require a preservative. Safety and effectiveness of these reformulations has generally been based on demonstrating in the laboratory that the physical and chemical properties are the same as the original product. As with all preservative-free vaccine formulations, manufacturers must continue to demonstrate sterility of the final formulated product, i.e., manufacturers must demonstrate that they can aseptically fill the final product in the absence of preservative.

7. We have repeatedly been told that when a new vaccine is licensed, it is reviewed in context of the vaccines it will be used in conjunction with. How did the FDA review the thimerosal use in all the vaccines given on the same day?

Pre-licensure clinical trials for new vaccines include the use of other vaccines administered according to the ACIP schedule. Safety data gathered during the clinical trial would support the use of multiple vaccines administered on the same day. Some of these vaccines contained thimerosal and therefore the safety data would reflect the use of multiple vaccines including those containing thimerosal.

Under the FDA Modernization Act of 1997, FDA reviewed the exposure of infants and young children to thimerosal in vaccines. The response provided to question 20 discusses this risk assessment and describes how exposure levels to thimerosal from the recommended childhood immunization schedule were calculated. It is important to recognize that our comparison of infant exposure to mercury from vaccines to existing Federal guidelines on methylmercury exposure was meant as a starting point in the risk assessment of thimerosal in vaccines.

FDA's Office of Vaccines Research and Review recognizes the concerns regarding possible risks from the use of thimerosal and has been recommending formally and informally that new vaccines under development be formulated without thimerosal as a preservative.

8. What other licensed drugs contain toxic substances such as mercury?

Toxicity is defined to be any interference with normal metabolism. Every medicinal product will, to some extent, interfere with normal metabolism. Yet, depending on the degree to which the administration can be controlled, toxicity can be managed and the medicinal product can be beneficial. The art and science of medicine is balancing the risk of toxicity against the benefit with the benefit outweighing the risk. Toxicity levels often depend on the amounts, concentrations, forms and or dosages of any particular substance. There are numerous drugs, such as chemotherapy drugs or coumadin, which are inherently and highly toxic substances. There are other drugs such as aspirin which, in the wrong amount, or administered to the wrong person, can be fatal. If the potential for benefit outweighs the potential risk, the product, whether the drug itself or a substance contained in the drug product, could be licensed for marketing.

9. Why has the FDA not recalled all mercury containing drugs including vaccines?

There is insufficient scientific data to justify a voluntary or mandatory recall of vaccines or other drugs containing thimerosal within prescribed limits. A mandatory recall requires that the product present "an imminent or substantial hazard to the public health." §351(d)(1) of the Public Health Service Act (PHS Act), 42 U.S.C. 262(d)(1). A voluntary recall may be requested when a marketed product is in violation of any FDA law or regulation and that present a risk of injury; voluntary recall is reserved for urgent

situations. 21 C.F.R. § 7.40. Current scientific data and information do not establish that products containing thimerosal within prescribed limits as a preservative creates an imminent or substantial hazard to public health or are in violation of FDA laws or regulations.

10. The FDA has warnings for dietary exposure to mercury, how is that different to vaccine exposure?

To determine whether a warning is appropriate for any specific product, FDA considers relevant scientific data regarding safety and weighs risks versus benefits from exposure or non-exposure to the product. The relevant scientific data regarding the use of vaccines containing thimerosal as a preservative within prescribed limits shows minimal if any risk from exposure to thimerosal and significant benefit from vaccination.

11. How many adverse events have been reported for mercury toxicity from foods, drugs, and vaccines?

To identify any events reported as attributable to thimerosal in vaccines, FDA queried approximately 90,000 VAERS reports from 1990-1998 by searching text fields for "thimerosal", "thiomersal", "merthiolate", and "mercury". Forty-five reports were identified. The types of events reported and vaccines administered are shown in Tables 1 and 2. Of note, one report described an individual who experienced anaphylaxis following hepatitis B vaccine. When rechallenged with a similar but thimerosal-free product, anaphylaxis occurred again, implying thimerosal was not the causative agent. In most cases, the reporter gave no basis for attributing the adverse event to thimerosal instead of a vaccine immunogen or any other vaccine constituent.

VAERS has several limitations, including lack of consistent diagnostic criteria, data acquired from a diverse group of voluntary reporters, underreporting, and the difficulty in determining whether a vaccine caused the adverse event reported. A cause and effect relationship between the reported adverse events and thimerosal in vaccines cannot be established because of these limitations.

Table 1: Reports to VAERS Attributed by Reporter to Thimerosal[§] by Vaccine Type

Hepatitis B	28
Influenza	10
Tetanus/Diphtheria	3
Haemophilus influenzae type b (HIB)	1
DtaP	1
DTP/HIB (TETRAMUNE)	1
DTP and HIB (Concurrent administration)	1

[§]Thimerosal, thiomersal, merthiolate, or mercury

Table 2: Types of Events Attributed by Reporter to Thimerosal[□]

Injection site reaction	13
Rash	9
Urticaria**	8
Edema†	5
Flu-like syndrome/joint aches¥	4
Anaphylaxis‡	1
"Severe allergic reaction"#	1
Wheezing**	1
Stridor	1
Malaise/agitation	1
Reaction not specified	2

[□]Thimerosal, thiomersal, merthiolate, or mercury

Note: Only one report (angioneurotic edema) required hospitalization. Most others reported doctor visits or emergency room visits.

**One report involved a patient with urticaria and wheezing, onset after vaccination not specified.

†One report of edema required hospitalization for angioneurotic edema, two reports of facial edema, one report of eyelid edema, one peripheral edema.

¥One patient also reported fever to 102°F.

#Not otherwise specified.

‡Patient had placebo-controlled rechallenge with similar vaccine formulated without thimerosal and had anaphylaxis; thus, anaphylaxis *not* thought to be due to thimerosal.

An additional 15 reports were identified through July 10, 2000, bringing the total to 60 reports alleging adverse events due to thimerosal in vaccines. Vaccines included in the 15 reports since 1998 were hepatitis B vaccine (7), influenza vaccine (6), tetanus toxoid (1), and DTP, Hib, and hepatitis B vaccines administered concurrently (1). In addition to the injection site and allergic reactions reported before 1998, the more recent reports included pain (2), developmental delay (1), pervasive developmental disorder (1), autism (1), and convulsions (1).

The FDA Adverse Events Report System (AERS) contains reports received for prescription and OTC drug products since 1969. For drugs other than biologics, as of August 4, 2000, there were 171 reports retrieved from AERS searched under the list of mercury-related products or ingredients.

Twenty-three were not mercury-related products, for flu vaccines, or events not directly associated with mercury products. In the remaining 148 reports, most were reported in earlier years, and reported on merthiolate or thimerosal containing topical or ophthalmic products (106). Accordingly, most of the adverse events were allergic type skin reactions. They were also mostly in adult (133) with 14 reported in pediatric age group as: 0-2: 1 case, 3-12: 6 cases, 13-19: 7 cases. Of the 14 reported in children, six had accidental exposure to metallic mercury resulting intoxication, one ingested mercurous chloride possibly as laxative for 6 months and one developed mercury poisoning after 3 months use of ammoniated mercury cream.

There were no deaths in any of the reports reviewed in AERS, but 10 were hospitalized or sent to the Emergency Room (ER) for treatment of the reported events. Three reported the events being life-threatening or disabling. The remaining cases reported patients received treatment and recovered.

The following are summaries of the case reports for each category of mercury products.

Organic mercuric compounds

1. Thimerosal (106 reports)

A. Thimerosal in Topical Antiseptic Solution or Tincture (80 reports)
All subjects were in adults and the reported adverse events usually occurred within three days following application of thimerosal. They were mostly skin related allergic reactions. One patient developed diarrhea and redness on skin whenever merthiolate was topically applied.

All but three patients reported recovery after treatment and discontinuing thimerosal use. Although three reported a serious outcome, hospitalization or life threatening, the patients did not use thimerosal according to direction. One prisoner had access to thimerosal and attempted suicide by ingesting large amount of thimerosal with high levels of mercury found in red cells and hair. One patient applied to ears and had ringing in both ears with permanent damage or 20 decibel hearing loss in both ears. Another reported local burn

from a new bottle and had an unlikely extreme reaction so called "cardiorespiratory arrest," but recovered without sequaele.

B. Thimerosal as Preservative in Contact Lens Cleaning or Soaking Solutions (15 reports)

The reported adverse events were allergic reactions, eye irritation, or inflammation of the eye, but none had a serious outcome.

C. Thimerosal as Preservative in Nasal Spray (11 reports)

The reported adverse events were mostly related to the decongestant ingredients such as - chest pain, hyperventilation, heart arrest, fainting or addiction. Few also reported hives, swollen mucous membrane, running nose, lost sense of smell, or burning sensation at application sites which might implicate allergic reactions to thimerosal contained in the products.

2. Mercuhydrin (ingredient name unknown) (16 reports)

Adverse events were reported form 1970 to 1974. The product was administered in 2cc dose to treat congestive heart failure. Immediately following injection, shaking, chills, and skin reactions or rash were reported. All subjects recovered.

3. Mercury Oxide Containing Ophthalmic Ointment (5 reports)

The reported adverse events were eye pain, eye swelling and edema, rash, burning, or irritation and inflammation of the eye. None had a serious outcome, except for temporary disability.

4. Phenylmercuric Nitrate in Preparation H (1:10,000) (4 reports)

The reported events were complaint of lack of effect, burning, rash and itching, or allergic reaction.

5. Miscellaneous:

Mercresin (mercocresols) (1 report)
Rash was reported.

Inorganic Mercury

1. Mercurous Chloride (2 reports)

One four year old female with five dental amalgam fillings, took Calomel in an over-the-counter Chinese medicine for 6 months. She was hospitalized for drooling, tremor, body

stiffening, flush, and irritability. Her urine mercury level was 39 ug/l. A 46 year old female with Lupus among other medical problems had used calomel for constipation over 10 years period. She developed pains in the extremities and had a urine mercury level 89 ug/l.

2. Ammoniated mercury cream (10%) (3 reports)

Two subject reported contact dermatitis. One report was of a five year old female who had significant kidney problem with protein spillage after three months of use. She was hospitalized with mercury level to 30 microgram, but recovered.

3. Metallic Mercury Poisoning (10 reports)

There were seven reports of either accidental or intentional ingestion/exposure of metallic mercury. All were serious but no deaths. The summary of cases follows:

A. 1969, a 2 year old male accidentally ingested mercury bichloride tablet, and had no urine output, vomiting , swelling, and burning, but recovered.
B. 1970, a 64 year old female with muscle weakness and decreased vision, had elevated mercury (23 ug units), suspecting mercury toxicity but without any indication of source of mercury.
C. 1971, a 22 year old female attempted suicide from mercuric chloride (20 tablets) of a "Poison", lavaged and recovered.
D. 1971, 15 year old female mistakenly took 1/2 tablet of mercury bichloride (500mg) for cold, vomiting was induced, recovered.
E. 1991, unknown patient overdosed by taking an unknown amount of mercury bichloride from collected medicine bottles had kidney function abnormality, hospitalized.
F. 1991, a 9 year old Texas female and family inhaled spilled metallic mercury scavenged from surplus medical equipment developed rashes, enlarged lymph nodes, enlarged liver, fever, vomiting, diarrhea.
G. 1996 (Turkey), a family of 4 (mother, 2 sons and one daughter) had acute metallic mercury poisoning (boiled from pieces of mercury found in the garbage) and accidental ingestion of Feldene with rash, blistering of the skin, hospitalized and recovered.

4. Mercury fillings (2 reports)

Only one reported sinus headache.

The Center for Food Safety and Applied Nutrition (CFSAN) is not aware of any adverse event reports for mercury toxicity in foods within the last ten years.

12. What studies has the FDA or HHS funded to look at mercury toxicity in thimerosal?

CBER is aware of one such study. DHHS sponsored a study in 1967 "Toxicology and carcinogenesis of various chemicals used in the preparation of vaccines" (contract #PH43-67-676) which included thimerosal. This was commissioned by the predecessor to CBER, the National Institutes of Health Division of Biological Standards, later the Bureau of Biologics, to assess the toxicity of thimerosal. The results of the study were detailed in the publication enclosed as TAB A(4).

Other agencies may have more detailed information concerning previous studies and ongoing studies.

13. You testified that there was no convincing data on mercury in vaccines harming children, but that the FDA was committed to removing all exposure of mercury to our children. If that is the case, why?

While there was no convincing evidence that children were being harmed, FDA concluded that removing or reducing thimerosal from vaccines was merited given the concern over the potential health effects of mercury exposure from all sources and the feasibility of removing thimerosal as a preservative.

14. Please provide to the Committee a list of the lots of vaccines that have been released for distribution and use that contain thimerosal.

The Committee has been provided a list of all childhood vaccines which contain thimerosal. This is provided again at TAB A (5). Samples of any lot of any licensed biological product and protocols showing test results may be required to be sent to CBER. Upon the request of CBER, a manufacturer may not distribute a lot of product until the lot is released by CBER. (21 CFR 610.2) Any manufacturer may apply for an exemption from the lot release requirement or alternatives to lot release. The manufacturer may request to send CBER samples and protocols on a schedule (such as quarterly) agreed upon by CBER and the manufacturer or may request that samples and protocols not be sent to CBER. CBER has approved alternatives lot release that include many different schedules for sample and protocols submissions and has approved certain manufacturers to no longer provide any samples or protocols to CBER. Because some manufacturers are approved for exemptions from or alternatives to lot release, CBER may not have records of all lots released by a manufacturer under an exemption from lot release. In addition, the information contained in the database on lot release includes all vaccines, allergenic products and related bacterial products. Consequently, there is no database that would have the information as requested.

15. What was the concentration of mercury of the over the counter creams referred to in the 1982 Federal Register Notice discussed during the hearing?

The mercurial concentrations (contained as active ingredients in topical preparations) in the products considered in the 1982 Federal Register notice were as follows:

Mercurochrome - 2% aqueous solution
Merphol Tr. (thimerosal 0.1%)
Corona Ointment (no active ingredient shown in the Federal Register or American Drug Index (ADI)-1975)
Merthiolate Cream, Glycerite, Ointment, Solution, Tincture (Thimerosal 0.001%)
Merthiolate Aerosol (Thimerosal 0.033%)
Kip Ointment (orthohydroxphenylmercuric chloride 0.1% (Federal Register indicates tha for OTC use the active ingredient concentration is 0.056%)
Sperti Ointment (no active ingredient shown in the Federal Register or ADI-1975) (believed to be phenylmercuric nitrate (PMN). Sperti used to contain live yeast cell derivative (LYCD) as an active ingredient with PMN 1:10,000 as a preservative)

16. How would the mercury in a topical cream affect the body differently than mercury injected into the body?

The proposed rule published in the Federal Register of January 5, 1982, reported on findings of the Advisory Review Panel on OTC Miscellaneous External Drug Products. This panel report referred to the use of thimerosal as an active ingredient (antimicrobial) in topical preparations. It not did not include an assessment of the low concentrations of thimerosal used as a preservative in vaccines. Mercury found in topical germicides may be absorbed into the body in the same way as low concentrations of mercury used as a preservative. The major difference is the dose.

Topical preparations containing mercury could be applied multiple times over an extended period of time, thus greatly increasing the potential dose of mercury absorbed. Existing data have shown no convincing evidence of adverse health effects on children who received vaccines containing low concentrations of thimerosal under the recommended childhood immunization schedule. Bacterial and fungal contamination of vaccines is a very serious concern in multi-dose vials, with the potential for significant illness and death. The risks of contaminated multi-dose vials must be weighed against the theoretical risk of thimerosal.

17. Does thimerosal cause cell damage?

An advisory review panel to FDA reports in the Federal Register of January 5, 1982, - "Mercury-Containing Drug Products for Topical Antimicrobial Over-the-Counter Human Use; Establishment of a monograph" (Enclosed as TAB A(6)) references one study that suggested thimerosal may be more toxic for human epithelial cells in vitro than other mercury-containing compounds. (Reference 1, Enclosed at TAB A(7)) The reference also notes that sensitivity of skin was greater than cord, heart or spleen tissue cells. There are other references that suggest thimerosal is not toxic in other cell types (e.g., corneal epithelium or endothelium). (Reference 2, Enclosed as TAB A(8)) Thus, the toxicity of a compound needs to be assessed in the context of other information available. As a consequence, it may be inappropriate to use thimerosal as a topical antiseptic but may be appropriate to use it as a preservative.

References:

1. Engley, F. "Evaluation of mercurial antimicrobic action and comparative toxicity for skin tissue cells," *Soap and Chemical Specialties*, 30: 199-205 and 223-225, 1
2. Goldman, K. N., Centifanta, Y., Kaufman, H. F., et al., "Prevention of Surface Bacterial Contamination of Donor Corneas," *Archives of Ophthalmology*, 96 (12) :2277-80, 12/78.

18. Please provide information as requested during the hearing by Chairman Burton and Congresswoman Chenoweth-Hage including the sequence of events that lead to the ruling in 1982 that thimerosal caused cell damage in skin creams, why injected thimerosal was still considered safe?

The advisory review panel to FDA report in the Federal Register of January 5, 1982 - "Mercury-Containing Drug Products for Topical Antimicrobial Over-the-Counter Human Use; Establishment of a monograph" contains detailed information as to the sequence of events that led to the Proposed Rule. This can be found in the section of the Proposed Rule entitled ***Supplementary Information***. (Enclosed as TAB A(6))

With respect to the safety of injected thimerosal, a license is granted for product formulations that have been shown to be safe and effective for the intended use or indication. There are vaccines that have been licensed for use that contain thimerosal. Prior to licensure, these products, with their specific formulations and routes of administration were shown to be safe and effective for their intended use. FDA does not license individual components of a product but rather the product as it is formulated for its use.

19. You stated during the hearing that there is no evidence that thimerosal has caused harm, yet you admit during the hearing that we have epidemic levels of autism and we also have huge increases in ADD. What studies has FDA required to rule out that thimerosal or any other ingredients, including aluminum, is linked in any way to these increases?

The reference made during the hearing to "epidemic" levels of autism was an acknowledgement of the reported increases in autism cases. It was not a scientific assessment concluding that an actual scientific epidemic has occurred. As stated at the hearing, there is no current scientific data to support any causation between thimerosal in vaccines and autism.

There are many possible explanations for the apparent increase in the number of cases of autism over the past two decades, including a broadening of the case definition to include less severe and more atypical presentations of autism and improved awareness of this disorder resulting in greater number of cases being diagnosed. It also should be noted that thimerosal had been in use as a preservative in vaccines for at least 30 years prior to the apparent increase in rates of autism.

An association that has been noted by some concerned parents of autistic children is that the increase in the prevalence of autism over the last few decades closely matches the introduction and spread of thimerosal-containing vaccines. This type of comparison is known as an ecological study. Ecological studies are generally not accepted as strong evidence of causality, because they do not link individual exposure to individual outcome, and can be subject to confounding by unknown or uncontrollable factors. For example, numerous other influences that have changed over time may be linked to the increase in reported autism cases such as dietary and environmental factors. In addition, it has been noted that some children with autism have high levels of mercury in hair, urine and blood. This observation cannot be interpreted without information on the levels of mercury in individuals without autism (i.e., case-control study). However, such observations do indicate that the hypothesis may be worthy of further study.

There have been no controlled studies of the relationship between thimerosal and autism, and those controlled trials that have been done using thimerosal containing vaccines have not been conducted in a way that would allow an evaluation of the relationship between thimerosal and autism. There have been two retrospective cohort studies conducted recently by the CDC using data from two different health maintenance organization (HMO) databases. Results from these studies were presented at the CDC's Advisory Committee on Immunization Practices (ACIP) meeting on June 21, 2000. The first study did not show a statistically significant association between thimerosal exposure and autism. There were not enough cases of autism in the second database to study. There have been no case control studies of autism and thimerosal.

FDA supports the continued efforts of DHHS to fund studies to determine the causes and genesis of autism.

20. What are the safety exposure levels are to mercury for a 1 month old, 3, 6, 9 and 12 month old?

In our review under the FDA Modernization Act of 1997, the FDA undertook a risk assessment of thimerosal in childhood vaccines. One component of this risk assessment was an exposure assessment for the United States (U.S.) recommended childhood immunization schedule based on thimerosal content in vaccines prior to licensure of thimerosal-free hepatitis B infant vaccines. FDA compared exposure levels of infants to ethylmercury from vaccines to existing guidelines for exposure to methylmercury, as there are no existing guidelines for safe exposure to ethylmercury, the metabolite of thimerosal. (Enclosed at Tab A(9) is an article on ethyl and methylmercury.) Several agencies including the U.S. Environmental Protection Agency (EPA), U.S. Agency for Toxic Substances and Disease Registry (ATSDR), FDA and the World Health Organization (WHO), have developed guidelines for methylmercury exposure from dietary exposures.

It is important to recognize that such guidelines are meant to be starting points for evaluation of mercury exposure, and should not be viewed as absolute levels above which

toxicity can be expected to occur. In their Mercury Study Report to Congress of December 1997, the EPA describes their reference dose, or RfD as follows:

> The RfD is a quantitative estimate of levels expected to be without effect even if exposure persists over a lifetime. It is not intended to be compared with isolated or one time exposures. Exceedance of the RfD does not mean that risk will be present. Acceptability or uncertain risks is a risk management decision. Risk management decisions may consider the RfD but will take into account exposures, other risk factors and non-risk factors as well.

It should also be recognized that the EPA guidelines were meant to be protective of the developing fetus. It is likely that EPA guidelines provide a greater margin of safety for infants and small children.

Under FDA's exposure assessment, the total amount of mercury by weight was calculated for each vaccine in the infant schedule. Depending on the particular vaccine formulation and schedule, an infant may have received a total mercury dose from thimerosal in vaccines of approximately 187.5 μg (or mcg) during the first 6 months of life. In special populations, influenza vaccine may have been administered at 6 months of age, increasing the total dose to approximately 200 μg.

Assessment of exposure to mercury from vaccines at 6 months of age was thought to be most relevant because the toxic effects of mercury could be cumulative in infancy, and most vaccines of the infant series are completed by that time. (Vaccines are not typically administered at 3 or 9 months of age). Exposure at 24 months of age was also assessed to capture exposures from booster doses administered in the 2nd year of life.

Maximum Exposure to Mercury from Thimerosal in Vaccines in U.S. Infants

Vaccine	6 months of age	24 months of age
DTaP x 3	75μg	100μg
Hib x 3	75μg	100μg
Hepatitis B x 3	37.5μg	37.5μg
Influenza [selected populations]	[12.5μg]	[25μg]
Total	187.5μg [200μg]	237.5μg [249.5μg]

Guidelines for exposure to methylmercury were used to determine whether the mercury dose from vaccines approached a level of concern. The EPA, ATSDR, FDA and WHO have developed recommendations for safe exposure to methylmercury. These range from 0.1 μg/kg body weight/day (EPA) to 0.47 μg/kg body weight/day (WHO) and include a safety margin.

The agency guidelines were applied to a female infant at the lowest 5th, 50th and 95th percentile of weight between birth and 26 weeks, the period during which most infant vaccines are given. Females were selected because their smaller body weight results in a more stringent safety guideline, and thus more likely to identify risk to vulnerable children. Application of these guidelines makes the conservative assumptions that the

toxicity of ethylmercury is the same as methylmercury and that susceptibility of the infant to toxicity from organic mercurials is the same as that of the fetus.

Methylmercury Exposure Limits Using Various Agency Guidelines by Female Infant Weight at 6 Months of Age

Agency	5th%	50th%	95th%
EPA	65 μg	89 μg	106 μg
ATSDR	194 μg	266 μg	319 μg
FDA	259 μg	354 μg	425 μg
WHO	305μg	417 μg	501 μg

Thus, it was observed that some 6-month old infants may have received doses of mercury from vaccines in excess of EPA guidelines, however guidelines established by the other agencies would not have been exceeded. By 24 months of age, the cumulative dose of mercury in vaccines would not exceed any established guidelines due to growth and increased weight of the older children.

Exposure to mercury from thimerosal in vaccines can be assessed at other times points, as suggested (see table below).

Mercury exposure from thimerosal in vaccines prior to July 1999 (μg)

Vaccine	1 month of age	3 months of age	9 months of age	12 months of age
DTaP	0	25	75μg	75 μg
Hib	0	25	75μg	100μg
Hepatitis B	25 μg	25	37.5μg	37.5μg
Influenza (selected groups)	0	0	[12.5μg]	[25μg]
Total	**25 μg**	**75**	**187.5μg [200μg]**	**212.5μg [237.5μg]**

EPA guidelines for mercury exposure may be calculated for exposures at 1, 3, 9, and 12 months by infant weight, as shown below:

Approximate Mercury Exposure Limits Based on EPA Guidelines (μg)

Age	5th percentile weight	50th percentile weight
1 month	7.4	10
3 months	27	36
6 months	65	89
9 months	118	147
12 months	173	216
24 months	445	514

- Calculated Exposure Limit at 1 month of age = dose/kg body weight/day X average weight X 30 days X 0.932 (mercury molecular weight/ methylmercury molecular weight); e.g., EPA calculated exposure limit = 0.1 μg/kg body weight/day X 30 days X (2.4 kg + 2.9 kg)/2 X 0.932 = 7.5 μg.
- Assumes average of 5th, 50th % weight for females at birth (2.4 kg, 3.2 kg) and 1 month (2.9 kg, 3.9 kg) = 2.65 kg, 3.55 kg. Females were selected because their smaller body weight makes them more susceptible than males.
- Recommended limits on methylmercury exposure: EPA: 0.1 μg/kg body weight/day

Thus, EPA guidelines for mercury exposure could have been exceeded by exposure to mercury from thimerosal in vaccines at 1, 3, 6, 9 and 12 months of age.

Since the licensure of thimerosal-free hepatitis B vaccines in 1999, and withdrawal of Hib vaccines in multi-use vials from the U.S. market, the maximum total mercury exposure from thimerosal in vaccines at 6 months of age is currently 75 μg.

Current maximum exposure to mercury from thimerosal in vaccines (μg)

Vaccine	1 month of age	3 months of age	9 months of age	12 months of age
DtaP	0	25	75	75
Hib	0	0	0	0
Hepatitis B	0	0	0	0
Influenza (selected populations)	0	0	[12.5μg]	[25μg]
Total	**0 μg**	**25 μg**	**75 μg [87.5μg]**	**75 μg [100 μg]**

Thus, the exposure to mercury from currently available infant vaccines in the U.S. could exceed EPA guidelines after routine vaccines are administered at 6 months of age. EPA guidelines for mercury exposure at the other assessed time points would not be exceeded.

21. Why is ATSDR's exposure limit of 0.3 micrograms per kilogram of body weight per day higher than EPA's? Would it not be prudent to go with the lower level?

This question is more appropriately directed to ATSDR.

22. What are the demographics of the population was that were tested to determine the safety limits? (Please provide all the background data.)

This question is more appropriately directed to ATSDR.

23. How are those exposure limits arrived at?

This question is more appropriately directed to ATSDR.

24. What has HHS funded in regard to the relationship between vaccines, autism and ADD?

This question is more appropriately directed to NIH and CDC. Also see response to question 19.

25. What studies are planned?

This question is more appropriately directed to NIH and CDC.

Summary of Nonclinical Toxicology

Alcon Laboratories, Inc., is developing Diclofenac Sodium 0.1% Ophthalmic Solution for the short-term treatment of postoperative ocular inflammation in patients who have undergone cataract extraction. Diclofenac sodium is a nonsteroidal anti-inflammatory drug (NSAID) with anti-inflammatory, antipyretic and analgesic activity. It is believed to inhibit the enzyme cyclooxygenase which is essential in the biosynthesis of prostaglandins. Prostaglandins are mediators of many types of inflammation, and thus Diclofenac Ophthalmic Solution is an effective therapy for ocular inflammation elicited by cataract extraction. Diclofenac sodium is the active ingredient in two approved NDA's: Voltaren Ophthalmic Solution (NDA 20-037) and Voltaren tablets (NDA 19-201).

Based on the results of preclinical safety evaluations conducted with diclofenac sodium, Diclofenac Sodium Ophthalmic Solution 0.1%, and its components, the conclusions are as follows:

Diclofenac Sodium (Information based on published data)

1. Primates are apparently more resistant to the acute toxicity of diclofenac sodium than rodents since the oral LD_{50} is 55 mg/kg and 3200 mg/kg in rats and monkeys, respectively.
2. Diclofenac sodium did not exhibit any mutagenic activity in point mutation assays in mammalian (mouse lymphoma) and microbial (yeast, Ames) test systems. Likewise, the compound was nonmutagenic in several mammalian *in vitro* and *in vivo* tests such as the mouse dominant lethal and male germinal epithelial assay along with the Chinese hamster nucleus anomaly and chromosome aberration assays.

3. Reproduction studies conducted in mice at oral doses up to 5,000 times (20 mg/kg/day) and in rats and rabbits at oral doses up to 2,500 times (10 mg/kg/day) the human topical ocular dose revealed no evidence of teratogenicity due to diclofenac sodium even though maternal and fetal toxicity were induced. In rats, the maternally toxic doses were associated with dystocia, prolonged gestation, reduced fetal weights and growth, and reduced fetal survival.
4. Diclofenac sodium administered to male and female rats at 4 mg/kg/day did not affect fertility.
5. A two year carcinogenicity study conducted in mice in which males were treated with up to 0.3 mg/kg/day of diclofenac sodium and females with up to 1 mg/kg/day did not reveal any oncogenic potential. Carcinogenicity studies in rats administered up to 2 mg/kg/day of diclofenac sodium revealed no significant increases in tumor incidence. A slight increase in benign mammary fibroadenomas was observed among mid-dose (0.5 mg/kg/day) females, but the increase was not significant for this common rat tumor.

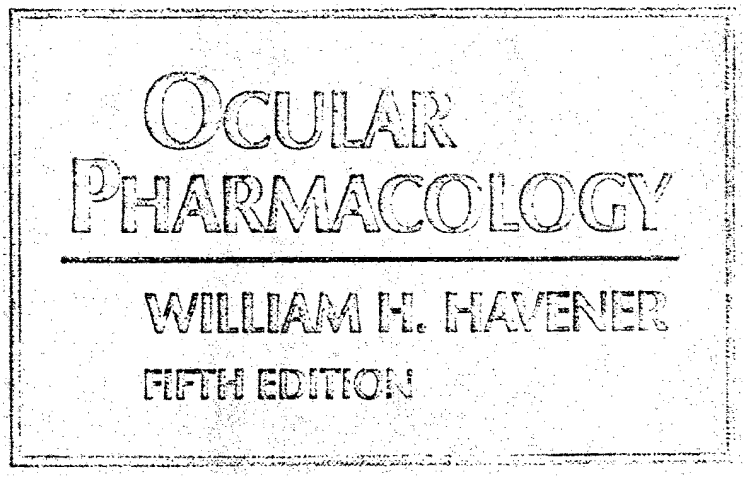
Diclofenac Sodium Ophthalmic Solution 0.1%

1. Diclofenac Ophthalmic Solution 0.1% preserved with POLYQUAD® (0.005%) and containing the solubilizer tocophersolan (5%) was administered four times per day (QID) to New Zealand White rabbits for up to three months. No signs of pharmacotoxicity were observed. Slit-lamp and indirect ocular evaluations and pachymetry measurements revealed no treatment-related findings. Clinical pathology data and histopathology were unremarkable which demonstrated the ocular and systemic safety of Diclofenac, POLYQUAD and tocophersolan in combination.

2. Topical ocular administration of aqueous solutions of 0.001, 0.01 or 0.05% of the preservative POLYQUAD three times daily (TID) for one year to rabbits did not produce any systemic toxicity and elicited only minimal ocular changes comparable to those effects observed in Untreated Control animals and animals treated with 0.001% Thimerosal or 0.01% BAC. Evaluation by scanning electron microscopy indicated either no corneal changes (Untreated Control, 0.001 and 0.01% POLYQUAD) or only minimal, reversible corneal changes with 0.05% POLYQUAD which were less severe than those changes observed in eyes receiving similar treatment with 0.001% Thimerosal or 0.01% BAC, the most commonly used ophthalmic preservative.

3. Tocophersolan (TPGS), used as a solubilizer in Alcon's Diclofenac Sodium 0.1% Ophthalmic Solution, is a vitamin E derivative and is used commercially as an oral Vitamin E dietary supplement. Chronic (one year) oral toxicity studies conducted in rats and dogs with TPGS at dose levels of 100, 300 and 1000 mg/kg/day elicited no treatment-related effects. This study was conducted by the National Cancer Institute.

Based on these preclinical toxicology studies, the opinion of Corporate Toxicology is that the change in the formulation of Diclofenac Sodium Ophthalmic Solution to include tocophersolan and POLYQUAD poses no increased risk or contraindications to its marketing.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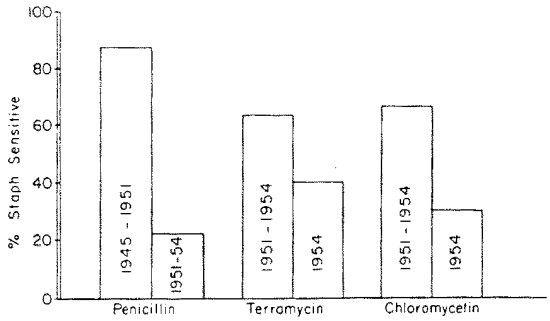

Fig. 6-1. In vitro studies of sensitivity of *Staphylococcus aureus* to various antibiotics, as measured in the years designated. Note the rapid and significant increase in resistant strains. (Modified from Locatcher-Khorazo, D., and Guiterrez, E.: Am. J. Ophthalmol. **41**:981, 1956. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)

"best" prophylactic antibiotic is a vain and illusory quest. Even if the concept of prophylactic antibiotics is valid (and it probably isn't), by the time a series of cases is reported, the sensitivity of microorganisms to the given antibiotic will have changed so much that the results will no longer have any relevance.

Let's assume that as you place the last conjunctival suture after a perfect cataract extraction in a one-eyed patient, the nurse tells you that the autoclave didn't cycle properly and your instruments have been unsterile. This really happened, and the management was prompt with massive use of prophylactic multiple antibiotics, both local and systemic. Do you suppose this prophylaxis worked? No. Endophthalmitis destroyed the eye. I'm not condemning use of antibiotics in such an instance. The message is that absolutely meticulous operating room technique is the key to a low rate of infection, providing that you have excluded patients who are themselves obviously infected. Do not try to substitute "prophylactic antibiotics" for observance of these two fundamental principles.

I use bacitracin, neomycin, and polymyxin B ointment following surgery, but without conviction. Their use makes the eyelashes easier to clean on the first postoperative dressing but probably doesn't accomplish anything else except to cause occasional neomycin allergy.

Donor cornea management

Antibiotic treatment of donor eyes for corneal transplantation is a special kind of prophylaxis. Despite sterile technique in removal and handling, in one study 50% of 1859 donor eyes were culture positive.[24] One hour after washing with chloramphenicol solution, only 30% of the eyes remained culture positive. Some of the eyes were washed with Neosporin; of these only 20% remained culture positive after 1 hour. Reducing by one half the number of culture-positive donor eyes seems like a worthwhile result of prophylaxis.

Generous irrigation with saline solution alone will greatly reduce the bacterial count on a postmortem eye. Soaking in 0.01% thiomersal was said to kill both fungi and bacteria, although the time required was not specified. The concentration of thiomersal generally used as a preservative is 0.001%. Up to 2% thiomersal was said not to harm corneal epithelium or endothelium.[25] (I have difficulty in believing that the endothelium is 2000 times as resistant to a chemical preservative as are microorganisms.)

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The Effect of Some Preservatives Used in Nasal Preparations on Mucociliary Clearance

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Abstract—The effect of methyl-*p*-hydroxybenzoate, propyl-*p*-hydroxybenzoate, chlorbutol, chlorocresol, EDTA, benzalkonium chloride, chlorhexidine, phenylmercuric nitrate and phenylmercuric borate on mucociliary transport rate of the frog palate has been examined. Following a variable number of applications all these preservatives halted transport, the first three reversibly. However, applications of thiomersal (0·01%) were well tolerated. The frog palate possesses a ciliated epithelium protected by mucus, since some of our findings are at variance with those previously reported results where the protective effect of mucus was negligible in the in-vitro model (usually trachea) employed, it would appear that the contribution of mucus to effective mucociliary clearance should not be underestimated.

Nasal drops and sprays are usually simple aqueous solutions containing substances with antiseptic, local analgesic and vasoconstrictor properties intended to act locally. However, the intra-nasal route may also be used to deliver compounds to the systemic circulation and provides a convenient and reliable means of self-administration which is likely to prove especially useful for those compounds which are difficult to deliver by the oral route. These include pharmacologically active polypeptides and proteins which are currently being developed, such as hormones and vaccines, which may fail to realize their full potential if the parenteral route is their sole means of administration.

The epithelium of the upper respiratory tract is covered by many hair-like cilia that beat in a co-ordinated manner within the periciliary fluid beneath a layer of viscoelastic mucus, the whole comprising the mucociliary apparatus. After inhalation, mucociliary clearance contributes to the body's primary non-specific defence mechanism by entrapping potentially hazardous substances such as dust and micro-organisms, allergens, carcinogens and cellular debris within the mucus blanket, which is then propelled by the claw-like tips of the underlying cilia towards the pharynx where it is swallowed or expectorated (Proctor 1977).

Compromised clearance may be associated with a variety of conditions including genetically misformed cilia (Afzelius 1976, 1979, 1981), cigarette smoking (Walker & Kiefer 1966) and bacterial or viral infection (Carson et al 1979; Iravani et al 1978). An alteration in the secreted mucus, such as is seen in cystic fibrosis, can also inhibit clearance (Di Sant Agnese & Davis 1976a,b,c; Wood et al 1976). Patients with such conditions suffer extensively from chronic respiratory infections such as bronchitis, sinusitis and rhinitis. These consequences of inhibited clearance emphasize that the constituents of preparations intended for nasal delivery should not adversely affect the clearance system.

Most nasal drops and sprays are presented as multi-dose preparations requiring a preservative to prevent the growth of micro-organisms upon repeated use. In studies investigating the effects of preservatives on the mucociliary clearance apparatus, ciliary beat frequency has been monitored using small portions of ciliated tissue usually from trachea (Greenwood et al 1946; Gallay 1960; Perrault et al 1978; Mostow et al 1979; Van de Donk et al 1980). We have examined the effect of a similar range of preservatives on mucociliary transport rate measured on the frog palate. This model has been shown to produce a good correlation with in-vivo tracheal clearance measured in mammals (Giordano et al 1977) and, since it possesses a ciliated epithelium protected by a visible and continuous layer of mucus (Morgan et al 1984), it might be expected to provide a better correlation with the human nasal epithelium than earlier models.

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Materials and Methods

Preparation of solutions

The control solution for most of the compounds was 0·9% w/v NaCl (May and Baker Ltd; UK) in distilled water. That for phenylmercuric nitrate was 1·3% w/v sodium nitrate or 5·07% w/v mannitol in distilled water. Chlorhexidine gluconate and phenylmercuric borate were also investigated using 5·07% mannitol as the control solution.

Preservative solutions were made by dissolving the required amount in the appropriate control solution. The concentrations investigated were: methyl-*p*-hydroxybenzoate 0·02 and 0·15%, propyl-*p*-hydroxybenzoate 0·02%, benzalkonium chloride 0·01% (Sigma Chemical Company, UK); chlorbutol 0·5%, 4-chloro-*m*-cresol 0·05% and 0·10%, thiomersal 0·01%, phenylmercuric nitrate 0·002% (BDH Chemicals Ltd; UK); ethylenediaminetetraacetic acid, disodium salt, dihydride (EDTA) 0·1% (Aldrich Chemical Company Ltd., UK); phenylmercuric borate 0·002% (Zyma S.A., Switzerland); chlorhexidine gluconate 0·01% (ICI PLC, UK).

Transport rate was measured in-vitro using a modification of the frog palate preparation described by Sadé et al (1970). After being pithed, the frog (*Rana temporaria*) had its upper palate exposed. The frog was then introduced into a transparent chamber maintained at 20°C with a relative humidity of 100% and the palate surface observed through a

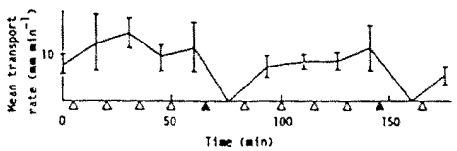

FIG. 1. The effect of propyl-*p*-hydroxybenzoate 0·02% w/v on mean transport rate. ▲; application of perservative, △; application of control solution.

stereo-microscope (Stereo Zoom 4, Bausch and Lomb UK Ltd), with a calibrated eyepiece (Bausch and Lomb UK Ltd 10× W.F. Stereo 31-15-71).

Control values were obtained for each experiment by applying 0·2–0·4 mL of the appropriate control solution to the palate, leaving it in contact for 10 min then draining it off. The transport rate was then measured by recording the time taken for graphite particles to travel a given distance, usually 0·3 cm, over the palate. This procedure was repeated three or four times before the test compound was similarly applied. If the preservative appeared to halt or decrease transport, the effect of rinsing the palate with the appropriate control solution was assessed. Each preservative was tested on at least six different palates.

Results

Figs 1–3 are examples of the results obtained for one of the six palates used. Values for mean transport rate are plotted with standard deviation bars. Methyl-*p*-hydroxybenzoate, propyl-*p*-hydroxybenzoate and chlorbutol halted transport, rinsing the palate reversed the toxic effect of methyl-*p*-hydroxybenzoate (0·02%) and propyl-*p*-hydroxybenzoate (Fig. 1), while reversal of the effect of methyl-*p*-hydroxybenzoate (0·15%) and chlorbutol was equivocal.

Chlorocresol (Fig. 2), benzalkonium chloride, EDTA and phenylmercuric nitrate halted transport irreversibly following one to two applications. Phenylmercuric borate in saline, halted transport after two to five applications, normally, but not always, irreversibly; in mannitol it caused transport to cease irreversibly, generally after a single application.

Chlorhexidine in 0·9% NaCl appeared to be well tolerated by the palate, and transport was still apparent after six applications. However, in a mannitol solution, one or two applications of chlorhexidine were generally sufficient to irreversibly halt transport.

Fig. 3 shows that activity could still be observed on the palate following nine applications of thiomersal, suggesting that in this model, this preservative is well tolerated.

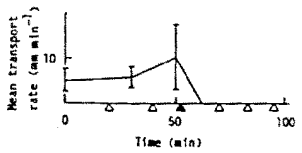

FIG. 2. The effect of chlorocresol 0·10% w/v on mean transport rate. ▲; application of perservative, △; application of control solution.

Discussion

The effects of methyl-*p*-hydroxybenzoate 0·15%, were similar to those published elsewhere (Gallay 1960; Perrault et al 1978; Mostow et al 1979; Van de Donk et al 1980). The reversibility of the observed effect appears to depend on the contact time and the concentration employed. This is substantiated by the observation that at the lower concentration (0·02%) the effect of methyl-*p*-hydroxybenzoate was always reversible, whereas at the higher concentration the reversal of the inhibiting effect was variable. Chlorbutol and propyl-*p*-hydroxybenzoate possessed similar properties to methyl-*p*-hydroxybenzoate, also in agreement with the results of Perrault et al (1978) and Van de Donk et al (1980). Methyl-*p*-hydroxybenzoate, propyl-*p*-hydroxybenzoate and chlorbutol are lipophilic and are believed to exert their toxic action upon micro-organisms following adsorption and subsequent diffusion through the lipophilic membrane.

Similar toxic effects may occur, following diffusion of the preservative across the ciliated epithelium, which halts transport. Subsequent rinsing may reverse the adsorption process and cause back-diffusion of the compounds from the cells of the mucous membrane, hence reversing the effect.

Chlorocresol, at both concentrations used, halted transport after a single application and this effect was irreversible. This could be explained by it possessing a higher oil-water partition coefficient than the previous three compounds such that rinsing with saline was insufficient to cause back-diffusion out of the cells. The oil-water partition coefficients of chlorocresol, methyl-*p*-hydroxybenzoate and propyl-*p*-hydroxybenzoate in vegetable oil are 117·0, 7·5 and 80·0, respectively, lending some support to this suggestion. It is also possible that transport over the frog palate was inhibited by an alteration of the well-defined viscoelastic properties the mucus gel must possess in order to flow on a ciliated epithelium (Litt et al 1976). Since this irreversibility contradicts the results of Van de Donk et al (1980) with trachea, it is likely that it is a consequence of the mucus layer covering the cilia of the frog palate.

In earlier studies the effect of preservatives has been assessed by monitoring ciliary beat frequency on isolated pieces of ciliated tissue, usually trachea, which were completely immersed in the test solution (Gallay 1960; Perrault et al 1978; Mostow et al 1979; Van de Donk et al 1980). Such immersion increases the likelihood of removal of any mucus layer that might be present, and in two of the studies mucus was deliberately removed (Gallay 1960; Mostow et al 1979).

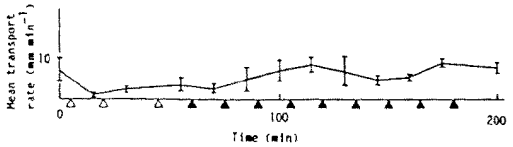

FIG. 3. The effect of thiomersal 0·01% w/v on mean transport rate. ▲: application of perservative, △: application of control solution.

With the tracheal preparation even if a mucus layer is present, the protection it affords the cilia is minimal since, when the ring is submerged in the test solution the compound is able to gain direct access to the cilia via the anterior and posterior (cut) surfaces of the ring. While such models supply useful information about the toxicity of compounds to the cilia, efficient mucociliary clearance is dependent upon the quantity and viscoelastic properties of the periciliary fluid and mucus as well as the number, beat frequency and co-ordination of the cilia (Mygind et al 1982).

The quaternary ammonium compound, benzalkonium chloride, halted transport irreversibly following one or two applications. Similar observations have been reported by Gallay (1960), Van de Donk et al (1980) who observed a slower onset of inhibition than we found with the frog palate. Benzalkonium chloride exhibits surfactant properties, it exerts its antibacterial action by damaging the external membrane of micro-organisms (Richards & Cavill 1976). Surface active compounds also have been shown to destroy the ciliary membrane (Summers & Gibbons 1971) and thus benzalkonium chloride might be expected to be toxic to cilia. Moreover, surfactants are likely to alter the viscoelastic nature of the mucus gel (Martin et al 1978). This dual effect could explain the faster onset of action we observed.

EDTA is an accepted preservative potentiator often used in conjunction with benzalkonium chloride. It is thought to aid penetration of the preservative into the bacterial cell by damaging certain outer layers of the cell envelope and, in some instances, to affect internal sites (Richards & Cavill 1976). It is possible that the irreversible cessation of transport caused by EDTA could be explained by a similar disruption of ciliated epithelium, since, via its chelating ability, it causes expansion of the intercellular spaces and therefore permits an increase in the permeability of the tissue to various molecules including EDTA itself (Grass & Robinson 1988). Calcium is believed to play a vital role in the regulation of ciliary activity. It is currently believed that two mechanisms exist for generating motility in cilia and eukaryotic flagella: a Mg^{2+}-dependent sliding of microtubules and a Ca^{2+}-sensitive system controlling the sliding and bending (Satir 1982). Hence, inhibition of mucus transport is likely to be related to decreased ciliary beating caused by the sequestration of Ca^{2+} and/or Mg^{2+} by EDTA. It has been stated that the calcium present in the mucus of the nose should be sufficient to counteract completely the effect of EDTA and render it of negligible toxicity (Van de Donk et al 1980). Our results suggest that this may not be the case and it should be noted that not all Ca^{2+} present in mucus is available for chelation since a proportion is bound to the glycoprotein molecule.

The cessation of transport resulting from applying phenylmercuric borate, in 0·9% NaCl, to the palate, was slower in onset than the other compounds. Although no precipitate was observed, the low solubility of the halide salts of phenylmercuric compounds is well documented therefore the experiments were repeated with mannitol as solvent. This rapidly halted transport, implying that not all the preservative was available from the saline solution.

Chlorhexidine, with its detergent-like properties, might be expected to be toxic to cilia. It is capable of thickening cervical mucus (U.S. Patent 4,590,070) which might also impair mucus transport. We found that transport was still observable after six, 10 min applications of chlorhexidine dissolved in 0·9% NaCl, however, in mannitol it halted transport after one or two 10 min applications. In saline it is likely that the dihydrochloride was formed, this has decreased solubility compared with the gluconate which is likely to explain the decreased activity observed. Van de Donk et al (1980) found chlorhexidine in Locke-Ringer solution to halt tracheal ciliary beat irreversibly after 80 min. The abundance of chloride ions in that solution might have decreased the activity.

Of the compounds investigated, thiomersal appeared the least toxic which contradicts [illegible] able ciliotoxicity in the absence of mucus was observed (Perrault et al 1978; Van de Donk et al 1980). This suggests that the cilia are protected by the mucus.

In comparing our results with earlier work, a number of differences emerge which may be attributed to the different models used. Since mucociliary clearance is a complex function of the physical properties of the mucus (Gelman & Meyer 1979), coupled to appropriately functioning cilia (Sleigh 1981), it is important that neither aspect is overlooked when choosing an in-vitro model. In possessing a ciliated epithelium protected by an intact layer of mucus the frog palate provides such a model.

A knowledge of the effect of preservatives on cilia protected by mucus as well as on unprotected cilia should lead to a greater understanding of the mode of action of compounds in such a system and should ultimately lead to the best choice of preservative for use in future nasal preparations.

Our results show that within the constraints of formulation and packing requirements, thiomersal should be preferentially included in nasal drops and sprays.

There are instances where a transient slowing or halt of mucus transport is desirable to increase the contact time between the active principle and nasal mucosa. Microspheres have been used as a nasal drug delivery system to increase the half life of nasal clearance (Illum et al 1987) and perhaps

those preservatives halting transport reversibly might be useful in a similar manner. It remains to be determined, however, whether a compound with a gradual but irreversibly toxic effect upon the mucociliary system is more, or less appropriate, in the long term, than a compound appearing immediately but reversibly toxic.

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PRESERVATIVES AND BIOLOGICAL REAGENTS

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Abstract

Biological reagents used for the *in vitro* diagnosis of disease have been selected as a result of research in a variety of disciplines over a considerable period of time; consequently a multiplicity of preservatives are in use. The selection of a preservative for such biologicals is mainly influenced by the test system and not usually by considerations of toxicity for man.

The reasons for adding preservatives to reagents are firstly to take care of any minimal contamination which might occur during the final stages of production, e.g. during filling; secondly with multitest containers the preservative is expected to protect the reagent against contamination resulting from several references to the container. Preservatives are not added with the aim of sterilizing reagents.

This paper reports:

(1) the results of a survey of the preservatives used in a wide range of biological reagents;

(2) the results of an investigation into the stability of these preservatives as used in the reagents;

(3) a comparison between sodium azide and thiomersalate as bacteriostats in a range of reagents.

It is over fifty years since our laboratories first prepared and issued diagnostic reagents. Salmonella agglutinating sera raised in rabbits were the first to be prepared and these after filtration through Berkefeld candles were preserved with 0·5 % phenol. Over the years the number of reagents prepared at the laboratories has grown to over 500 and of these more than 400 are preserved by chemical means. Very few reagents are issued in single-test containers, and preservation is desirable to prevent the growth of small numbers of organisms which may be accidentally introduced during use. For most reagents physical methods of preservation, which from some points of view are preferable, are not practicable. (If all reagents were issued in single-test containers, could be filtered through membranes of a sterilizing porosity, or would withstand autoclaving for an hour at 15 lb pressure there would be no problem.)

As the numbers of reagents produced grew, so did the number of preservatives used. There were several reasons for this; reagents are almost always research based, arise from the efforts of workers in different disciplines who tend to take advice from many sources and in the end often use what is available in their

Table I. *Compounds used for the preservation of diagnostic reagents*

	Concentrations (%)	No. of reagents using
Preservatives		
Formaldehyde	0·20	1
Glycerol	33·00	2
Orthocresol	0·35	13
Phenol	1·00	2
	0·50	99
	0·25	4
Sodium azide	0·10	36
	0·08	20
Thiomersalate	0·025	2
	0·02	36
	0·01	16
Preservatives used in combination		
Boric acid	1·0	30
Thiomersalate	0·01	
Formaldehyde	0·25	21
Thiomersalate	0·01	
Glycerol	50·0	1
Thiomersalate	0·01	
Glycerol	25·0	2
Thiomersalate	0·02	
Glycerol	10·0	1
Formalin	1·0	
Phenol	0·5	30
Thiomersalate	0·02	
Richardson's sol. A		
Boric acid	0·06	1
Borax	0·14	
Sorbitol	0·74	
Richardson's sol. B		
Borax	0·04	
Sodium azide	0·05	

particular laboratory and if it apparently works they stick to it. In many cases also reagents are prepared to formulae and only rigidly adhering to the prescribed method in all details including preservation is one justified in labelling the reagent with the inventor's name.

Table I lists in alphabetical order the preservatives currently in use. Some reagents for good practical reasons wear a belt and braces, that is contain two preservatives. An example is the *Escherichia coli* antisera where both phenol and thiomersalate (sodium ethylmercury-thiosalicylate) are used because the raw serum must be preserved as soon as it has been separated from the clot in order

Table II. *Effective concentrations of thiomersalate in reagents stored for 2 years at 4 °C*

No. tested	Preservative	% of starting concentration after 2 years' storage	Type of reagent
4	Thiomersalate Boric acid	12·5–17 Not measured	Streptococcal grouping sera
4	Thiomersalate	50–100	Skin test antigens
10	Thiomersalate	6·25–25	Agglutinating sera
6	Thiomersalate Phenol	10–25 40–44	Agglutinating sera
12	Phenol	38–80	Agglutinating sera

to hold down the growth of organisms to a reasonable level during the repeated absorptions which are commonly required to render the serum specific; phenol is used for this purpose. After processing it has been found that the level of phenol remaining is often too low to be relied on during use and therefore thiomersalate is added before filtration.

An example where the use to which the reagent may be put determines the preservative which can be used is in the antisera to the Salmonella H non-specific phase, where it may be necessary to neutralize the antibacterial effect of the preservative when the reagent is used in plates or Craigie tubes by workers trying to establish the specific phase of the organism. Here thiomersalate is used alone as its antibacterial activity can be readily neutralized with thioglycollate, and these sera normally require less absorption than the *E. coli* sera.

You will see that we are still faithful to 0·5% phenol for some reagents, particularly for somatic agglutinating sera where it has been found to work well. In a number of cases the reasons behind the use of a particular preservative are not known; so a natural desire for rationalization coupled with an equally natural caution which dictated that changes in preservatives should only be made when it could be shown that the new was at least as good as the old, prompted us to start looking into the situation.

As it is our normal practice to retain samples of all reagents for variable periods of time after they reach their expiry date (the period is at least six months but variable because of the difficulty of finding time to turn out cold rooms) it seemed that a good place to start would be by looking at as many as possible of such retained samples. Some of the results obtained when the residual preservative was measured are shown in Table II. The reagents are grouped according to type of reagent and preservative used.

It will be noted that only with the skin test antigens, where the amounts of protein present are very low, is the concentration of thiomersalate remaining after two years' storage of the same order as that added. With the agglutinating sera – undiluted rabbit sera – the apparent concentration of thiomersalate is reduced to between a fifth and a sixteenth of the initial concentration. Phenol, however,

Table III. *Sodium azide concentration in reagents after storage at 4 °C for varying times (0·1 % azide added)*

		Age (months)	Sodium azide (%)
Freeze-dried reagents			
Fluorescent-labelled globulins (sheep)		8	0·03
		9	0·05
		12	0·05
		23	0·05
Unlabelled globulin (sheep)		18	0·04
Liquid reagents (immune sera)			
Species	Concentration of serum		
Human	1/6	3	0·068
	1/50	3	0·1
Sheep	Neat	1	0·05
		21	0·05
		22	0·075
		36	0·05
Rabbit	Neat	26	0·05
	2/3	22	0·03
	2/3	24	0·05
	1/20	32	0·1
	1/20	32	0·1125
Goat	Neat	24	0·05
	Neat	21	0·1125
Glycine Buffer		21	0·113

appears either to be longer lasting or not to be fixed to the same extent and the reduction in its concentration is only by a third to a fifth.

In contrast, Table III shows the residual sodium azide in reagents arranged according to type and age. Sodium azide was introduced in the forties primarily for reagents which were particularly liable to instability resulting from contamination, for example complement and anti-Rh agglutinins and which were easily denatured in the presence of thiomersalate(5, 6). It was found to be of value in enzyme studies and it is also used for viral reagents where it has been found that thiomersalate may impair the precipitation of some viruses by their respective antisera(1, 3, 4). We do not know whether this is because the quaternary structure breaks up or because there is a direct interaction with sulfhydryl-containing antigenic determinants or as a result of the release of mercury ions. Sodium azide is also used in reagents which are to be freeze-dried, in order to avoid the denaturation which could occur as a result of local increases in concentration of preservatives such as phenol. The residual concentration of azide ranges from 27% of the starting concentration to 100%, but no clear pattern emerges.

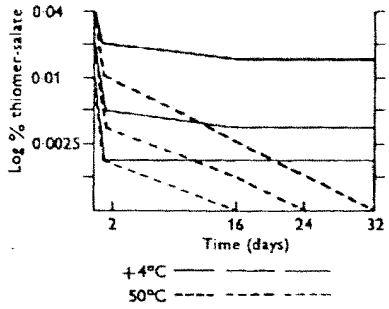

Fig. 1. Accelerated deterioration test of thiomersalate in rabbit serum in plastic containers.

It should be stated at this point that despite the reduction in preservative in these samples held at 4 °C for two years there was no evidence to suggest that any minimal undetected contamination which might take place during filling was not held by the preservative and all samples appeared to be sterile.

We were already looking at the stability of thiomersalate in rabbit serum in plastic containers for another purpose. We were assaying the thiomersalate biologically by comparing the diameter of the zones of inhibition of the growth of *Staphylococcus aureus* on nutrient agar with those obtained using standard solutions of thiomersalate as we considered that the biological activity of the residual preservative was our main concern.

The results of these assays (Fig. 1) show that, within the first 24 h, there is a marked reduction in the activity of the thiomersalate, presumably due to rapid chemical inactivation of the mercury by sulphides or thiol groups in the serum. The percentage reduction in concentration is greatest with the weaker solutions, but not all activity is lost and that remaining is unchanged after a month at +4 °C. However, when higher temperatures are used to accelerate reactions and to indicate trends, it is seen that at 50 °C the concentration of thiomersalate in the plastic containers is reduced to an undetectable level within a month. These findings and our increasing interest in the fate of preservatives prompted an investigation into the situation in glass containers.

Fig. 2 indicates that the activity of thiomersalate falls to undetectable levels within a month at 50 °C in glass bottles also, although this happens more slowly than in plastic containers. At +4 °C and 25 °C a similar initial drop is seen but the activity then remains constant throughout the month. At 37 °C the rate of fall in activity following the usual initial drop is slower than at 50 °C, as might be expected. The continuing fall in activity at the higher temperature may be the result of a permanent loss of activity or it may be that the serum protein and thiomersalate are in a different state of equilibrium as the higher temperature results in more denatured protein to react with the thiomersalate. This may be reversible if the temperature is lowered but it seems unlikely. The finding of up

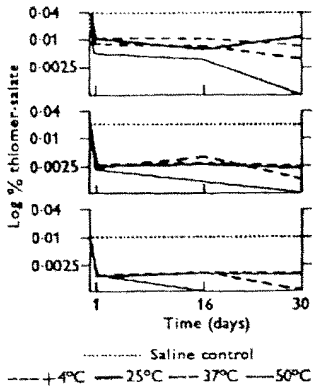

Fig. 2. Accelerated deterioration test of thiomersalate in rabbit serum in glass bottles.

to an eight-fold immediate reduction of activity of thiomersalate in the presence of serum at all temperatures is in keeping with the previous results, as shown in Table IV.

Similar assays were made on serum containing sodium azide. A serum preparation simulating a control serum was assayed for inhibitory activity, i.e. residual azide, over a period of 6 weeks. The effective concentration of azide is reduced far less than is that of thiomersalate, and there is little difference between the results obtained at +4 °C, 25 °C, 37 °C and 50 °C. In all cases at least half the added sodium azide remains.

Whilst seeking a suitable organism for the assay of sodium azide it was noticed that many organisms were relatively insensitive to sodium azide on agar plates. Sodium azide has therefore been compared with thiomersalate on the basis of activity against a number of organisms commonly isolated in the laboratory (Table V). The comparison was made on nutrient agar plates and the results are shown in Figs. 3 and 4. Acinetobacter was the one selected for the assay of sodium azide.

The results of similar tests to determine the activity of the two preservatives against fungi were particularly interesting in that all fungi tested showed similar zones of inhibition as a result of the action of thiomersalate, as did the bacteria. However, on the plates on which the discs soaked in sodium azide were placed, none of the fungi grew. As a result of our concomitant reading we then realized that hydroazoic acid, the active agent of sodium azide volatolized by the incubation temperature, could be acting in the gaseous phase against the moulds which tend to be markedly aerobic in respiration(2). Additional plates were therefore set up for these fungi and sodium azide and the lids of the dishes were raised for 24 h during incubation. The results confirmed that the inhibitory activity was in the vapour phase, because after raising the lids during incubation all plates

Table IV. *Assay of zero samples of normal rabbit serum containing thiomersalate*

The preservative was added to the serum at 09.00 h and the assay was set up at 15.00 h. The inhibition zones were read 24 h later.

Standard 1 % thiomersalate solution in distilled water	
Concentration (%)	Zone (mm)
0·02	23·5
0·01	21·5
0·005	19·5
0·0025	16·5
0·00125	13·5

Serum preparations plus standard 1 % thiomersalate solution		
	6 h later	
Initial concentration (%)	Zone (mm)	Concentration (%)
0·04	24	0·026
0·02	19·5	0·005
0·01	16	0·002

Standard 1 % thiomersalate solution	
	Zone (mm)
Dil. to 0·01 %	21·5

Table V. *A comparison between the inhibitory effects on certain bacterial species commonly associated with contamination*

	Thiomersalate		Sodium azide	
	0·01 % (mm)[a]	0·0025 % (mm)	0·1 % (mm)	0·05 % (mm)
Bacillus subtilis	29	18	C	C
B. cereus	30	22	20[b]	C
Aerobacter aerogenes	26	17	17[b]	C
Pseudomonas aeruginosa	30	22	C	C
Proteus vulgaris	18	C	15	C
Acinetobacter sp.	32	25	32	25
Serratia marcescens	36	25	24	15[b]
Pseudomonas sp.	C	C	26[b]	21[b]
Micrococcus sp.	30	15	C	C
Escherichia coli	23	15	23[b]	15[b]
Staphylococcus sp.	33	24	C	C
Achromobacter sp.	45	33	47	37

C = Confluent growth up to disc.

[a] Diameter of zones of inhibition on nutrient agar plates containing the test organism after 24 h incubation at 32 °C.

[b] Area of reduced growth.

138

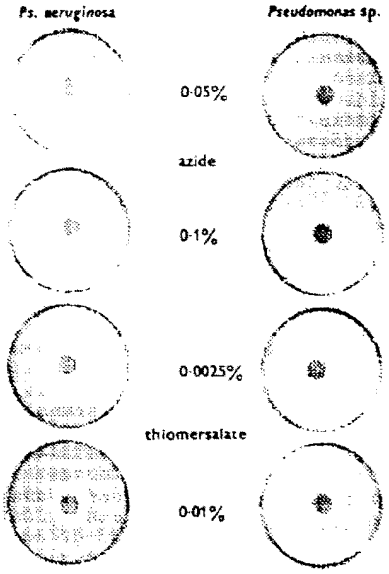

Fig. 3. Effect of azide and thiomersalate on *Ps. aeruginosa* and *Ps.* sp.

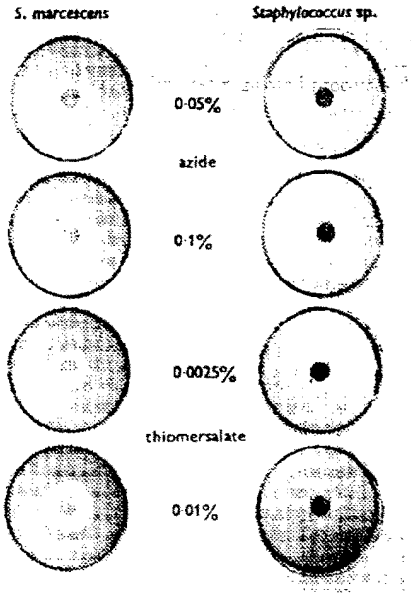

Fig. 4. Effect of azide and thiomersalate on *Serratia marcescens* and *Staphylococcus* sp.

Table VI. *A comparison between the effect of thiomersalate and sodium azide on fungi*

	Thiomersalate 0·01 %		Sodium azide 0·1 %			
	2 days	5 days	2 days	5 days	2 days*	5 days
Penicillium citrinum	42 mm	—	NG	Sl.G	Sl.G	C
Mucor albo-ater	38 mm	—	NG	Sl.G	C	—
Aspergillus quercinus	50 mm	—	NG	Sl.G	C	—
Rhizopus nigricans	NG	65 mm	NG	NG	NG	C
	2 days		1 day	2 days*		
Candida albicans	40 mm		NG	C		
Saccharomyces cerevisiae	42 mm		NG	C		
Mucor albo-ater	38 mm		NG	C		

NG, No growth. Sl.G, Slight growth. C, Confluent growth up to disc.
* Lids of Petri dishes were raised.

showed good growth, completely covering the surface up to the edge of the disc to which the sodium azide had been added (Table VI). Some years ago we also made a comparison of the inhibitory concentration of preservatives on a range of 65 common moulds and yeasts with the following results. We compared phenol, diphenylene iodonium sulphate and thiomersalate at concentrations ranging from 1000 μg/ml to $<0{\cdot}1$ μg/ml and found that the growth of all 65 fungi was completely inhibited by 0·02% phenol, 0·002% DPI and 0·00002% thiomersalate. Fig. 5 shows some of the plates involved. The top row of plates contains the aspergilli, the second row the penicillia and the third row the yeasts.

Even in the best regulated processes during the preparation of reagents contamination may occur and we have, on rare occasions, found organisms contaminating products containing thiomersalate or sodium azide, which were apparently resistant to these preservatives.

From the results of the experiments on the effect of thiomersalate and sodium azide on various strains of bacteria, it appears that thiomersalate is effective against a wider range of bacterial species than is sodium azide. However, some organisms in the Pseudomonas group have been found in thiomersalate-preserved products which appear to be able to metabolize the preservative.

A small experiment was therefore undertaken to investigate the competence of these preservatives to protect serum against a bacterial challenge under conditions which might be encountered in production. The results are given in Table VII. The sample of serum to which 0·01% thiomersalate was added was able to cope with the challenge by Acinetobacter within four days after which it appeared to be sterile, i.e. no organisms could be grown, whilst the sample of serum to which 0·1% sodium azide was added, although it showed a reduction in the number of organisms after seven days, only became apparently sterile after 13



Fig. 5. Effect of phenol, diphenylene iodonium sulphate and thiomersalate on fungi.

days. Both samples of serum were held at 4 °C. However, when further samples of the two sera were challenged with a small number of a *Pseudomonas* sp. it was seen that in the presence of thiomersalate the inoculum multiplied four to five hundred fold in 7 days and after 13 days the number of organisms present was so great as to be uncountable. In contrast, after four days in the serum containing sodium azide, the number of organisms which could be recovered was considerably reduced and after six days the serum appeared to be sterile. Again, both samples of serum were held at 4 °C.

We are currently looking at the possibility of using methyl parahydroxybenzoate (Nipagin M). To date we have not found any obvious advantages but some disadvantages in that it is relatively ineffective at neutral or alkaline pH, and there are also solubility problems at low temperatures. There have been reports that, although effective in many areas, it is no more active at the levels used than thiomersalate in destroying organisms of the Pseudomonas and Flavobacterium group.

From this very small and necessarily superficial survey it would seem that thiomersalate is a more effective agent than sodium azide against both bacteria and fungi at the concentrations usually recommended, but neither preservative can be expected to cope with a massive challenge and there is a place for both

Table VII. *Bacterial challenge to preservatives added to rabbit serum*

(1) *Thiomersalate* 0·01 % *added. Culture:* Acinetobacter *sp.*

Culture dilution	Orgs. added to 5 ml serum	=/ml	Orgs./ml after 4 days 4 °C
10/1	19000	3800	0
10/2	1900	380	0
10/3	190	38	0
10/4	19	4	0
10/5	4	<1	0
10/6	0	0	0

(2) *Sodium azide* 0·1 % *added. Culture:* Pseudomonas *sp.*

Culture dilution	Orgs. added to 5 ml serum	=/ml	4 days 4 °C (orgs./ml)	7 days 4 °C (orgs./ml)
10/1	98000	19600	8300	0
10/2	9800	1960	1500	0
10/3	980	196	50	0
10/4	98	20	0	0
10/5	15	3	0	0
10/6	2	<1	0	0
10/7	0	0	0	0

(3) *Sodium azide* 0·1 % *added. Culture:* Acinetobacter *sp.*

Culture dilution	Orgs. added to 5 ml serum	=/ml	7 days 4 °C (orgs./ml)	13 days 4 °C (orgs./ml)
10/1	12500	2500	1000	0
10/2	1250	250	50	0
10/3	125	25	0	0
10/4	20	4	0	0
10/5	0	0	0	0
10/6	0	0	0	0

(4) *Thiomersalate* 0·01 % *added. Culture:* Pseudomonas *sp.*

Culture dilution	Orgs. added to 5 ml serum	=/ml	7 days 4 °C (orgs./ml)	13 days 4 °C (orgs./ml)
10/4	67	13	5000	UC
10/5	5	1	500	UC
10/6	1	<1	200	UC
10/7	0	0	0	0
10/8	0	0	0	0
10/9	0	0	0	0

in biological reagents. As all the products discussed are for laboratory use and not for injection into man or animals, it is possible that the preservatives could be added to give higher residual concentrations, although one would need to assess the effect on the performance of the reagents and one must remember that sodium azide is not without hazard.

In conclusion it must be emphasized that we have only been able to present

the observations of a quality control and sterility control section together with such *ad hoc* experiments as could be fitted into an already very full schedule. The material presented is not the result of carefully planned experiments in a research project. However, a computer search for papers published during the last five years using preservatives and biological reagents as key words produced a great weight of print-out listing many hundreds of papers but only produced two really relevant papers. It is now felt that there are sufficient findings to demonstrate how little is known and it is hoped that a screen through which preservatives, organisms and products can be fed before deciding which preservative is the most effective in a given circumstance can be devised.

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Discussion

CHRISTENSEN Your finding of *Pseudomonas* resistant to thimerosal, was it only in the presence of rabbit serum?

BATTY Our first observation was with an agglutinating serum which, despite filtration through Millipore membrane of 0·22 porosity, and the presence of 0·02% thimerosal, was not rendered sterile. This came as a shock to us. When we isolated the organism, we found it not only to tolerate thimerosal, but also to thrive in its presence.

DRUBE I cannot quote the reference, but a recent report commented on L-forms of *Pseudomonas* which were resistant to various antimicrobial agents, and this may have some bearing on your findings.

BATTY In a way, that would be a comforting answer to the problem.

WILSON Concerning the loss of preservative over a period of time, was any attempt made to determine how much was bound to the rubber stoppers?

BATTY We do not use rubber stoppers. We use plastic screw caps which, in our tests, do not seem to absorb the preservative.

MÖLLER I was interested to hear about the loss in concentration of thimerosal in contact with rabbit serum. I found the same to occur in the presence of human serum which we keep in glass containers with no rubber. We used a chemical assay to quantitate thimerosal.

BATTY This is very interesting because of the use of chemical assay. Ours was a biological method of determination, and I have always been prepared to believe that the thimerosal was there, but was fixed in some manner. But at least it is not detectable chemically either.

A comparison of thiomersal and 50% alcohol as preservatives in urinary cytology

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SUMMARY The efficacy of 50% ethyl alcohol and of thiomersal as preservatives in urinary cytology were compared. In both methods over 80% of the cells were sufficiently well preserved after three days to allow cytomorphological evaluation, and over 50% on the seventh day. In the specimens without preservative, only 54% and 28% were intact after the same time intervals. In contrast with 50% ethyl alchohol, thiomersal is a more effective bactericide, it does not increase the volume of the sample, it is cheaper, and it does not affect the cytomorphology.

With the increasing incidence of carcinoma of the urinary bladder in industrialised countries the use of cytology has become more important. For a mass screening project a centralised cytology service is preferable, but, as this may lead to a delay in the processing of specimens, preservation of the urine is desirable. The maintenance of life-like features of the cells is not essential, only the retention of morphological and diagnostic features in the fixed and stained cells (Bahr, 1974). This can be achieved either by initial fixation of the whole specimen, for instance with 50% ethyl alcohol (Durfee, 1968), or by using a bactericide such as thiomersal (Merthiolate), the sodium salt of ethyl mercuric thiosalicylic acid (Jamieson and Powell, 1931; O'Connor, 1939).

The present study compares the efficiency of thiomersal and of 50% ethyl alcohol as preservatives for urinary cytology specimens.

Material and methods

The study was carried out on specimens of freshly voided urine obtained from 31 female and 9 male patients attending the Urological Clinic of the University Hospital, Leyden. Six patients had proved carcinoma of the urinary bladder and 34 had non-malignant diseases of the urinary tract. All the patients with carcinomas were males.

Each urine sample was divided into four equal portions. The first portion (sample 1) was used for culture and bacterial counts, and for performing the trypan blue exclusion test to determine the percentage of living cells present. No preservative was added to the second portion (sample 2); 50 mg thiomersal per 100 ml was added to the third portion (sample 3), and an equal quantity of 50% ethyl alcohol was added to the fourth portion (sample 4). The samples were kept at room temperature. The trypan blue exclusion test was also performed on sample 2 on the third and fifth days.

Smears were made from centrifuged aliquots of sample 1 immediately and from all four samples on the third, fifth, and seventh days. The smears were fixed with spray fixative and stained by the Papanicolaou method.

The proportion of intact cells in the stained smears was determined as a percentage of the total number of intact and degenerate epithelial cells present, using the following criteria for an intact cell: well-circumscribed cell border, presence of intact cytoplasm, a well-defined nuclear border, and a clear-cut unblurred nuclear pattern. The presence of bacteria (graded +, ++, or +++), crystals, and background material was also evaluated in each smear.

Results

The quantitative bacteriological examination carried out on the freshly voided urine (sample 1) showed that there was a significant difference in the number of viable bacteria per millilitre cultured from urines with pathogenic and non-pathogenic bacteria. In seven cases, pathogenic bacteria (citrobacter, entero-

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bacter or pseudomonas) were present. The number of bacteria in these specimens was 10^5/ml or more. In the other 33 specimens no pathogens were found and the bacterial count was less than 10^4/ml.

Bacterial growth took place within 24 hours in those urine samples kept at room temperature to which no preservatives had been added, and most of the urines without preservative became cloudy after three days because of the numerous bacteria present. In the male urines containing no or few bacteria, the cells were still morphologically intact up to the fifth day provided that there was no bacterial contamination from the environment. The urines from the tumour cases all contained blood, and the urines from males with cystitis and from all females contained mucus or protein. In these cases the multiplication of the bacteria was visible by the third day, and most cells had lost their normal morphology by the fifth day.

There was neither increased bacterial growth nor accelerated cellular degeneration in those cases with pathogenic bacteria. On the day of taking the specimen, seven of the cases showed significant bacterial contamination (graded + +/+ + +), and an additional 21 of the specimens without preservative contained numerous bacteria by the third day. In contrast to this there was no increase in bacterial contamination when thiomersal or ethyl alcohol were used. By the seventh day, 38 of the samples without preservative contained numerous bacteria as compared with an additional two of the cases treated with ethyl alcohol and none with thiomersal. One of the ethyl alcohol treated samples was overgrown with fungi on day 7.

In the freshly voided urine of the six patients with urothelial carcinomas, 46% (±4) of the cells were vital and most of these cells appeared to be malignant: but only 26% (±5) of the cells from cases with non-malignant diseases were vital. After three days almost all the cells in the cases with positive and negative cytology were dead.

There was a difference in the rate of degeneration of epithelial cells in samples with and without added preservative (Figure). In the urine without added preservative, 93% (±9) of the epithelial cells were intact on the day of taking the specimens, 54% (±15) on the third day, 28% (±6) on the fifth day, and 19% (±5) on the seventh day. In contrast to this, 81% (±7) of the cells in the samples treated with thiomersal and ethyl alcohol were intact on the third day, and by the seventh day 51% (±12) were still satisfactory for cytodiagnostic purposes. The difference in the percentages of intact cells when thiomersal and ethyl alcohol were used is not statistically significant.

The cell yield in the smears made from the ethyl alcohol-treated specimens was approximately one-

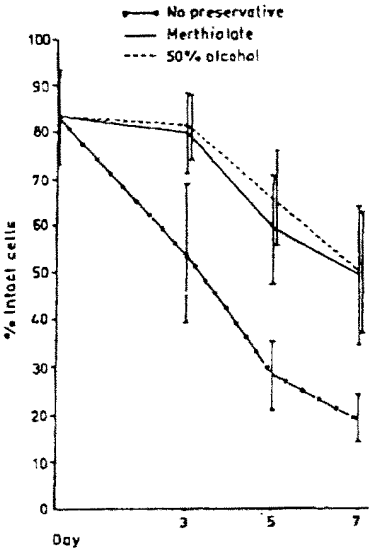

Figure. Preservative effect of thiomersal and 50% ethyl alcohol compared with untreated urine.

third of that obtained from the thiomersal treated specimens. Crystals were often present on the fifth and seventh days.

Discussion

Any increase in the interval between the time of collection of the sample and the preparation of the smear results in an exponential growth of bacteria in the urine if no preservative is added, and degenerative changes occur in the epithelial cells as a result of bacterial toxins. Thus, if there is little or no bacterial contamination (as frequently occurs in healthy males) intact cells can be harvested after three days, while in the majority of urine specimens from female controls (with heavy contamination by vaginal bacteria) the cells show degenerative changes after the same time interval (Beyer-Boon *et al.*, 1977). When thiomersal is added to freshly voided urine bacterial growth is stopped. Thiomersal has these advantages: its low toxicity, its high degree of solubility in water, and, of particular importance in cytology, its devitalising properties (Jamieson and Powell, 1931). Thiomersal has been

proved to be a potent bactericide for pathogenic bacteria (Powell and Jamieson, 1930) and effective against both anaerobic and aerobic bacteria. A high concentration of thiomersal is required, however, to stop all bacterial growth (Elliott *et al.*, 1940; Arden, 1956). When 50% ethyl alcohol is added to freshly voided urine, bacterial growth is slowed down in the majority of cases, but the efficacy of 50% ethyl alcohol as a safe bactericidal agent should be viewed with caution as some mycobacteria and fungi can still grow in specimens treated with this concentration of alcohol (Mitchell, 1977; Tucker, 1977). We also noted fungal proliferation in one alcohol-treated specimen. In the light of these observations, the use of thiomersal is recommended in preference to ethyl alcohol as a safer bactericide in the handling of infectious cytological material, such as sputum, especially if the technical procedures used involve blenders, which are particularly liable to produce potentially infectious aerosols Harris (1977). 50% ethyl alcohol prefixes the cells immediately. However, in specimens containing large quantities of protein the resultant precipitate makes the preparation of smears difficult. This problem does not occur in thiomersal treated specimens where the cells are not fixed until after the smear has been made. An additional drawback to using prefixed cells is the reduced adherence of the cells to the slides, which causes loss of cells and a greatly reduced yield (Beyer-Boon, 1977).

Our results show that when bacterial growth is prevented, although almost all cells are dead by the third day, over 80% are sufficiently well preserved to allow cytological evaluation. After this time there is a marked reduction in the percentage of intact cells which may be due partly to the effect of toxic substances released by dead cells (Mohr, 1969). Thiomersal and 50% ethyl alcohol are equally effective in preserving cells for the first three days and a delay of up to three days is therefore possible before cytological preparations need to be made. We prefer the use of thiomersal because it is cheaper, it does not increase the volume of the specimen, it does not affect cytopreparation, it permits a higher cell yield, and it is a safer bactericidal agent.

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Merthiolate = Thimerosal

Sterility testing: detection of fungi and yeasts in the presence of preservatives*

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Thirty-four strains of fungi and yeasts were studied for growth in six media in the presence of Merthiolate. All strains were killed in a 1 : 500,000 dilution; 1 : 5,000,000 was the maximum concentration that permitted recovery of all strains in Fluid Thioglycollate Medium (FTM). Fluid Sabouraud Medium (FSM) containing either sodium thioglycollate or sodium hydrosulphite was almost as effective. FTM with sodium hydrosulphite substituted for sodium thioglycollate and Bonnel–Raby medium were inferior to FTM, also to FSM. Rate of initiation of growth was reduced in the low concentration of 1 : 7,000,000 with maximum recovery at 21 days, whereas maximum recovery occurred in 7–10 days in the six control media which were similar in promoting growth. Phenylmercuric borate, phenol, benzethonium chloride and parabens were also fungicidal. Results are discussed relative to the discontinued use of FSM in the United States in official sterility testing and for the use of FTM in the test of mercurial-preserved biologics incubated at 20–25°C.

INTRODUCTION

In the early 1960's work on sterility testing procedures for detection of fungal and yeast contamination was initiated. At that time a large number of media were being employed in different countries. Due to lack of comparative data the use of one or more media could not be recommended in General Requirements for Biological Substances (WHO, 1960). In the first phase of this study Pittman & Feeley (1962) showed that Fluid Thioglycollate Medium (FTM) was only slightly less effective than Fluid Sabouraud Medium (FSM), Sabouraud Agar or Malt Agar in promoting growth of fungi and yeasts, but the

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rate of initiation of growth was slower. The temperature of incubation was more important than the type of medium. The optimum temperature was 22°C as compared with 16, 30 or 35°C.

In the second phase the influence of the presence of Merthiolate (thimerosal) and other preservatives commonly used in biological products on the growth of fungi and yeasts in several media was studied. FTM in general promoted better growth than FSM and equal or better growth than four other media which contained sulphydryl molecules. The results of both studies gave support to the recent omission of FSM as a required medium for the sterility test for pharmaceutical products (U.S. Pharmacopeia, 1970) and for biological products (U.S.P.H.S. Regulations, 1971b) as well as the specification that if a biologic contains a mercurial preservative FTM be used for the sterility test incubated at 20–25°C in place of Soybean–Casein Digest Medium. The latter does not contain a mercurial inhibitor. The results of the second phase of the study are reported in this paper.

MATERIALS AND METHODS

Media

Six media were employed: Fluid Thioglycollate Medium (FTM) and Fluid Sabouraud Medium (FSM) (U.S.P.H.S. Regulations, 1960–1971a); FSM plus 0·05% sodium thioglycollate (FSMT); FSM plus 0·05% sodium hydrosulphite (FSMH); FTM with 0·05% sodium hydrosulphite substituted for sodium thioglycollate (FTMBH); and Bonnel–Raby sodium hydrosulphite medium (BRHM) (WHO, 1960). For FTM and FSM, commercial, desiccated preparations were used. FTMBH and BRHM were prepared in the laboratory using the individual ingredients. Each medium distributed in 15 ml amounts in 20 × 150 mm test tubes (vessels) was prepared the day before use.

Cultures

The 34 fungal and yeast cultures employed are listed in Table 1. All except the last two were used in the first study (Pittman & Feeley, 1962). Although only four cultures, two yeast-like organisms, one *Penicillium* sp. and another unidentified member of the *Fungi imperfecti* were actually recovered from biologics, most of the collection represented organisms which could be regarded as potential airborne contaminants. Unfortunately more contaminants from biologics were not available.

Spore suspensions for inoculation of the test media were prepared and standardized as previously described by Pittman & Feeley (1962). In each experiment, the inoculum per vessel of medium was 1·0 ml of a 10^{-5} dilution prepared in 0·1% trypticase (Baltimore Biological Laboratories). It usually contained 10–100 spores as determined by plate count.

Preservatives

The preservatives and the concentrations studied are given in Table 2. Just prior to the spore inoculation, appropriate dilutions of the preservatives were added to the vessels containing the respective media. The range of the dilutions was selected to cover the minimum dilution that would not be fungicidal but this was not always attained.

Procedure

The day of an experiment appropriate dilutions of the preservatives were added to the one-day-old media. Vessels containing a preservative and control vessels without

TABLE 1. Identity and source of yeast and fungal cultures

Group	Number of strains	Identity	Source
Yeast and yeast-like	1	*Rhodotorula* sp.	Medium contaminant, 4°C
	1	*Candida guillermondi*	Heart-lung machine
	1	*Candida albicans*	Dr C. W. Emmons
	1	*Candida tropicalis*	Dr C. W. Emmons
	1	*Saccharomyces cerevisiae*	Dr C. W. Emmons
	2	Not identified	Dr J. H. Brewer
Phycomycetes	1	*Cunninghamella* sp.	Sterile glucose solution
	1	*Absidia corymbifera*	Dr C. W. Emmons
	1	*Mucor anguliosporus*	Dr C. W. Emmons
	1	*Rhizopus arrhizus*	Dr C. W. Emmons
Streptomycetes	4	*Streptomyces* sp.	Medium contaminant, 4°C
Fungi imperfecti	1	*Cephalosporium* sp.	Medium contaminant, 4°C
	7	*Penicillium* sp.	Medium contaminant, 4°C
	1	*Penicillium* sp.	Sterile horse serum, 4°C
	1	*Penicillium* sp.	Dr C. W. Emmons
	3	Not identified	Medium contaminants, 4°C
	1	*Aspergillus flavus*	Dr C. W. Emmons
	1	*Aspergillus terreus*	Dr C. W. Emmons
	1	*Paecilomyces variotii*	Dr C. W. Emmons
	1	*Scopulariopsis brevicaule*	Dr C. W. Emmons
	1	Not identified	Dr J. H. Brewer
	1	*Penicillium* sp.	Dr E. B. Seligmann Adenovirus Reference Vaccine

TABLE 2. Preservatives and range of concentrations employed

Preservative	Final concentrations (number of steps)
	Dilution
Merthiolate	0·5 – to 7 million (12)
Phenylmercuric borate (Merfen)	0·64 – to 3·04 million(5)
Phenol	3444 to 30,400 (6)
Benzethonium chloride	0·64 – to 3·04 million (5)
	mg/ml
Parabens*	(5)
methyl	0·09375 to 0·0197
propyl	0·0125 to 0·0026

* Parabens were used in fixed combinations of 7·5 parts methyl *p*-hydroxybenzoate to 1 part propyl *p*-hydroxybenzoate.

preservative were inoculated with the designated spore suspensions. The number of strains used in all experiments per medium ranged from 12 to 34. The vessels were incubated at 21° ± 1°C for 21 days. Each vessel was examined visually for growth on days 3, 7, 10, 14 and 21. If no growth had occurred by the end of 21 days, 1·0 ml was subcultured into FSM, also into FTM if a mercurial preservative were present. The subcultures were incubated for 21 days. This step was to determine if the failure of growth in the first culture was due to a fungistatic or fungicidal reaction.

The results were expressed as the cumulative percentage of tubes per medium per preservative which showed visible growth of all test organisms employed.

RESULTS

Merthiolate

A comparison of the growth of fungi and yeast in FTM, FSM and FSMT containing dilutions of Merthiolate ranging from 1 : 500,000 to 1 : 7,000,000 is given in Fig. 1. Growth occurred in 90–93% of the control vessels of the three media. Comparable percentages occurred in FTM containing 1 : 5,000,000 or less Merthiolate; with increasing concentrations to 1 : 500,000 the percentages of growth declined to near zero. Growth in

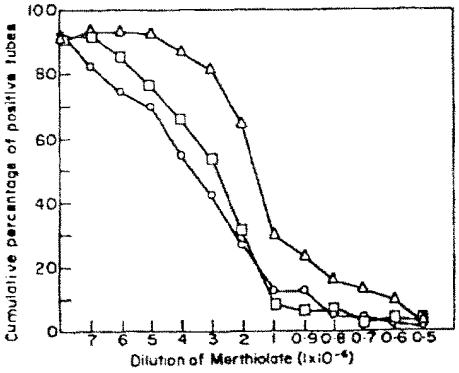

Fig. 1. Comparison of the recovery of fungi and yeasts in the presence of increasing concentrations of Merthiolate from 1 : 7,000,000 to 1 : 500,000 in FSM, FSMT and FTM. ○—○, Fluid Sabouraud; □—□, FSM + Na thioglycollate; △—△, Fluid Thioglycollate.

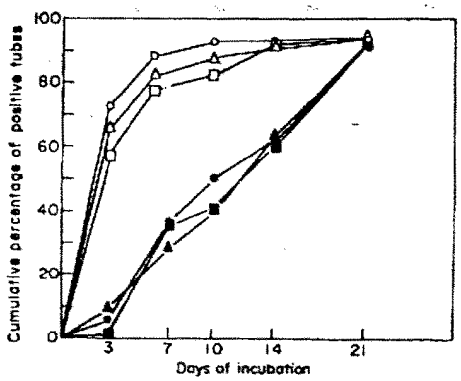

Fig. 2. Rate of initiation of growth of 23 strains of fungi and yeasts in FSM, FSMT and FTM in the absence or presence of 1 : 7,000,000 dilution of Merthiolate. ○—○, Fluid Sabouraud; ●—●, FSM + Merthiolate; □—□, FSM + Na thioglycollate; ■—■, FSM + Merthiolate; △—△, Fluid Thioglycollate; ▲—▲, FTM + Merthiolate.

FSM was somewhat less and the addition of sodium thioglycollate provided a slight advantage. Subcultures from all vessels without growth were negative. This indicated

TABLE 3. Percentage of the tubes with growth of fungi and yeasts in six media containing low concentrations of preservatives

Medium	Day	Controls*	Merthiolate 1 : 5,000,000	Phenyl-mercuric borate 1 : 3,040,000	Phenol 1 : 30,400	Benze-thonium chloride 1 : 3,040,000	Parabens†
		78 : 34	66 : 34	36 : 12	36 : 12	36 : 12	36 : 12
FTM	3	67	6	0	25	0	6
	7	94	32	0	31	6	19
	10	96	44	0	31	8	25
	14	97	70	0	31	14	28
	21	99	91	0	31	19	31
		88 : 34	76 : 34	36 : 12	36 : 12	36 : 12	36 : 12
FSM	3	78	3	0	8	0	6
	7	97	26	3	28	17	19
	10	99	38	6	31	17	25
	14	99	47	6	31	17	25
	21	100	67	6	31	17	25
		70 : 34	58 : 34	36 : 12		36 : 12	36 : 12
FSMT	3	67	0	3		3	11
	7	91	28	3		17	28
	10	93	38	8		22	28
	14	99	60	11		22	28
	21	100	90	14		22	31
		47 : 23	35 : 23	36 : 12		36 : 12	36 : 12
FSMH	3	77	3	11		6	11
	7	98	46	22		19	25
	10	98	51	22		19	28
	14	98	69	22		19	31
	21	100	86	28		19	31
		35 : 23	35 : 23				
FTMBH	3	66	0				
	7	97	6				
	10	100	14				
	14		17				
	21		17				
		12 : 12	12 : 12				
BRHM	3	92	0				
	7	92	0				
	10	92	8				
	14	92	8				
	21	100	8				

* Each test carried a control of the medium. Since all tests were not performed on the same day and some tests were repeated, the number of control tubes may exceed the number of cultures tested. Number of tubes : Number of cultures.

† The fixed mixture provided a final concentration of 0·0197 mg methyl *p*-hydroxybenzoate and 0·0026 mg propyl *p*-hydroxybenzoate per ml.

that the Merthiolate had been fungicidal and that a few strains were susceptible to as little as one part in 7 million and all were susceptible to 1 part in 500,000. These concentrations are much less than those employed in biologics.

Figure 2 shows that the rate of initiation of growth of 23 cultures in the presence of 1 : 7,000,000 dilution of Merthiolate was significantly lower than in the control vessels. In the controls, maximum recovery was reached in 10 days in FSM; in FSM containing sodium thioglycollate, there was a slight lag, with maximum recovery being at 14 days. In contrast, in the presence of this low concentration of Merthiolate only 40–50% of the vessels had visible growth at 10 days and maximum recovery was not attained until 21 days. The percentages of tubes with growth approached the percentages of the control vessels.

Merthiolate and other preservatives

Table 3 summarizes the results of several tests in which six media were employed. The number of strains tested per medium ranged from 12 to 34. Since strains may differ in susceptibility absolute comparisons cannot be made. Nevertheless, the results as a whole indicate that FTM was the best medium.

The growth-promoting properties of the six media (controls) were similar. Only at the three-day reading was there a suggestion of a small difference. High percentage of recovery in all media was attained in 7–10 days. However, in each of five media growth occurred in one more tube at 21 days than at 14 days. In the presence of 1 : 5,000,000 Merthiolate, FSMT was superior to FSM and comparable to FTM. FSMH approached FSMT in promotion of growth and was slightly superior to FSMT and FTM in the recovery of fungi from the 1 : 1,500,000 dilution of Merthiolate which was included in the test but not recorded in Table 3. On the other hand, the other two media which also contained sodium hydrosulphite, FTMBH and BRHM, were very inferior to the other four media.

The majority of the cultures were susceptible to phenylmercuric borate, phenol, benzethonium chloride and parabens in the highest dilutions studied. Each preservative had a relatively high fungicidal activity when compared with the concentrations employed in biologics.

DISCUSSION

A number of media have been used for the detection of bacterial and fungal contaminants in biologics (cited in WHO, 1960; Bonnel, 1950; Bonnel & Raby, 1957; Ježková, 1960; Desbordes & Ninard, 1961). In 1960 the U.S. Public Health Service Regulations prescribed the use of a mycotic sterility test in order to conform with International (WHO, 1960) and U.S. Pharmacopeia (1947) requirements. The Fluid Sabouraud Medium (FSM) formula as specified in the U.S. Pharmacopeia was used. **The high susceptibility of fungi and yeast to preservatives shown in our report and to Merthiolate by Ikuta, Arima & Kurokawa (1963) betokens evidence that safety of biologics had not been affected adversely by lack of a specific mycotic sterility test prior to 1960 and supports the 1971 deletion of FSM and the prescribed use of FTM for mercurial-preserved biologics.**

Scarcity of mycotic cultures isolated from biologics was noted when Pittman & Feeley (1962) were able to obtain only three such strains. One additional culture was obtained

for the present study. This attests to a very low recovery rate from biologics. Besides susceptibility to preservatives, two interrelated factors, namely, time of incubation and type of medium utilized, may possibly have played a role. In the absence of preservatives, Pittman & Feeley obtained a high rate of recovery within seven days, but 21 days were required for maximum recovery. In the presence of low concentrations of Merthiolate, we have found a marked lag period with a significant increase in percentage of tubes with growth after 14 days of incubation. Prior to the latest U.S. revisions (U.S. Pharmacopeia, 1970; U.S.P.H.S. Regulations, 1971b) 10 days of incubation was acceptable. The international requirements specified not less than 14 days. Current specifications for not less than 14 days fall short of 21 days which were required for maximum recovery in our study.

On the other hand, our results show fungicidal activity of Merthiolate in a concentration of 1 : 500,000 which is 25–50 times less than the concentrations usually employed in biologics. Even when a medium containing 0·05% sodium thioglycollate was employed, the concentration had to be reduced to 1 : 5,000,000 for near complete recovery. Therefore, from a practical standpoint, a minimum period of 14 days is reasonable for the mycotic sterility test. Of course a longer period should be used if the risk of fungal contamination is high.

FTM and FSM containing 0·05% sodium thioglycollate were almost equal in promoting growth of fungi in the presence of 1 : 5,000,000 Merthiolate. Growth in the anaerobic medium may have been influenced by the mixing of the tube content at each period of examination. Denmark (Scheibel & Bentzon, 1957) has used for the mycotic sterility test an enzyme digest of casein broth containing 0·05% sodium thioglycollate. It is of particular interest that Ikuta *et al.* (1963) found that better recovery of fungi in the presence of Merthiolate was obtained when a concentration of 0·15–0·20% sodium thioglycollate was added to FSM. They noted, however, that these concentrations may be too high for thioglycollate-sensitive organisms and that the addition of agar favoured the inactivation of the preservative.

The toxicity of thioglycollate for micro-organisms has not been clearly defined. One of the authors (M. P., unpublished) found that even fresh Alternate Thioglycollate Medium (Difco) inhibited the growth of both bacteria and fungi and that the addition of 0·075% agar neutralized this inhibition. She can find no justification for the use of this alternate medium at any time as a sterility test medium. Mossel & Beerens (1968) reported that sodium thioglycollate was inhibitory to the germination of spores of several species of *Clostridium* on solid agar medium. However, they made no comparison between each test medium with and without thioglycollate or with Fluid Thioglycollate Medium.

In the present study, FSM containing 0·05% sodium hydrosulphite (FSMH) was almost as good as FTM in promoting the growth of fungi in the presence of 1 : 5,000,000 Merthiolate, but the other two media containing this compound, FTMBT and BRHM, were very inferior (Table 3). In the absence of this preservative the latter media had excellent growth promoting properties.

The recovery of fungi in the presence of the other preservatives, phenylmercuric borate, phenol, benzethonium chloride and parabens in FTM, FSM, FSMT and FSMH, was very low. Subcultures indicated fungicidal activity. Whether or not this action was due to the preservatives *per se* or factors in the medium was not investigated.

Since the completion of our experimental work, Soybean–Casein Digest Medium (SCD) has replaced FSM for the sterility test incubated at 20–25°C (U.S. Pharmacopeia, 1970; U.S.P.H.S. Regulations, 1971b) except FTM is specified for this sterility test of

biologics which contains a mercurial preservative (U.S.P.H.S. Regulations, 1971b). We have made no experiments to determine the effect of mercurial neutralizers in SCD on the growth of fungi. The advantage of FTM for the lower temperature test will be largely for the detection of psychrophilic bacterial contaminants (Pittman, 1953). Bacteria are less susceptible to mercurial preservatives than fungi (Ikuta *et al.*, 1963). It is realized that FTM may fail to initiate the growth of a low incidence of contamination of aerobic spore-forming organisms and a rare occurring fungi (F. W. Bowman, unpublished). FTM is not satisfactory for recovery of aerobic organisms when they are entrapped in a membrane filter or other substances (Doyle, Mehrhof & Ernst, 1968). Bowman, White & Calhoun (1971) have shown that SCD is superior to FSM for the sterility test by membrane filtration.

From a practical standpoint FTM seems to be the medium of choice for the general sterility test incubated at 30–32°C and for the sterility test incubated at 20–25°C if a mercurial preservative is present. However, no medium is capable of detecting the presence of all possible contaminants. The present formula, except for a reduction of the amount of L-cystine from 0·75 g/l to 0·5 g/l in 1955, has been in use in the United States since the mid 1940's. Differences in growth-promoting properties of different products and of lots of the same product of FTM do occur. Current studies on ingredient specifications by the U.S. Pharmacopeia Advisory Panel on Microbial Attributes and Procedures may provide a better formula for the detection of fungi and bacterial as well as consistency between products.

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Prevention of Surface Bacterial Contamination of Donor Corneas

Kenneth N. Goldman, MD; Ysolina Centifanto, PhD; Herbert E. Kaufman, MD; Thomas E. Slappey

• A simple method has been developed to reduce contamination in postmortem donor human eyes in anticipation of corneal transplantation. In vivo investigation of albino rabbits demonstrates that vigorous saline solution irrigation is extremely effective in decreasing the surface bacterial counts of the postmortem eye. In vitro and in vivo studies show that Neosporin kills bacteria at room temperature and further show that a tenfold increase in the thimerosal concentration of the Neosporin will kill fungus. Postmortem eyes contaminated by pathogenic organisms can be effectively cleaned by a combination of saline solution irrigation and the new Neosporin-thimerosal solution. No substantial damage of the donor tissue was noted by scanning electron microscopy. Human eyes cultured before this procedure were all contaminated, but after cleansing and immersion, no bacterial or fungal growth occurred.

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After any intraocular surgical procedure, the occurrence of endophthalmitis is a devastating complication. In corneal transplantation, there is one additional source of possible bacterial contamination of the eye, ie, the corneal donor button itself. To avoid this possible route of infection, we have investigated methods to provide for surface sterilization of the donor tissue whether it be subsequently stored in a moist chamber or in McCarey-Kaufman medium.

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MATERIALS AND METHODS

Pathogenic Organisms

Pseudomonas aeruginosa, Staphylococcus epidermidis, S aureus, Proteus mirabilis, Streptococcus viridans, and *Escherichia coli* bacterial strains were used as bacterial test organisms. Stock suspensions were grown overnight in trypticase soy broth. The suspensions were diluted in phosphate buffered saline solution (PBS) (pH 7.2). Several log dilutions were made, and 0.2 ml of these dilutions were plated on blood agar plates to quantify the inoculum. The concentration of the final bacterial inoculum was approximately 10^6 to 10^7 bacteria per milliliter. The fungus *Candida albicans* was initially grown in Sabouraud's agar in a 60-ml bottle, kept refrigerated, and used as the source of *Candida* in this investigation. The *Candida* inoculum was quantified in the same manner as that for the bacteria.

Drugs

The ophthalmic solution we used (Neosporin) contains polymyxin B sulfate (Aerosporin) (5,000 units), neomycin sulfate (2.5 mg), gramicidin (0.025 mg), 0.5% ethyl alcohol, and 0.001% thimerosal per milliliter; the mixture was selected because it is most commonly used by eye banks. To increase the concentration of thimerosal in the Neosporin solution, a thimerosal solution was made of 10 mg/ml in twice-distilled water. This stock solution was then filtered through a 0.45 mμ Millipore filter. The stock was kept refrigerated and was prepared fresh at one-month intervals. An aliquot of 0.1 ml of this solution was then added to 10 ml of the Neosporin solution to bring the final concentration of thimerosal to 0.01%.

Animal Experiments

Two 2- to 3-kg albino rabbits were used for in vivo experiments for each concentration of each organism tested.

The rabbit was killed with a lethal injection of barbital sodium. Immediately following death, 0.1 ml of a quantitated bacterial suspension was placed on the dome of the cornea. The lids were closed and gently massaged to distribute the bacteria. The lids were then sewn closed with a double-arm 4-0, black, silk, mattress suture. After an hour's inoculation in the conjunctival sac of the killed animal, the lids were opened and the eye was enucleated using sterile technique. The eyes were then subjected to different sterilizing preparations and programs (to be discussed with each individual experiment), after which the corneas were cultured.

Human Experiments

Twenty human corneas were cultured for bacteria and fungi when initially obtained. They were then recultured after vigorous irrigation and immersion of the intact globe for five minutes in Neosporin with 0.01% thimerosal. Cultures were done by thoroughly swabbing the cornea and scleral rim with a thioglycollate-moistened swab, putting the swab in 1 ml of thioglycollate broth and placing 0.2 ml on each of blood agar and Sabouraud's agar plates.

Cornea Culture Technique

To culture the corneas and quantitate bacterial contamination, the cornea was excised from the eye using sterile technique. The anterior chamber was entered with a dissecting blade and then using curved corneal scissors, the whole cornea was excised. The cornea was then placed in 1 ml of thioglycollate broth to neutralize any remaining thimerosal on the cornea.

Following this, 0.2 ml of thioglycollate was placed in blood agar plates for quantitation of the corneal bacterial count.

Experiments

Experiment 1.—Irrigation.—On four separate occasions, an animal was killed and an inoculum of quantitated *Pseudomonas* was placed in the conjunctival sac of both eyes and left for one hour. The paired eyes were then enucleated in sterile fashion and subjected to one of two procedures. One eye of the pair was vigorously irrigated with a jet of 20 ml of normal saline solution using a syringe and 20-gauge hypodermic needle. The eye was then fully immersed in 10 ml of normal saline solution. The other eye was not irrigated, but was directly immersed in 10 ml of normal saline solution. After 30 minutes, the corneas were excised and cultured.

Experiment 2.—Neosporin Effect at Room Temperature (25 °C).—Using a tuberculin syringe, 0.1 ml of a quantitated pathogen suspension was injected into 1 ml of Neosporin solution and likewise into 1 ml of the prepared PHS-thimerosal-alcohol solution (0.01% thimerosal and 0.05% alcohol) and left at room temperature. At the appropriate times, 0.1 ml of each mixture was inoculated into 0.9 ml of thioglycollate broth (this neutralized thimerosal). Then, 0.2 ml of this broth was plated onto individual blood agar plates. To prevent a Neosporin carry-over effect (a "prozone") in the case of the *S epidermidis*, several dilutions of the 0.2 ml of inoculated thioglycollate broth were made, and each dilution was plated out. The figures in Table 1 represent a 1:100 dilution. The carry-over effect of the Neosporin is negligible. The three pathogens used in this experiment were inocula of 10^6 bacteria per milliliter of *Proteus*, *S epidermidis*, and *Candida*.

Experiment 3.—Combined Irrigation and Neosporin.—An in vivo model of a donor eye setting was prepared. Briefly, the animals were killed, large quantities of a specific pathogen were inoculated into the conjunctival sac and left for one hour, and the globes were enucleated (as in experiment 1). One eye of a pair was irrigated by a strong jet of normal saline solution from a 20-gauge hypodermic needle. The eye was then immersed for five minutes in 10 ml of the Neosporin 0.01% thimerosal.

The other eye was not treated or irrigated but was immediately immersed in 10 ml of normal saline solution for five minutes. The corneas of both eyes were excised and cultured. The 10 ml saline depository of the untreated (control) eye was also cultured and quantitated to establish a control bacteria count for the globes (after enucleation) themselves.

Experiment 4.—Morphologic Examination of Treated Eyes.—The eyes of an albino rabbit that weighed 2 to 3 kg were enucleated and then subjected to the treatment of irrigation and Neosporin-thimerosal solution bath for five minutes (see experiment 3). The endothelium and epithelium were then examined by scanning electron microscopy.

Tissue for scanning electron microscopy was first fixed in 2.5% glutaraldehyde in Millonig buffer for one hour. The tissue was then rinsed in buffer and postfixed in 1% osmium tetroxide that was also in Millonig buffer for 90 minutes. Both fixations were done in cold temperatures.

After fixation, the tissue was dehydrated in increasing concentrations of ethanol. Final dehydration was performed in an apparatus with carbon dioxide.

The tissue was then coated with palladium-gold and viewed with an electron microscope.

Table 1.—Neosporin Effect at Room Temperature on *Staphylococcus epidermidis**

Time, min	Average Counts Organism per Blood Agar Plate: Neosporin (With Preservatives)	Average Counts Organism per Blood Agar Plate: 0.01% Thimerosal + 0.5% Ethyl Alcohol
5	1,147	TNTC†
10	586	TNTC
15	755	TNTC

*Inoculum, 10^6 bacteria per milliliter; 30-minute percent kill, 99.9%.
†TNTC, too numerous to count.

Table 2.—Effect of Irrigation on Bacterial Counts

Initial Pseudomonas Inoculum, Bacteria per Milliliter	Final Bacterial Counts of Excised Cornea, Average Bacteria Count per Plate: Irrigation of Globe	Final Bacterial Counts of Excised Cornea, Average Bacteria Count per Plate: No Irrigation
4.05×10^6	0	Confluent
2.20×10^6	15	288
1.70×10^6	1	50
6.05×10^6	1	15

Table 3.—Neosporin Effect at Room Temperature on *Proteus**

Time, min	Average Counts Organism per Blood Agar Plate: Neosporin (With Preservatives)	Average Counts Organism per Blood Agar Plate: 0.01% Thimerosal + 0.5% Ethyl Alcohol
0	TNTC†	TNTC
15	261	TNTC
30	135	TNTC

*Inoculum, 10^6 bacteria per milliliter; 30-minute percent kill, 92.4%.
†TNTC, too numerous to count.

Table 4.—Neosporin Effect at Room Temperature on *Candida**

Time, min	Average Counts Organism per Blood Agar Plate: Neosporin (With Preservatives)	Average Counts Organism per Blood Agar Plate: 0.01% Thimerosal + 0.5% Ethyl Alcohol
15	978	370
30	590	133
45	397	42

*Inoculum, 10^6 fungi per milliliter; 30-minute percent kill of 0.01% thimerosal, 83%; 45-minute percent kill of 0.01% thimerosal, 97.8%.

RESULTS

Animal Studies

Experiment 1.—Vigorous irrigation alone can substantially clear bacteria from a contaminated globe (Table 2).

Experiment 2.—At room temperature, Neosporin is an effective bactericidal agent. At room temperature, a tenfold increased concentration of thimerosal is an effective fungicidal agent, whereas Neosporin alone is not. (Using a *t* test and the kill rates determined by measuring the slope of the line best fitting the data, the 0.01% thimerosal was significantly more effective against *Candida*, with a confidence of >95%) (Tables 1, 3, and 4).

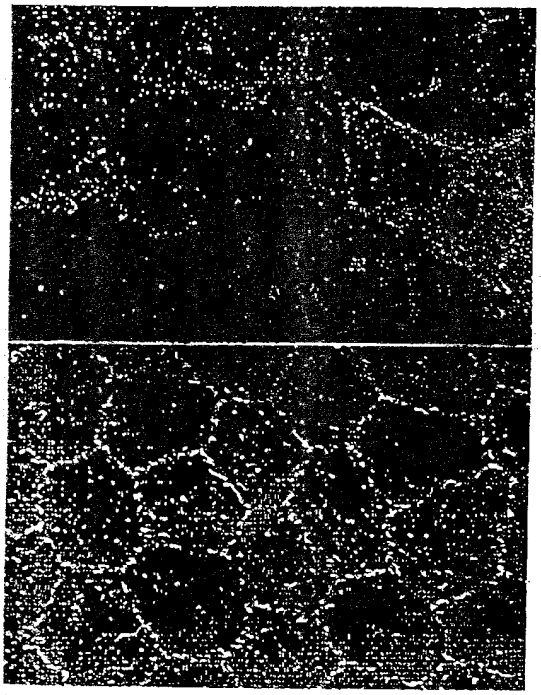
Experiment 3.—The combination of forceful jet stream irrigation of the globe and five minutes immersion into Neosporin-0.01% thimerosal solution gave a kill rate of more than 95% of bacterial contamination despite a massive inocula (Table 5).

Experiment 4.—No notable damage

Table 5.—Effect of Irrigation and Neosporin-0.01% Thimerosal

Organism	*Staphylococcus epidermalis*	*S aureus*	*Proteus*	*Escherichia coli*	*Pseudomonas*	*Streptococcus*	*Candida*
Initial inoculum into conjunctival sac	1.0×10^7	1.05×10^8	3.5×10^7	2.8×10^8	6.0×10^8	3.1×10^8	2.0×10^8
Organisms recovered from treated cornea (irrigation and neosporin-0.01% thimerosal)	395	80	85	842	245	250	180
Organisms recovered from untreated cornea	390	4,362	1,250	1,715	2,460	2,175	36
Organisms in 10 ml saline depository of untreated cornea	8,400	9,870	58,400	TNTC*	42,550	74,200	5,450
Total organisms from control globe (untreated)	8,790	14,332	60,650	TNTC	45,010	76,375	5,486
Percent kill with treatment							
Compared with initial inoculum	99.1	99.5	99.8	99.9	99.9	99.8	99.9
Compared with control globe	95.5	99.9	99.8	...	99.5	99.7	99.7

*TNTC, too numerous to count.



Rabbit donor cornea after vigorous irrigation and five-minute immersion into Neosporin-0.01% thimerosal solution showing essentially normal epithelium with no damage from thimerosal. Top, Epithelium (×1,750). Bottom, Endothelium (×1,500).

or morphologic change was observed in corneas treated with irrigation and immersion into Neosporin-0.01% thimerosal solution (Figure).

Human Studies

Experiment 5.—Swab cultures taken before cleansing were all positive for bacterial contamination. Quantitation was not attempted since growth was often profuse. *Staphylococcus pyogenes* and *S epidermis* were most common, but *S aureus*, *Streptococcus* sp, *Pseudomonas* sp, and occasionally, *Proteus* sp were seen. Following the cleansing procedure, all cultures for bacteria and fungi were negative.

COMMENT

This investigation was undertaken to minimize the risk of the donor corneal button being a possible source of contamination in corneal transplantation. Other investigators have reported that the surface of 50% to 100% of all donor eyes enucleated is bacterially contaminated.[1-3] Numerous methods have been suggested for decreasing bacterial counts in donor tissue. Neosporin has long been used for this purpose and has been suggested by numerous authors to be effective in diminishing the bacterial contamination of the donor eye.[3-6] Mechanical clearing of bacteria both by irrigation[3,4] and by removal of the donor corneal epithelium[2] have also been suggested as adjuncts in preparing bacteria-free donor tissue. In the present study, we have attempted to quantitate the effects of both mechanical and pharmacologic clearing of pathogens. By this approach we have tried to develop a simple, safe, and rational method of decreasing pathogen contamination of donor tissue.

The results of experiment 1 show

that there is a notable effect of vigorous mechanical irrigation alone. It may very well be that irrigation and washing of the globe is the single most important factor in diminishing bacterial contamination.

The purpose of experiment 2 was to observe the relative effectiveness of Neosporin with its normal preservative constitution (0.001% thimerosal and 0.5% alcohol) and a solution of increased concentration of thimerosal (0.01%) without antibiotic as bacteriocidal and fungicidal agents. The experiment was designed to prevent any carry over of the Neosporin onto the culture plates. The in vitro study demonstrated that Neosporin clearly had a bacteriocidal effect at room temperature. However, *Candida sp* was not cleared by Neosporin with its present preservative level (0.001% thimerosal, 0.5% alcohol). Therefore the increased concentration thimerosal solution was prepared and tested primarily to observe its effect on fungus. Topical thimerosal of up to 2% concentration has no deleterious effects on corneal epithelium or endothelium.[3] The results show that the increased thimerosal concentration of 0.01% indeed had fungicidal properties well in excess of Neosporin alone.

Taking cognizance of the bacteriocidal effect of Neosporin and the fungicidal effect of 0.01% thimerosal, experiment 3 was devised to test a method of producing bacteria-free corneas by using the combined actions of saline solution irrigation and immersion into a Neosporin-0.01% thimerosal solution. In experiment 3, an in vivo study was designed to simulate conditions found when obtaining human donor material. A very large bacterial inoculum was used in this experiment, far in excess of what may be found in any inapparent eye infection. The choice of bacteria used was based on those bacteria considered to be the most frequent pathogens of donor eyes.[2] A combination of jet-stream saline solution irrigation and immersion into a Neosporin-0.01% thimerosal solution, was found to be highly effective in clearing of the pathogens. However, the inocula used were massive and would likely occur in the human situation only in the presence of frank, obvious infection. Despite the large numbers of organisms in the inocula and those infecting the globes, the method used herein of clearing pathogens was 90% effective in most of the tests, and the method was never below 95% effective.

The results of experiment 4 show that the integrity of donor corneal tissue (endothelium and epithelium) is maintained with the proposed regimen of sterilization. This is in agreement with another report[3] in which concentrations of thimerosal up to 2% had no harmful effect on the cornea as shown by light microscopy; however, neither that study nor the present study utilized transmission electron microscopy on the corneas.

There is now evidence that vigorous saline solution irrigation of the globe—the importance of which must be underscored—and the immersion of the globe in a solution of Neosporin with increased thimerosal concentration—which has potent bacteriocidal and fungicidal properties at room temperature—seems effective in cleansing the surface of donor corneal tissue with the concentrations of organisms that might reasonably be expected. This procedure is now being used by the North Florida Eye Bank. Studies of 20 donor eyes showed contamination before this cleansing procedure, but all cultures for bacteria and fungi were negative afterward.

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CONTACT LENSES

Evaluating the Preservative Effectiveness of RGP Lens Care Solutions

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We examined the antimicrobial preservative efficacy of nine rigid gas permeable (RGP) contact lens care solutions by challenging them in a laboratory study with both standard test organisms and preservative-resistant strains. Solutions containing polyhexamethylene biguanide (PHMB), such as Boston Advance (15 ppm) and a Boston Advance Enhanced Comfort Formula (5 ppm PHMB + 30 ppm chlorhexidine gluconate [CHG]) were most effective at rapidly killing vegetative cells, killing all bacteria and yeast by 6 hours. Boston Advance only slightly reduced the number of *Aspergillus niger* spores during the 28 day study, but Boston Advance Enhanced Comfort Formula reduced the spores by almost 3 logs by 14 days and by 4 logs by 21 days. Thimerosal-preserved Soaclens only reduced *Staphylococcus aureus* by 1 log at 6 hours, but at 1 day all tested organisms including *S. aureus* and *A. niger* were killed. Barnes Hind Gas Permeable Wetting and Soaking Solution, containing 50 ppm CHG, had little effect on adapted *Serratia marcescens* or *Pseudomonas cepacia* during the 28 day study. Allergan Wet-N-Soak Plus, containing 30 ppm benzalkonium chloride (BAK), was also unable to kill adapted *S. marcescens* or *P. cepacia*. CIBA Vision Premus (40 ppm BAK) was unable to kill adapted *S. marcescens*. Alcon Opti-Free, with 50 ppm polyquaternium-1 (polyquad), did not kill *P. cepacia*. Sherman Stay-Wet 3, containing 0.1% benzyl alcohol, was not effective against *S. marcescens* (adapted or unadapted), *P. cepacia*, or *A. niger*. Sherman DeStat 3, which contains 0.1% benzyl alcohol plus surfactants and five times the concentration of EDTA as in Stay-Wet 3, was able to kill all the vegetative cells by 7 days but did not significantly reduce *A. niger*.

Introduction

The most serious complication associated with contact lens use is microbial keratitis.[1] In a study from one major referral center, 70% of all recently infected corneal ulcers were from contact lens wearers.[2] Microbial contamination of preserved multiuse lens care products used for disinfecting lenses can represent the source of the infecting organisms.[3-5] Studies of patients with contact lens associated corneal ulcers also have demonstrated contamination of lens care systems.[4] Improper hygienic practices and subsequent failure of some preservative systems were found to be the primary cause of contamination of lens care systems.[6]

Recent investigations have demonstrated that isolates of *Pseudomonas aeruginosa* from corneal ulcers and contaminated saline solutions of a given patient were of the same strain.[4] *Serratia marcescens*, which is currently the etiologic agent in approximately 5 to 10% of gram-negative corneal ulcers, has also been found in contact lens solutions of patients with keratitis.[7,8] *S. marcescens* is the organism most frequently isolated in preserved ophthalmic solutions.[4]

This study was designed to compare the antimicrobial capabilities of a number of rigid gas permeable (RGP) lens care solutions by employing standard laboratory methods for the assessment of the preservative effectiveness of such solutions. The United States Pharmacopeia (USP)[9] and European Pharmacopeia (EP)[10] guidelines for determining the efficacy of chemical disinfection were followed; however, in addition to the organisms required by the USP and EP, *Pseudomonas*

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TABLE I Lens care products and primary preservatives

Lens care product		Primary preservatives*
Allergen Wet-N-Soak Plus	Lot 06T11	0.003% BAK
CIBA Vision Premus	Lot B0012105	0.004% BAK
Sherman DeStat 3	Lot 1112	0.1% benzyl alcohol
Sherman Stay-Wet 3	Lot 1672	0.1% benzyl alcohol
Barnes Hind Gas Permeable Wetting & Soaking Solution	Lot 20323	0.005% CHG
Polymer Technology Boston Advance	Lot GA264A	0.0015% PHMB
Polymer Technology Boston Advance Enhanced Comfort Formula	Lot GC211X	0.0005% PHMB + 0.003% CHG
Alcon Opti-Free for Hard Lenses	Lot G-02A	0.005% polyquad
Alcon Soaclens	Lot 1KPL	0.004% thimerosal

*All the solutions also contain EDTA at 0.1% or less except DeStat 3, which contains 0.5%.
BAK = benzalkonium chloride; CHG = chlorhexidine gluconate; PHMB = polyhexamethylene biguanide.

(*Burkholderia*) *cepacia* ATCC 25416 and *S. marcescens* 48 (a product isolate) were included as challenge organisms. *P. cepacia* is a highly resistant organism that has been isolated from a variety of health care products containing various preservatives. *S. marcescens* 48 is a lens care product isolate, and cultures of *S. marcescens* 48 that had been adapted to chlorhexidine gluconate (CHG) also were included in this study. The adaptation of *S. marcescens* to CHG by growth in sub-lethal concentrations in saline has been shown to lead to eightfold higher resistance than that seen in unadapted cells.[1] Adaptation to CHG also allowed survival of *S. marcescens* in higher concentrations of other antimicrobial agents, including benzalkonium chloride (BAK) and polyquaternium-1 (polyquad), than occurred with unadapted cells.[1]

Materials and methods

Solutions Tested: The tested solutions and their primary preservatives are shown in Table I. All the solutions also contain EDTA at 0.1% or less, except Destat 3, which contains 0.5%. In addition, Stay-Wet 3 contains 0.05% sorbic acid, and DeStat 3 contains unspecified surfactants.

Test Microorganisms: In addition to the required organisms specified by the European Pharmacopeia (EP)[10] and U.S. Pharmacopeia (USP) XXII[11], *P. cepacia* ATCC 25416, *S. marcescens* 48 (an ophthalmic product isolate), and *S. marcescens* 48 adapted to CHG were used.

Working cultures were kept on trypticase soy agar (Difco Laboratories, Detroit, MI). Suspensions of 1×10^7 to 1×10^8 cfu/mL of the following microorganisms were prepared in 0.85% saline according to USPXXII guidelines: *P. aeruginosa* ATCC 9027, *Staphylococcus aureus* ATCC 6538, *Aspergillus niger* ATCC 19606, *Candida albicans* ATCC 10231, *S. marcescens* 48, unadapted and adapted to CHG, *Escherichia coli* ATCC 8739, and *P. cepacia* ATCC 25416. CHG-adapted *S. marcescens* 48 was prepared by overnight growth in 1 g/L trypticase soy broth (Difco Laboratories) containing 10% v/v Barnes Hind Gas Permeable Wetting and Soaking Solution.

Preservative Efficacy Assay: Twenty milliliter samples of each product were inoculated with 0.1 mL of the different microbial suspensions to obtain challenge concentrations of between 1×10^3 and 1×10^4 cfu/mL. The inoculated products were maintained at 22 ± 2°C for the duration of the study.

The initial inoculum and number of viable microorganisms contained in the test samples were determined after 6 hours and after 1, 2, 7, 14, 21, and 28 days of microbial challenge by duplicate platings onto Letheen agar after dilution in neutralizing broth (Letheen broth; Difco Laboratories).

The results are expressed as the average number of cfu/mL of test sample for each lens care product.

Results

Results for preservative efficacy tests of the different solutions are shown in Table II.

Thimerosal (10 ppm in Alcon Soaclens) killed all organisms within 24 hours but not in 6 hours. The number of *S. aureus* decreased by only 1 log at 6 hours, *S. marcescens* by about 2 logs, and *E. coli* by 5 logs. *S. marcescens* adapted to CHG was killed at 6 hours.

The polyhexamethylene biguanide (PHMB)-containing solutions (Boston Advance Enhanced Comfort Formula and Boston Advance) were similar to thimerosal except for a slower kill of *A. niger*. A 1 log reduction of *A. niger* was obtained with Boston Advance by 28 days, whereas there was a 4 log reduction by 21 days with the Boston Advance Enhanced Comfort Formula. In contrast with the thimerosal-preserved formulation, both the Boston Advance Enhanced Comfort Formula and Boston Advance killed all the bacteria and yeast by 6 hours.

The BAK preserved systems (Allergan Wet-N-Soak Plus with 30 ppm and CIBA Vision Premus with 40 ppm) were ineffective against adapted *S. marcescens*. Also, Allergan Wet-N-Soak Plus, with the lower BAK concentration of the two (30 ppm) was ineffective against *P. cepacia*.

The CHG-preserved system (Barnes Hind Gas Permeable Wetting and Soaking Solution with 50 ppm CHG) was ineffective against adapted *S. marcescens* and *P. cepacia*.

Alcon's polyquad-preserved Optifree lowered *A. niger* spore counts 3 logs by 28 days and was ineffective against *P. cepacia*. DeStat 3 (benzyl alcohol-preserved) was ineffective against *A. niger* and was slow killing *C. albicans*. Stay-Wet 3, also benzyl alcohol-preserved but with less EDTA and no surfactants, was unable to kill most of the test strains by 28 days, only killing *P. aeruginosa*, *S. aureus*, and *E. coli*.

Discussion

Whereas most studies of microbial keratitis affecting contact lens wearers have involved daily wear or extended wear

TABLE II Efficacy of RGP care systems preservatives

Formulation	Organism	Inoculum	Viability (cfu/mL) 6 hour	1 day	2 days	7 days	14 days	21 days	28 days
Allergan	1. *P. aeruginosa* 9027	2.6E6	<10	<10	<10	<10	<10	<10	<10
Wet-N-Soak	2. *S.aureus* 6538	3.0E6	<10	<10	<10	<10	<10	<10	<10
Plus	3. *A. niger* 19606	4.0E6	1.7E4	<10	1.0E1	<10	<10	<10	<10
	4. *C. albicans* 10231	4.6E5	<10	<10	<10	<10	<10	<10	<10
Lot 06T11	5. *S. marcescens* 48	3.0E6	<10	<10	<10	<10	<10	<10	<10
(Exp. 1-94)	6. Adapted *S. marcescens*	1.8E6	1.8E6	>1.0E6	>1.0E6	8.4E5	4.7E5	3.8E5	2.1E5
	7. *E. coli* 8739	3.2E6	<10	<10	<10	<10	<10	<10	<10
	8. *P. cepacia* 25416	3.1E6	4.0E4	4.4E4	9.7E4	>1.0E6	>1.0E6	>1.0E6	>1.0E6
CIBA Vision	1. *P. aeruginosa* 9027	2.1E6	<10	<10	<10	<10	<10	<10	<10
Premus	2. *S. aureus* 6538	1.1E6	<10	<10	<10	<10	<10	<10	<10
	3. *A. niger* 19606	9.2E5	2.0E1	<10	2.0E1	<10	<10	<10	<10
Lot B0012105	4. *C. albicans* 10231	4.8E5	<10	<10	<10	<10	<10	<10	<10
(Exp. 4-94)	5. *S. marcescens* 48	2.3E6	<10	<10	<10	<10	<10	<10	<10
	6. Adapted *S. marcescens*	6.0E6	1.4E5	9.5E5	>1.0E6	3.3E5	6.4E4	4.8E4	9.8E4
	7. *E. coli* 8739	1.7E6	<10	<10	<10	<10	<10	<10	<10
	8. *P. cepacia* 25416	1.1E6	<10	<10	<10	<10	<10	<10	<10
Sherman	1. *P. aeruginosa* 9027	2.6E6	<10	<10	<10	<10	<10	<10	<10
DeStat 3	2. *S. aureus* 6538	3.0E6	<10	<10	<10	<10	<10	<10	<10
	3. *A. niger* 19606	4.0E6	1.0E6	6.2E5	5.2E5	2.7E5	3.1E5	3.3E5	2.5E5
Lot 1112	4. *C. albicans* 10231	4.6E5	3.9E5	1.8E5	1.8E4	<10	<10	<10	<10
(Exp. 4-95)	5. *S. marcescens* 48	3.0E6	8.1E5	1.0E1	<10	<10	<10	<10	<10
	6. Adapted *S. marcescens*	1.8E6	4.4E5	<10	<10	<10	<10	<10	<10
	7. *E. coli* 8739	3.2E6	<10	<10	<10	<10	<10	<10	<10
	8. *P.cepacia* 25416	3.1E6	6.8E5	3.0E1	<10	<10	<10	<10	<10
Sherman	1. *P. aeruginosa* 9027	2.1E6	<10	<10	<10	<10	<10	<10	<10
Stay-Wet 3	2. *S. aureus* 6538	1.1E6	1.2E5	1.1E5	6.2E4	<10	<10	<10	<10
	3. *A. niger* 19606	9.2E5	3.3E5	4.1E5	3.1E5	2.5E5	2.5E5	2.0E5	7.4E4
Lot 1672	4. *C. albicans* 10231	4.8E5	3.6E5	3.7E5	3.9E5	9.2E4	6.0E3	4.0E1	2.0E1
(Exp. 6-95)	5. *S. marcescens* 48	2.3E6	1.8E5	5.3E4	8.0E3	8.4E4	>1.0E6	>1.0E6	>1.0E6
	6. Adapted *S. marcescens*	6.0E6	3.4E5	4.2E4	5.4E4	3.1E5	>1.0E6	>1.0E6	>1.0E6
	7. *E. coli* 8739	1.7E6	5.7E5	6.6E4	5.9E2	<10	<10	<10	<10
	8. *P.cepacia* 25416	1.1E6	9.8E5	9.8E5	1.1E6	>1.0E6	>1.0E6	>1.0E6	>1.0E6
Barnes Hind	1. *P. aeruginosa* 9027	2.6E6	<10	<10	<10	<10	<10	<10	<10
Gas Permeable	2. *S. aureus* 6538	3.0E6	<10	<10	<10	<10	<10	<10	<10
Wetting and	3. *A. niger* 19606	4.0E6	7.6E5	4.0E3	6.4E2	3.0E1	<10	<10	<10
Soaking	4. *C. albicans* 10231	4.6E5	<10	<10	<10	<10	<10	<10	<10
	5. *S. marcescens* 48	3.0E6	<10	<10	<10	<10	<10	<10	<10
Lot 20323	6. Adapted *S. marcescens*	1.8E6	8.9E5	>1.0E6	>1.0E6	2.5E5	3.1E5	1.1E6	4.0E5
(Exp. 4-94)	7. *E. coli* 8739	3.2E6	<10	<10	<10	<10	<10	<10	<10
	8. *P. cepacia* 25416	3.1E6	3.0E5	1.0E6	>1.0E6	>1.0E6	>1.0E6	>1.0E6	>1.0E6
PTC Boston	1. *P. aeruginosa* 9027	2.6E6	<10	<10	<10	<10	<10	<10	<10
Advance	2. *S. aureus* 6538	3.0E6	<10	<10	<10	<10	<10	<10	<10
	3. *A. niger* 19606	4.0E6	7.8E5	6.6E5	5.5E5	3.4E5	3.2E5	4.9E5	3.5E5
Lot GA264A	4. *C. albicans* 10231	4.6E5	<10	<10	<10	<10	<10	<10	<10
(Exp. 1-94)	5. *S. marcescens* 48	3.0E6	<10	<10	<10	<10	<10	<10	<10
	6. Adapted *S. marcescens*	1.8E6	<10	<10	<10	<10	<10	<10	<10
	7. *E. coli* 8739	3.2E6	<10	<10	<10	<10	<10	<10	<10
	8. *P.cepacia* 25416	3.1E6	<10	<10	<10	<10	<10	<10	<10
PTC Boston	1. *P. aeruginosa* 9027	2.1E6	<10	<10	<10	<10	<10	<10	<10
Advance	2. *S. aureus* 6538	1.1E6	<10	<10	<10	<10	<10	<10	<10
Enhanced	3. *A. niger* 19606	9.2E5	2.9E5	3.8E5	1.7E5	1.4E4	1.3E3	8.0E1	8.0E1
Comfort	4. *C. albicans* 10231	4.8E5	<10	<10	<10	<10	<10	<10	<10
Formula	5. *S. marcescens* 48	2.3E6	<10	<10	<10	<10	<10	<10	<10
	6. Adapted *S. marcescens*	6.0E6	<10	<10	<10	<10	<10	<10	<10
Lot GC211X	7. *E. coli* 8739	1.7E6	<10	<10	<10	<10	<10	<10	<10
	8. *P. cepacia* 25416	1.1E6	<10	<10	1.0E1	<10	<10	<10	<10
Alcon	1. *P. aeruginosa* 9027	2.6E6	<10	<10	<10	<10	<10	<10	<10
Opti-Free	2. *S. aureus* 6538	3.0E6	<10	<10	<10	<10	<10	<10	<10
	3. *A. niger* 19606	4.0E6	1.0E6	4.0E5	4.0E5	1.7E5	9.6E4	1.5E4	9.5E2
Lot G-02A	4. *C. albicans* 10231	4.6E5	3.8E2	<10	<10	<10	<10	<10	<10
(Exp. 7-93)	5. *S. marcescens* 48	3.0E6	<10	<10	<10	<10	<10	<10	<10
	6. Adapted *S. marcescens*	1.8E6	<10	<10	<10	<10	<10	<10	<10
	7. *E. coli* 8739	3.2E6	<10	<10	<10	<10	<10	<10	<10
	8. *P. cepacia* 25416	3.1E6	1.8E6	2.1E5	1.6E5	7.1E5	3.4E5	2.2E5	1.8E5
Alcon	1. *P. aeruginosa* 9027	2.1E6	<10	<10	<10	<10	<10	<10	<10
Soaclens	2. *S. aureus* 6538	1.1E6	1.3E5	<10	<10	<10	<10	<10	<10
	3. *A. niger* 19606	9.2E5	<10	<10	<10	<10	<10	<10	<10
Lot IKPL	4. *C. albicans* 10231	4.8E5	<10	<10	<10	<10	<10	<10	<10
(Exp. 7-93)	5. *S. marcescens* 48	2.3E6	6.6E3	<10	<10	<10	<10	<10	<10
	6. Adapted *S. marcescens*	6.0E6	<10	<10	<10	<10	<10	<10	<10
	7. *E. coli* 8739	1.7E6	3.0E1	<10	<10	<10	<10	<10	<10
	8. *P. cepacia* 25416	1.1E6	<10	<10	<10	<10	<10	<10	<10

soft lenses, several have compared the incidence of keratitis in soft, hard (PMMA), and RGP lens wearers. In one study in the U.S. and a second in the U.K., the relative risk of keratitis was estimated to be from slightly more to four times greater for daily wear soft lens wearers than for RGP lens wearers. The risk for extended wear soft lens wearers was much higher than the risk for any other group.[12,13]

Because of the strong relationship between the use of microbially contaminated contact lens care products and microbial keratitis,[3-5] the antimicrobial effectiveness of lens care solutions can be important in preventing infection. This study compared the preservative effectiveness of nine common RGP lens care solutions.

We previously had shown that microorganisms originally isolated from a preserved product may die when inoculated into sterile full strength product unless first "adapted" to the preservatives by growth in diluted product.[14,15] More recently, Gandhi and coworkers[11] have shown that organisms surviving in full strength lens care solutions containing CHG were more resistant than "unadapted" cells. We have also previously reported that an accurate prediction of whether a product is well preserved or is susceptible to microbial contamination during use by consumers may require the inclusion of preservative-resistant strains for challenge testing.[16] We have observed a correlation between the ability of a preserved contact lens solution to kill adapted, resistant microorganisms and the frequency of contamination of that product; those solutions that are best able to kill resistant strains in the laboratory are least likely to become contaminated during use. The resistant strains that best allowed one to predict whether or not a contact lens solution was susceptible to contamination were adapted *S. marcescens* and unadapted *P. cepacia*, and, therefore, those microorganisms were included in this study.

In most respects the results of this study confirm what might be predicted based on the known activities of the preservatives employed in each of the tested products. All of the solutions except for those containing benzyl alcohol or thimerosal rapidly killed *P. aeruginosa*, *S. aureus*, *C. albicans*, and *E. coli*, which are the specified bacterial and yeast strains required for the USP and (minus *E. coli*) the EP. The same solutions also rapidly killed unadapted *S. marcescens*. The thimerosal-containing Alcon product allowed survivors among several of the required bacterial strains at 6 hours but eliminated all organisms by 1 day; the slow but effective killing by thimerosal is well known. The Sherman products, which contain benzyl alcohol, varied greatly in their effectiveness; DeStat 3, which contains a much higher concentration of EDTA, is more effective than is Stay-Wet 3, the latter of which permitted very high levels of the three rigorous bacterial strains to persist for the entire 28 day test period.

The Allergan and CIBA Vision products containing BAK were very effective against *A. niger*, whereas those containing CHG and polyquad were moderately active and benzyl alcohol or PHMB were relatively ineffective. By combining reduced levels of PHMB and CHG, Polymer Technology's Boston Advance Enhanced Comfort Formula retained the effectiveness of the Boston Advance solution against the bacteria and yeast, while enhancing the killing of *A. niger*.

The frequent occurrence of *S. marcescens* in lens care solutions preserved with CHG or BAK is well documented.[4,7,8] The data reported here that show long-term survival of adapted *S. marcescens* in solutions preserved with CHG or BAK seem to further confirm that use of adapted rigorous product isolates can identify products at risk for in-use contamination. The persistence of both adapted and unadapted *S. marcescens*, as well as *P. cepacia*, in a lens care product containing benzyl alcohol plus 0.1% EDTA suggests that this product also may be vulnerable to in-use contamination. However, the latter product, Stay-Wet 3, is not designated as a storage or disinfecting solution, but is only recommended for wetting or lubricating lenses and therefore may be less exposed to environmental contamination.

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BRONOPOL AS A SUBSTITUTE FOR THIMEROSAL

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Abstract

Thimerosal, chlorhexidine digluconate and bronopol (2-bromo-2-nitropropane-1,3-diol) are of broad bacteriostatic spectrum covering *Ps. aeruginosa*, while other conventional preservatives are not.

In gamma-globulin solution (10 %) contaminated with sewer water, and to which various antiseptics were added and kept for three months at 30 °C, bacterial growth was totally inhibited by 100 p.p.m. of chlorhexidine or thimerosal, by 300 p.p.m. of benzalkonium, benzethonium chloride or bronopol, and by 1000 p.p.m. or more of the others. Only bronopol inhibited non-bacterial precipitations.

Combined with similar findings with another protein solution, 300 p.p.m. bronopol proved as effective a preservative as 100 p.p.m. thimerosal. Consequently, a dose of 0·5 mg/kg b.w. of the substance has become the object of safety studies. In this range of dosage, bronopol is acutely and chronically less toxic than thimerosal. No allergic response has been observed with rabbits.

Antitoxin titer of tetanus-hyperimmune globulin showed no difference between bronopol (500 p.p.m.) and thimerosal (100 p.p.m.) as preservative after incubating for three months at 30 °C.

Elimination studies with ^{14}C-labelled bronopol revealed rapid urinary excretion of the substance and unlikelihood of long-term storage in liver.

Electron microscopy of *Ps. aeruginosa* incubated with bronopol revealed destruction of cell wall and leakage of nucleic acid and protein-like substance.

BACTERIOSTATIC SPECTRUM

Since the possibility of an allergenic effect of thimerosal is now common knowledge, studies for finding a replacement have been of great importance. Toward this objective, renewed and comparative studies of the minimum inhibitory concentration (MIC) of several antimicrobial agents such as acriflavin, acrinol, benzalkonium chloride, benzethonium chloride, ethyl *p*-oxybenzoate, hexachlorophene, nitrofurazone, phenol, tricresol, thimerosal, chlorhexidine digluconate and bronopol were made with common Gram-positive and Gram-negative bacteria (Fig. 1). Only thimerosal, chlorhexidine digluconate and bronopol(1, 2) (2-bromo-2-nitropropane-1,3-diol*) were found to be of broad bacteriostatic spectrum including *Ps. aeruginosa*.

* Bronopol (non-proprietary name), *WHO Chronicle* (1966) 20, no. 11.

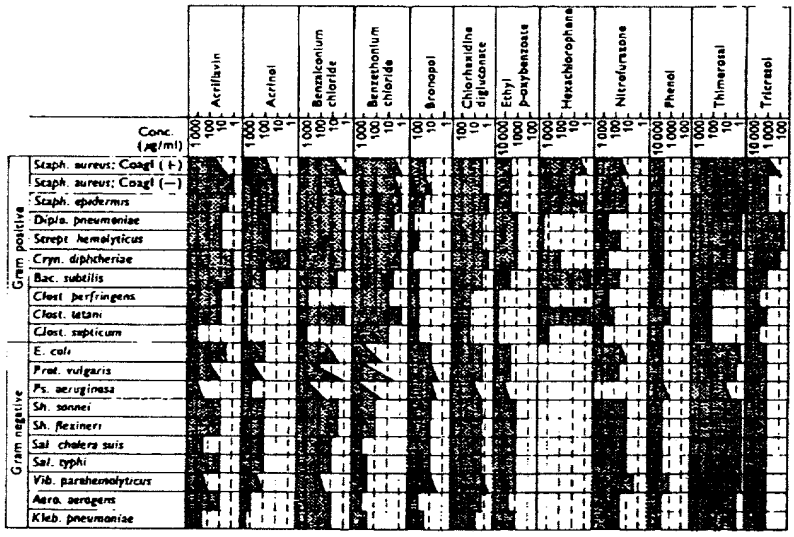


Fig. 1. Bacteriostatic spectrum of antimicrobial agents, the dark columns indicating inhibition.

ACUTE TOXICITY

By acute toxicity test or LD_{50} on mice (intraperitoneal, 72 h), no remarkable difference was found among the antimicrobial agents tested, except for *p*-oxybenzoate esters. However, the quotients of MIC against *Ps. aeruginosa* over LD_{50} indicate the lowest toxicity of those three at the effective inhibitory concentrations against *Ps. aeruginosa* (Table I).

BRONOPOL AND ITS MECHANISM OF ACTION

Bactericidal effect of bronopol in terms of phenol coefficient was compared with that of thimerosal and other agents. In contrast to the values of MIC, the effect of bronopol was not as acute as that of the others, especially with *Staphylococcus* (Table II).

To study the influence of protein on the bacteriostatic effect, cultures of *Staphylococcus aureus* and *Ps. aeruginosa* in heart-infusion broth, with and without 1·5 % human albumin solution, were treated with antimicrobial agents and incubated for 20 h at 37 °C, and increase or decrease of microbial growth was noted. Bronopol showed much less reduction of bacteriostatic action than thimerosal under these conditions (Table III).

Electron micrography, agar- and ultrathin section methods, of *Ps. aeruginosa* exposed to bronopol in phosphate-buffered saline (pH 6·8) at concentrations of

Table I. (1) *Minimum inhibitory concentration*, (2) LD_{50} *and* (3) *Relative toxicity* (*quotients* (1)/(2))

Agents	(1) MIC (μg/ml): *Ps. aeruginosa*	(2) LD_{50} (mg/kg): mice, 72 h	(3) Relative toxicity (1)/(2)
Acriflavin	1000	37·0	27·0
Acrinol	> 100	72·0	> 1·3
Benzalkonium chloride	1000	62·5	16·0
Benzethonium chloride	1000	30·0	33·3
Bronopol	5	86·8	0·0058
Chlorhexidine digluconate	2	60·5	0·033
Ethyl *p*-oxybenzoate	10000	1340	7·46
Hexachlorophene	> 3000	86·8	> 34·5
Nitrofurazone	5000	282	17·7
Phenol	3150	2·36	1335
Thimerosal	5	53·6	0·093
Tricresol	3150	284	11·1

Table II. *Phenol coefficient*

Agents	*Staphylococcus aureus*	*Salm. typhi*	*Ps. aeruginosa*
Acriflavin	1·2	33	68
Acrinol	0·9	17	18
Benzalkonium chloride	470	630	160
Benzethonium chloride	470	830	170
Bronopol	<0·5	1·1	1·8
Chlorhexidine digluconate	40	1460	230
Hexachlorophene	4·0	<0·1	0·1
Thimerosal	130	25	4·5

Table III. *Reduction of bacteriostatic effect by protein*

(MIC in μg/ml)

Agents	With protein	Without protein	Reduction
	Ps. aeruginosa		
Acrinol	300	1000	+
Bronopol	15	3·2	+
Chlorhexidine digluconate	15	2·0	+ +
Hexachlorophene	1000	> 3000	
Thimerosal	32	3·2	+ +
	Staphylococcus aureus		
Acrinol	10	100	+ +
Bronopol	32	32	—
Chlorhexidine digluconate	3·2	2·0	+
Hexachlorophene	100	3·2	+ +
Thimerosal	1·5	0·1	+ +

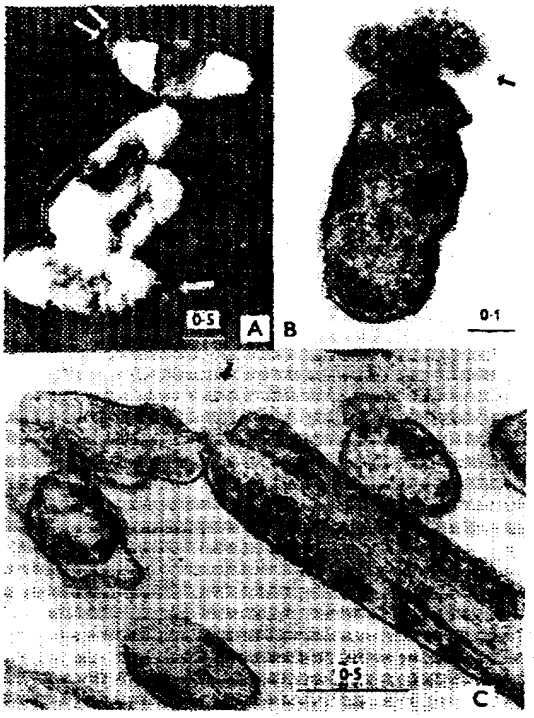


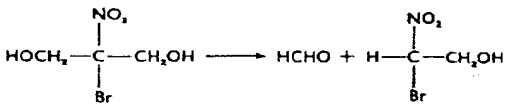
Fig. 2. Electron micrographs of *Ps. aeruginosa* after 8 h contact with bronopol (100 μg/ml). A: Shadowing. B, C: Sections. Bronopol-treated *Ps. aeruginosa* showed an uneven surface (A) and a large projection (A ↓ ↓). Some parts of the bacterial cell wall were cracked (A ↓), and the efflux of cytoplasmic materials (B ↓) and fibrous nucleic acid (C ↓) was recognized. Scales in μm. (Photo: H. Arimura.)

50 p.p.m. or higher for 8 h, revealed large granular deformation or whole destruction of bacterial cell wall and cytoplasmic membrane. In the latter case, the efflux of cytoplasmic substance and fibrous nucleic acid resembled the effect of polymixin (Fig. 2). In the supernatant obtained from centrifugation after eight hours' incubation, a remarkable increase of optical density at 260 nm and 280 nm was observed.

From these findings, bronopol could be classified in the slow-acting, cell-wall-affecting group.

CHEMISTRY

Bronopol in aqueous solution can be extracted with ethyl acetate, and quantitatively analyzed by gas-chromatography. It was shown that 6·8% bronopol



	Bronopol →	Formaldehyde	+ Bromonitro-ethanol
	μ mol	μ mol	μ mol
In phosphate buffer pH 7·0	100 →	4·7	8·3
In distilled water pH 5·0	100 →	3·5	3·3

Fig. 3. Decomposition of bronopol in aqueous solution.

in aqueous solution (pH 5·0) was decomposed to formaldehyde and bromonitroethanol (Fig. 3). The latter was as bacteriostatic as bronopol. In phosphate buffer (pH 7·0) the rate of decomposition is higher than in water.

USE AS PRESERVATIVE

In studying the practical use of bronopol as preservative, vials of gammaglobulin (GG) solution (10%) were prepared with various antiseptics, contaminated with town sewer water containing 10^6 micro-organisms, and kept for six months at 30 °C. Bacterial growth was totally inhibited by 100 p.p.m. of chlorhexidine and thimerosal, by 300 p.p.m. of benzalkonium and benzethonium chlorides and *bronopol*, by 1000 p.p.m. or more of the others. Non-bacterial precipitations appeared with all preservatives at the effective concentrations, but not with bronopol, although the latter showed a trace of coloring. In view of the precipitation which appeared with thimerosal, bronopol is preferred to the latter (Fig. 4).

With solutions of heparin sodium containing 1000 units/ml at pH 7, 300 p.p.m. bronopol proved as effective a preservative as 100 p.p.m. thimerosal. Assuming that 100 ml of any solution should be safe given parenterally for an adult of 70 kg of body weight, 0·5 mg/kg body weight of bronopol would then be the object of safety studies.

SUBACUTE TOXICITY OF BRONOPOL

Intraperitoneal administration of a large dose of bronopol (4 mg/kg daily) to Wistar-strain rats for four successive weeks, resulted in a slight disturbance of the growth of test animals, caused by peritoneal adhesion and consequent deformation of intestine; anemia and leucopenia, especially in lymphocytes, were also observed. Liver and kidney function, however, remained normal. Except for slight edema in heart muscle, Kupffer cells in the liver, and hyaline

Concentration (μg/ml)	3150	1000	315	100	31·5
Benzalconium chl.	M ▲▲▲	M ▲▲▲	+ + + +	+ + + +	+ + + +
Benzetonium chl.	M ▲▲▲	M ▲▲▲	▲▲▲	+ + + +	+ + + +
Bronopol	C	C	C	+++ c	+ + + +
Chlorhexidine digl.	▲▲▲	▲▲▲	M ▲▲▲	+++	+ + + +
Dihydrostreptomycin sulf.	/	/	+ + + +	+ + + +	+ + + +
Kanamycin sulf.	/	/	+ + + +	+ + + +	+ + + +
Nitrofurazone	▲▲▲	▲▲▲	+++	+ + + +	+ + + +
Phenol	▲▲▲	+ +	+ + + +	/	/
p-Oxybenzoate, methyl	▲▲▲	+++	+ + + +	+ + + +	/
p-Oxybenzoate, ethyl	▲▲▲	+++	+ + + +	+ + + +	/
p-Oxybenzoate, propyl	M ▲▲▲	+ +	+ + + +	+ + + +	/
Thimerosal	/	▲▲▲	▲▲▲	▲▲▲	+ + + +
Tricresol	▲▲▲	▲▲▲	+ + + +	/	/

Bacterial growth with visible turbidity

4	8	12	24 weeks
+ + + +	+++	+ +	+

M: Mold growth only
▲▲▲ : Sterile precipitation
C: Coloring
c: Slight coloring
/: Not tested

Fig. 4. Bacterial growth and other changes in 10% gamma-globulin solution, heavily contaminated and stored for 24 weeks at 30 °C. Effect of preservatives.

droplet degeneration of tubular epithelium in the kidney, no pathological changes were found in the brain, lung and other organs. With daily doses of 1 mg/kg of bronopol, the pathological changes were less manifest than those caused by the same dose of thimerosal (Table IV).

INFLUENCE OF BRONOPOL ON TISSUE CULTURE

The effect of antimicrobial agents inhibiting growth of cultured chicken embryo fibroblasts was compared at the seventh day of culture. The concentration allowing growth of fibroblasts to 70% of the normal culture indicates that thimerosal is the least harmful, followed by bronopol and chlorhexidine (Table V).

INFLUENCE OF BRONOPOL ON ANTITOXIN TITER IN GG

Two preparations of tetanus-hyperimmune globulin, one with 500 p.p.m. bronopol and the other with 100 p.p.m. thimerosal, incubated at 30 °C for three months, exhibited no difference in antitoxin titer between them.

Table IV. *Subacute toxicity*

Agents	Daily 1 mg/kg for 4 weeks	
	Bronopol	Thimerosal
Neutrophils	↑	—
Lymphocytes	↓	—
Total serum protein	—	↓
Serum albumin	—	↓
A/G	—	↓
SGPT	↓	—
Weight of spleen	—	↑
Hematocrit	No change	
Hemoglobin		
Leucocytes count		
BSP retention		
PSP excretion		
Urine		
Heart weight		
Liver weight		
Pancreas weight		
Kidney weight		
Ovary weight		

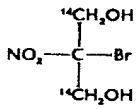
Table V. *Concentration of antimicrobial agents allowing 70% growth of fibroblasts*[a]

Agents	Concentration (μg/ml)
Acriflavin	< 1
Benzalkonium chloride	1
Bronopol	3
Chlorhexidine digluconate	3·2
Hexachlorophene	0·9
Thimerosal	31·5

[a] Chick embryo, at 7th day plasma culture in Carrel flask.

ELIMINATION

^{14}C-labelled bronopol was synthetically prepared from ^{14}C-labelled formaldehyde.



(3·17 μCi/mg)

After intravenous and oral administration of 1 mg/kg in rabbits, radioactivity in

Table IV. *Subacute toxicity*

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	Bronopol	Thimerosal
Neutrophils	↑	—
Lymphocytes	↓	—
Total serum protein	—	↓
Serum albumin	—	↓
A/G	—	↓
SGPT	↓	—
Weight of spleen	—	↑
Hematocrit	No change	
Hemoglobin		
Leucocytes count		
BSP retention		
PSP excretion		
Urine		
Heart weight		
Liver weight		
Pancreas weight		
Kidney weight		
Ovary weight		

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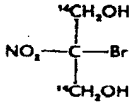

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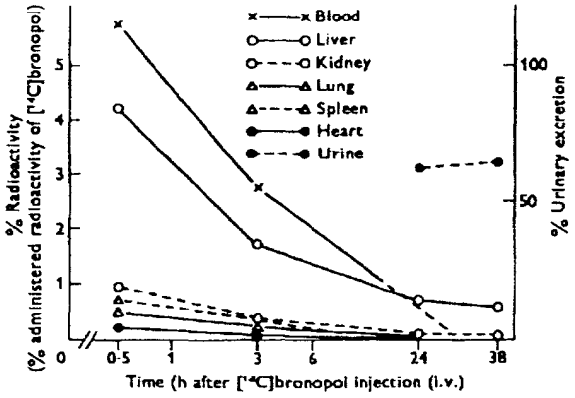

Fig. 5. Elimination of bronopol after intravenous administration.

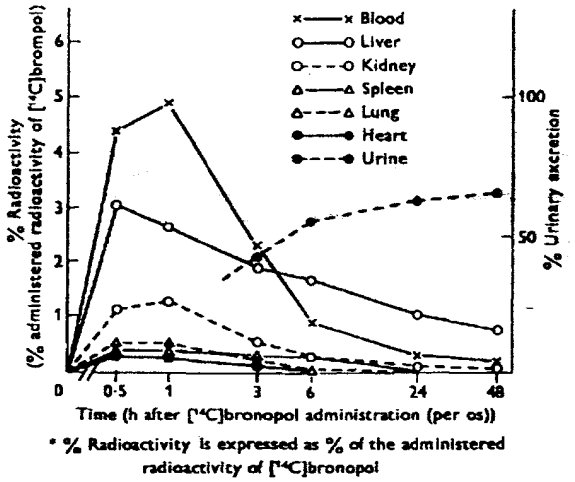

Fig. 6. Elimination of bronopol after oral administration.

blood and other organs was measured by a scintillation counter. ^{14}C-bronopol given intravenously was rapidly eliminated from circulation and the concentration in blood was down to 6% of the given dose after 30 minutes, 0–0·5% after 24 h. In lung, spleen, kidney and heart, only about 1% of the given bronopol was counted after 30 min. This decreased to zero after 24 h, while 60% of the

given radioactivity was excreted in urine in 48 h. In liver, 4·2% of given substance after 30 min decreased to 1 % or less after 24 h (Fig. 5).

When bronopol was given orally, its level in blood reached its peak at 5 % of the given dose; from the blood it was rapidly excreted, as after intravenous administration. Appearance, elimination, and excretion in and from the organs through urine were quite identical to the intravenous administration (Fig. 6).

Though studies on chronic toxicity, allergenicity and teratogenicity of bronopol are still in progress, bronopol is offered as one of the candidate substitutes for thimerosal.

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Discussion

E. B. SELIGMANN (Discussant) Thank you, Dr Naito, for a most interesting paper. You have condensed a tremendous amount of work into this presentation. I agree with your desire to discover or develop improved preservatives. While under certain conditions thimerosal is an excellent preservative, it also possesses a number of serious disadvantages. Dr Naito mentioned the fact that certain individuals have developed a sensitivity that makes it hazardous for them to receive products containing thimerosal. One of the attributes of this preservative is also one of its disadvantages. Fungi are exquisitely sensitive to thimerosal. Experimentally it has been demonstrated that extremely high dilutions are necessary in order to permit the growth of inocula of fungi containing only a few cells. This presents serious problems to be overcome in order to perform valid sterility tests. While fungal spores may not germinate in the presence of thimerosal, there is always the chance that they will still be capable of multiplication when introduced into the body. Neutralizers for thimerosal have been proposed to be used in sterility testing but at effective concentrations by themselves the ones studied so far all possess some degree of toxicity for micro-organisms.

Thimerosal is not unique. All present preservatives have some disadvantages. Therefore it is necessary to press the search for more suitable preservatives. While certain preservatives may not be compatible with some products, all preservatives must be capable of preventing the growth of and of killing all types of micro-organisms. The possibility exists that any type of micro-organism may become a contaminant of a product. However, for test purposes, it is sufficient to use only those types known to have caused infections and known to gain access to products during manufacture. These should include *Staphylococcus*, *Clostridium*, *Bacillus*, *Pseudomonas*, and *Aspergillus* species as well as coliforms and yeasts. Tests should be quantitative so that the number of viable cells introduced is known in order to determine the degree and rate of kill. Both the microbiostatic and microbiocidal effects of a candidate preservative must be ascertained.

After it has been determined that a relatively low concentration of a candidate chemical will kill representative micro-organisms, it becomes necessary to establish its compatibility with specific products. Furthermore, it is necessary to determine the compatibility of various products with the candidate preservative. In addition, the safety of the preservative in combination with specific products when administered to man must be established following exhaustive testing in animals.

Bronopol seems to have certain properties that make it a candidate preservative. However, more must be learned concerning its activity against fungi. It would be desir-

able to differentiate between its microbiostatic and microbiocidal activities. Ultimately it must be combined with specific biological products. The road to new preservatives is a long one. It may be easier to investigate preservatives that have been proven safe through years of use when it becomes necessary to replace a specific preservative in specific products. However the basic research involved in the development of new and safer preservatives must be continued so that we will always have a variety of effective preservatives to select from as new products are developed. Thank you.

MOZEN Dr Naito has described the great number of studies carried out to qualify this candidate preservative, and Dr Seligmann has pointed out areas for additional study. I would like to mention another study that I think might be necessary before qualifying this material. You mention, Dr Naito, that the studies with the immune serum globulins at 10% concentration, showed that in the presence of all the preservatives, except bronopol, precipitation was observed, which on first glance, would appear to be a plus in the favor of bronopol. I might say the precipitation of 10% gamma-globulin, of course, is fairly well known in the field. The cause is not totally understood. We generally go to the 16·5% concentration because the presumed protein–protein interaction maintains the solution. The fact that the material in the presence of bronopol did not precipitate suggests that there may have been some chemical interaction between bronopol and immune serum globulins, in which case it would seem to me that it may be necessary to determine whether any new antigenic sites, or new antigenic determinants, may have been formed due to such interaction. These kinds of study could, perhaps, be carried out in animals, and then subsequently, cautiously in man. As you know, particularly with some of the immune globulins, administration is very prolonged, and at times for life, such as in immune deficiency diseases. It would certainly be important to know whether we are dealing with a new antigenic material.

NAITO Thank you very much for your kind suggestions. I have to confess that our experimental programs were designed in terms of 10% gamma-globulin. So, in compliance with your kind suggestions, we will renew our studies and do the experiment again, using the 16% gamma-globulin.

CHRISTENSEN We are going to discuss tomorrow the question of safety, but I should like to say that data indicate that thimerosal has a very high degree of safety, and I think that a new substance like bronopol has to compete with this very safe substance. So I think that it is necessary to go through clinical trials before knowing if bronopol is acceptable.

HIATT Dr Naito, I should mention that acroflavine is one of the classic compounds whose cytotoxic activity is, to a large extent, a function of the light intensity which existed during the experiment. This may account for the extraordinary cytotoxicity of acroflavine against chick fibroblasts.

NAITO I fully agree; acroflavine was the most toxic inhibitor of chick fibroblasts, and was used in our experiment only for comparison with bronopol.

MRS BATTY Could Dr Naito tell us a little more about the solubility of bronopol, and particularly at 4 °C? We have had some difficulty in maintaining the recommended amount in reagents with a pH of about 7·0.

NAITO So far as I know, bronopol is a substance with good solubility. It is quite stable at pH 5·0–6·0, but rather unstable at pH 7·0.

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trends

New approach to preserving eye drops

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The effects of antimicrobial preservation of eye drops have been investigated and several proposals have been put forward for effective preservation based on microbiological criteria and chemical compatibility. The mixtures that have been proposed, and which are discussed in this article, act rapidly and are bactericidal for a wide spectrum of bacteria, including Pseudomonas aeruginosa. *Furthermore, these mixtures do not irritate the eye. Tests have established which of the proposed mixtures can be used with which of the therapeutic constituents of eye drops.*

Les effets d'agents conservateurs de gouttes opthalmiques sont étudiés et plusieurs propositions avancées quand à leur efficacité en termes de critères microbiologiques et de compatibilité chimique. Les formules suggerées et discutées dans cet article agissent rapidement et présentent un large spectre bactéricide, y compris contre Pseudomonas aeruginosa. Ces mélanges n'irritent en outre pas les yeux. Des essais ont établi lesquels peuvent être utilisés avec quels constituants thérapeutiques de gouttes opthalmiques.

The problem of preserving opthalmic preparations is currently a matter of great interest[1,2]. The isolation of living micro-organisms, which are often pathogenic, from ophthalmic drugs, and the large number of eye infections from the use of these products, indicates that their method of preparation is defective. Among the factors affecting the production of eye drops, besides aseptic working conditions, insurance against secondary contamination during use is very important, particularly in the case of multidose containers.

The fact that living micro-organisms have been isolated from these preparations while they were being used shows that the preservatives utilized do

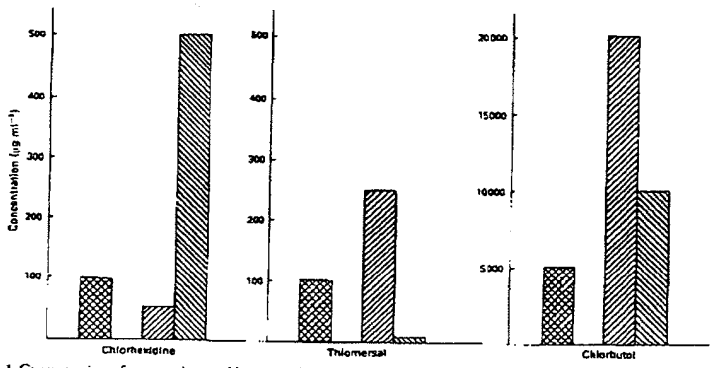

Fig. 1. Concentrations of preservatives used in practice for eye drops and bactericidal effect obtained in researches. ▩ *Concentrations used in practice;* ▩ *Bactericidal concentration for Gram-positive bacteria;* ▧ *Bactericidal concentration for Gram-negative bacteria.*

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not fulfil their role of protecting the eye against secondary infection. This situation is particularly dangerous when *Pseudomonas aeruginosa* is present in the preparation, as this microbe can damage the cornea and even cause blindness. Therefore, in our studies of the problem of preservation we analysed the effectiveness of antimicrobial preservatives that are used most often in eye drops. Also, a search had been made for the most effective substances against *Ps. aeruginosa* based on theoretical considerations and the results of our own tests. The preservatives proposed by us were tested with respect to irritation *in vivo* and their compatibility with the constituents of those preparations that are used most often.

MICROBIOLOGICAL TESTS

In the first part of our studies, the bacteriostatic and the bactericidal effect of the preservatives was tested against 30 strains of Gram-positive and Gram-negative bacteria that were isolated from drugs and clinical materials. Also, the speed of the bactericidal effect with respect to *Ps. aeruginosa* was established[3,4,5].

In our opinion, a good preservative for eye drops ought to show a rapid bactericidal effect against a large inoculum. For this reason, the time of observation for our tests was chosen to be 60 min

TABLE I. Compatibility of preservative mixtures with substances in eye drops

Substance	Compatible preservative mixture
Adrenalin	II, III, IV
Atropine sulphate	
Physostygmine salicylate(B)	
Sodium borate	
Benzylpenicillin (buffered with sodium citrate)	III, IV
Chloramphenicol	
Cocaine hydrochloride(B)	
Neomycin sulphate(B)	
Resorcinol	
Sodium citrate	
Sodium salicylate	
Zinc sulphate(B)	
Boric acid	I, III, IV
Homatropine hydrobromide	I, II, IV
Ephadrine hydrochloride	I, III
Ethylmorphine hydrochloride(B)	II, III
Procaine hydrochloride(B)	I, II
Di-sodium edetate	II
Scopolamine hydrobromide	
Procaine hydrochloride(A)	III
Fluorescein sodium	IV
Sulfacetamide sodium	



Fig. 2. Time of bactericidal effect of preservatives alone and in mixtures (against Pseudomonas aeruginosa*). A, benzalkonium chloride – 50 µg; B, chlorhexidine – 50 µg; X, with phenethyl alcohol – 4000 µg; Y, with bronopol – 500 µg; Z, with chlorhexidine – 50 µg.*

and the inoculum size between 10^5 and 10^6. For our analyses, we chose the following chemical preservatives: benzalkonium chloride and bromide, chlorhexidine acetate and gluconate, methyl hydroxybenzoate and propyl hydroxybenzoate phenylmercuric borate and nitrate, bronopol, thiomersal, chlorbutol, boric acid and phenethyl alcohol. These preservatives were used at concentrations normally utilized to preserve eye drops. All trials were done first in media and then in eye drops, because the antimicrobial effect depends on both the medium and the form of the drug.

It has been established that the majority of preservatives act only bacteriostatically and that this effect is [illegible] bronopol and [illegible] against Gram-negative bacteria. Compounds of mercury, benzalkonium and chlorhexidine yielded good results with Gram-positive bacteria. The following were ineffective for our purposes: chlorbutol, methyl- and phenyl-hydroxybenzoate, and boric acid (Fig. 1).

In the second part of our experiments, it became evident that the bactericidal effect was slow and noticeable only after many hours of contact with the microbial cells. Only benzalkonium and chlorhexidine compounds showed rapid activity[4,5]. For this reason further studies were limited to finding other compounds which showed a rapid bactericidal effect.

To obtain a faster synergetic effect, a mixture of two compounds was used according to the following guidelines:

1. Combining two preservatives which have shown rapid bactericidal effects (chlorhexidine and benzalkonium);

2. Combining an antimicrobial preservative with a compound that has the ability to alter the permeability of a microbial cell wall and in this way

facilitates the penetration of the antimicrobial substance (in our case, a mixture of a preservative with bronopol or phenethyl alcohol).

The results of our experiments confirmed the theoretical assumptions[6]. In all cases, except for boric acid, satisfactory results were obtained. In some cases a considerable decrease in killing time became evident, and was reduced from many hours to 10 or 15 min (Figs 2 and 3).

Moreover, other useful phenomena were observed. It was noticed that *Ps. aeruginosa* develops resistance with more difficulty to mixtures of preservatives than to a single substance. In many cases bacterial resistance was not observed.

The results of experiments in bacterial media were confirmed by tests in eye drops (ten of the most frequently used drugs were chosen). It was also shown that the combinations of preservatives were not irritant to the eye (methodology according to NF XIII, American Pharmaceutical Association, 1970).

In connection with these positive results, the following mixtures of preservatives were chosen to test their compatibility with drugs.

	PRESERVATIVE	CONC
I	Benzalkonium bromide (chloride)	0.005%
	Chlorhexidine gluconate (acetate)	0.01%
II	Benzalkonium bromide (chloride)	0.005%
	Phenethyl alcohol	0.4%
III	Phenylmercuric borate (nitrate)	0.001%
	Phenethyl alcohol	0.4%
IV	Thiomersal	0.02%
	Phenethyl alcohol	0.4%
V	Phenylmercuric borate (nitrate)	0.001%
VI	Thiomersal	0.02%

(The preservatives V and VI are recommended to be used when mixtures I, II, III and IV are incompatible with the constituents of the various drugs.)

COMPATIBILITY OF PRESERVATIVES WITH DRUGS AND ADJUVANTS

The above mentioned mixtures of preservatives were tested for their compatibility with those medicinal substances most often used in the eye drops. The solutions of drugs in their maximal used concentrations were prepared according to general regulations of Polish Pharmacopoeia with sodium chloride (A) or boric acid (B) as isotonic agents. The mixtures of preservatives I–IV were then added at the concentrations mentioned above. After thermal sterilization (if not contraindicated), solutions were stored in closed bottles protected from light for 2 weeks at room temperature. Visual observations were made every day to compare test solutions with

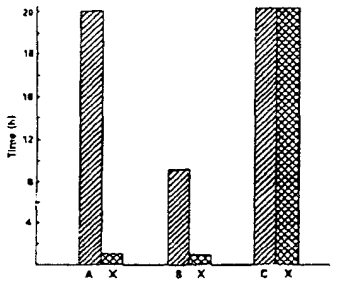

Fig. 3. Time of bactericidal effect of preservatives alone and in mixtures (against Pseudomonas aeruginosa*). A, chlorbutol – 5000 g; B, methyl- and phenyl-hydroxybenzoate – 1000 + 500 μg; C, boric acid – 2000 μg; X, with phenethyl alcohol – 4000 μg.*

standards (i.e. the same solutions but without preservatives). Any discolouration or cloudiness of the solution was assumed to be a symptom of incompatibility.

It was shown that the four mixtures of preservatives that were studied were compatible with calcium chloride, pantocaine, pilocarpine hydrochloride and sodium chloride. Those substances that were compatible with selected preservative mixtures are shown in Table I. Only a few substances, that were not compatible with the mixtures of preservatives appeared to be compatible with the simple preservatives: potassium and sodium iodide – VI; sodium thiosulphate – V; oxytetracycline hydrochloride – V, VI; tetracycline hydrochloride – V, VI.

Solutions of silver nitrate, chlortetracycline hydrochloride, streptomycin sulphate and tannin ought to be prepared without any added substance on account of their incompatibility with all the preservatives that have been studied.

The results of these investigations were confirmed by separate trials at laboratories in Cracow, Wroclaw and Warsaw. The preservative mixtures were officially introduced in Polish pharmacies by a decree of the Ministry of Health and Social Welfare. Their compatibility with thickening agents such as methylcellulose, hydroxyethylcellulose and polyvinyl alcohol was also investigated. The measurement of turbidity and antibacterial activity were taken as the criteria of compatibility. All thickening agents were compatible with the preservatives with one exception; one batch of

methylcellulose was incompatible with I, but another two batches of methylcellulose were compatible. The studies also excluded any complex formation between the preservatives and thickening agents and showed no essential influence of thickening agents on antimicrobial activity of the preservatives.

REVIEW OF PRESERVATIVE ACTION

The compounds currently used for the preservation of eye drops are mainly bacteriostatic; the bactericidal effect is slow and limited, and, as a result, they offer no protection against secondary contamination while in use. The contamination of eye drops in their containers by living microorganisms and the infections due to this contamination are, therefore comprehensible.

In searching for effective preservatives, the hypothesis that the effect of preservatives can be increased by other compounds that alter the permeability of the microbial cell wall has been confirmed. The same result was observed in the case of mixtures of two preservatives that had shown rapid bactericidal action when tested individually. These results were obtained under rigorous testing conditions. Of particular interest is the effectiveness of mixtures against Gram-negative bacteria because the structure of their cell walls presents a strong barrier against the penetration of undesirable substances.

Combinations of preservatives have also been studied by other investigators[8,9,10]. However, their experiments were principally 'model' studies and random from the microbiological point of view, and were unconfirmed by tests on the various eye drops for compatibility. Therefore, it is clear why those experiments have not found direct application in drug preparations.

Our methods for the preparation of eye drops, as well as the requirements for their preservation, are currently recommended for general public use in Poland, and will be published in the new edition of the Polish Pharmacopoeia. The results of these microbiological experiments indicate that eye drops prepared in such a way are protected against secondary contamination during their use.

The rapid bactericidal effect that was observed against *Ps. aeruginosa* suggests, in our opinion, that no other microorganisms were present, because *Pseudomonas* is especially resistant to the effects of antimicrobial substances and its sensitivity can be used as a general indicator of the antibacterial effectiveness of these preservatives.

Confirmation of the compatibility of the proposed compounds with the constituents of the preparations permits their application in the preparation of the majority of eye drops utilized in ophthalmic therapy. The lack of an irritating effect of the proposed preservatives on the eye lends additional support to their possible wide application in the field of medical care.

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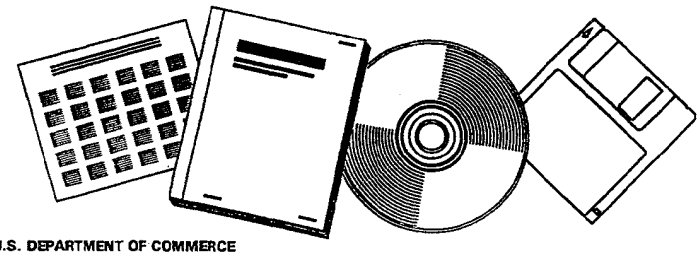

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TOXICOLOGY AND CARCINOGENESIS
OF VARIOUS CHEMICALS USED
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Final Report

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16. Abstracts. Benzethonium chloride, ethylene chlorohydrin, ethylene glycol, methylparaben, phenol red, thimerosal, and pyridine were injected in high doses subcutaneously into Fischer rats. One hundred injections were made over 50 weeks. The rats were observed for six months, after completion of the injection schedule, before necropsy. Each chemical was given to 200 rats. Benzethonium chloride produced numerous injection-site indurations. Twenty-six of these rats developed site-related fibrosarcomas. All other compounds produced 2-4 site-related tumors. There was no evidence of metastasis in any of the rats. One hundred saline-injected rats had no site-related tumors, however, the 100 uninoculated rats had one subcutaneous fibrosarcoma.

17. Key Words and Document Analysis. (a). Descriptors

Toxicology
Carcinogenesis
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Ethylene glycol
Methylparaben
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Thimerosal
Pyridine

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A

UNITED STATES GOVERNMENT
Memorandum

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

TO : Contract #PH-43-67-676 DATE: November 26, 1969

FROM : Dr. Carl E. Miller, Project Officer

SUBJECT: Statistical analysis of the summary data from Mason Research Institute

The summary data was subjected to statistical analysis using the method of Binomial Approximation. The following were found to differ significantly from the controls:

Benzethonium Chloride 3.0 mg/kg x 100 doses

Benzethonium Chloride 1.0 mg/kg x 100 doses

Thimerosal at 1.0 mg/kg x 100 dose level approached significance having a value of 1.94 as compared to the P = 0.05 level of 1.96.

No other significant reactions were found.

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TABLE OF CONTENTS

	Pages	Tables
Abstract and Summary	i-iii	
Introduction	1	
Materials and Methods	1 - 3	1 - 2
Toxicity Studies	4 - 5	3
Chronic Studies	6 - 7	4
Controls	6 - 7	
Formulation	8	
Results	9 - 35	5 - 27
Testicular Tumors in Fischer Rats	36-39	28 - 29
Nickel Sulfide Induced Tumors	40-47	30 - 34

Toxicology and Carcinogenesis of Various Chemicals
Used in the Preparation of Vaccines

(Contract No. PH43-67-676)

ABSTRACT AND SUMMARY

Since many chemical compounds are used in the manufacture of vaccines it was decided to determine the toxic and carcinogenic potential of seven representative compounds: Benzethonium Chloride, Ethylene Chlorohydrin, Ethylene Glycol, Thimerosol (Merthiolate), Methyl Paraben, Phenol Red and Pyridine.

Fischer rats were used in both the toxicity as well as the carcinogenic trials. The following table gives the single dose LD_{50}, the repeated dose-maximum tolerated dose and the selected maximum dose for the twice weekly injection schedule that continued for one year.

Summary Toxicology Table

Compound	LD_{50} (mg/kg)	Maximum Tolerated Dose (mg/kg)	Maximum Dose For 100 Injections
Benzethonium Chloride	119.0	3.0	3.0
Ethylene Chlorohydrin	71.6	<30.0	10.0
Ethylene Glycol	5300.0	<1700.0	1000.0
Thimerosol (Merthiolate)	98.0	<5.0	1.0
Methyl Paraben	>500.0	-	3.5
Phenol Red	>600.0	-	1.0
Pyridine	866.0	<180.0	100.0

Two hundred animals were assigned for the testing of each compound. One hundred and twenty animals were assigned for each group of negative and vehicle controls, while

160 rats were used for the injection of nickel sulfide as a positive control.

The toxicity of the compounds given over a period of one year did not exceed the estimates based on the preliminary toxicity trials. At the end of one year, the mortality of the treated groups (1.85%) did not exceed that of the negative and vehicle controls (2.0%). This largely held true for the 18-month period at which time the treated groups had a mortality of 6.5% while the average of the controls was 7.05%. After 18 months, Benzethonium Chloride and Merthiolate at their highest dose level showed decreased weight gains as compared to the controls of 12% and 22%, respectively. At the lower dose levels all the compounds showed weight gains similar to the controls.

The only remarkable histopathology was related to a late bronchopneumonia which developed in many of the Merthiolate treated animals. It was clearly a dose-related finding.

Benzethonium Chloride was the outstanding compound which gave rise to 26 injection site-related tumors in the 200 treated animals. All the other test compounds had from two to four such tumors, while the controls had none. The high incidence of injection site tumors was correlated with a high incidence of induration and granulomas caused by the irritating activity of the subcutaneously injected compounds. The tumors were fibrosarcomas of which none metastasized. Merthiolate had numerous injection site indurations and was second highest with fibromas.

Complete autopsies were carried out on almost all of the 1800 rats in the trial. Many tumors were observed that had no relation to the injection site. Mammary fibroadenomas were [redacted] common to all groups and the incidence varied from 2% to 5%. Only the Methyl Paraben group showed an incidence of 8%.

Testicular tumors were found in most of the males that lived to 18 months. These are interstitial cell tumors peculiar to the Fischer rat. It is noteworthy that Merthiolate caused a dose-related inhibition of these tumors.

Uterine polyps were seen commonly in all groups and the test groups had an incidence range of 4% to 11% as compared to 10% in the controls.

Eighteen pituitary adenomas were found in the 1800 rats. Fifteen of these were in females. Ethylene Chlorohydrin had 7 in the 100 females with none in the males. Of

the eight adrenal tumors seen, six occured in males but there was no significance in the test group incidence. Seventeen leukemias were found distributed throughout all the groups. The only noteworthy finding here was that 15 out of the 17 occured in females.

Nickel Sulfide served well as a positive control since over 90% of the Fischer rats showed characteristic sarcoma formation at the site of injection. The sarcomas were pleomorphic with variations from the rhabdomyosarcomas to the more collagenous fibrosarcomas. Many of these were metastatic, especially to the lungs.

Toxicology and Carcinogenesis of Various Chemicals Used in the Preparation of Vaccines

INTRODUCTION

The objective of this study was to determine the toxic and carcinogenic potential of seven compounds, commonly used as preservatives or inactivating agents in the preparation of commercially available biologics.

In order to assure the public that its use of biological products is free of the danger of initiating neoplasms by virtue of the preservatives used, carcinogenic trials have been run on the following chemicals: Thimerosol (Merthiolate), Benzethonium Chloride, Methyl Paraben, Phenol Red, Pyridine, Ethylene Glycol and Ethylene Chlorohydrin.

The investigation was divided into three stages:

(1) acute toxicity and an approximation of the LD_{50}.

(2) a four week injection period at five dose levels to determine the maximum tolerated dose.

(3) a long term (1 year) inoculation series (twice weekly), subcutaneously into rats at four dose levels with careful evaluation of the incidence of tumors.

MATERIALS AND METHODS

Animals:

Caesarean-derived, Fischer 344 weanling (4 weeks old) rats of both sexes were used in this project. The animals weighed approximately 60 grams on arrival, and were placed on test within two weeks after arrival. They were housed two to a cage in air conditioned quarters and were maintained on Purina Rat Chow and water ad libitum. The animal quarters were divided into four separate rooms all on one floor. Approximately 2300 rats were used in this trial with 1800 continuing on long-term study (See Table 1).

Chemicals:

The compounds were provided by the Division of Biologics Standards, National

TABLE 1

ANIMAL DISPOSITION TABLE

Treatment Group	Preliminary Trial		Long Term Trial			Total Animals Used
	Preliminary Trials	Died or Discarded	Continued from Preliminary Trial	New Animals Added	Replacements	
Negative Control	-	-	-	120	2	122
Vehicle Control	-	-	-	120	-	120
Positive Control	-	-	-	160	-	160
Benzethonium Cl.	80	62	18	182	-	262
Eth. Chlorohydrin	80	62	18	182	1	263
Ethylene Glycol	80	28	52	148	-	228
Merthiolate	107	107	-	200	-	307
Methyl Paraben	82	42	40	160	1	243
Phenol Red	78	16	62	138	-	216
Pyridine	83	71	12	188	-	271
			202	1598		
			1800			

Total Rats Odered 2300
Total Rats Used in Direct Study 2192

722

TABLE 2

SOURCES OF COMPOUNDS AND ANALYTICAL DATA

Compound	Manufacturer	Selective Physical Constants			Selected Parameters for Purity Checks at M.R.I.
		M.P. (°C)	B.P. (°C)	U.V. (ε)*	
Benzethonium chloride (Phenol chloride)	Rohm and Haas Company	164 - 166	-	ε(236 mm) = 2968	U.V. ε(236 mμ) = 2968
Ethylene chlorohydrin (2-chloroethanol)	Distillating Products, Ind. Division of Eastman Kodak Company.	-	128 - 130	-	B.P. (uncorrected) 125.5°-126.5°C (slight brown residue)(1)
Ethylene glycol	Fischer Scientific Company	-	197 -198.3	-	B.P. (uncorrected) 194°-194.8°C
Merthiolate (thimerosol)	Eli Lilly and Company	dec. > 233	-	→	M.P. 235-238 U.V. Similar cyclic structures (acetylsalicylic acid) have molar extinction coefficients of about 600 Merthiolate, yielded an ε(272 mμ) of 648 which would be in agreement with molecular structure.
Methyl paraben (Methyl p-Hydroxy benzoate)	Heyden Division of Tenneco Chemicals, Inc.	131	-	ε(259 mμ) = 16,538	U.V. ε(259 mμ) = 16,126
Phenol red (P.S.P.)	National Aniline Div. Allied Chemical Corp.	> 300	-	→	U.V. ε (266 mμ) = 9976. Absorption bands and relative intensities were in agreement with those observed for a sample of phenol red from another source.
Pyridine	Fischer Scientific Company	-	115-11.5	-	B.P. (uncorrected) 112°-113°

* ε = molar extinction coefficient.

(1) residue probably associated with rubber lined caps used on shipping vials.

Institutes of Health. A list of the compounds is provided in Table 2.

Experimental Procedure:

The project was begun in three stages:

(a) an initial toxicologic study to determine the acute lethal dose (LD_{50});

(b) a supplementary study to determine the maximum tolerated dose; and

(c) the final four dose level study to determine carcinogenicity of the compounds in animals treated for at least one year and held another year for observation.

The compounds were prepared in solution with sterile physiological saline (Cutter Saftiflask "28"® sodium chloride, injection, U.S.P., N.S.S.), and administered subcutaneously, twice weekly, for the required period. The syringes used were individually packaged, sterile, nonpyrogenic, 1 cc. disposable tuberculin syringes (TOMAC® Catalog No. 15085 25 D), with a 25 X 5/8 needle size. The volume of compound injected was adjusted according to animal weight, so that the mean injection volume for each compound approximated 0.25 ml during the chronic study, except where the solubilities necessitated a larger dose volume. Dosages of the compounds were administered on a mg/kg basis. A fixed volume of 0.25 ml per injection of saline was used in the vehicle control group.

Initial Toxicity Study (Single Dose):

Five dose levels, at half-log intervals, were administered to groups of approximately 20 animals each, with equal numbers of males and females. The middle dose level was selected on the basis of literature data to closely approximate the LD_{50}. Lethality information calculated from the results was used to determine the starting dose in the supplementary study.

Supplementary Study:

Sixty animals were separated into five groups of 6, 12, 24, 12 and 6 animals each, with equal numbers of males and females, and administered injections of compounds twice weekly for four weeks at dose levels separated by quarter or half log intervals. The information from these results was used to determine the maximum

TABLE 3

TOXICOLOGICAL DATA FROM PRELIMINARY STUDIES

Compound	Single Injection			Repeated Injections	Maximum Dose Selected for Chronic Study
	LD_{50} (mg/kg)	95% Confidence Limits	$LD_{0.1}$ (mg/kg)	MTD (mg/kg)	
Benzethonium chloride	119.0	67-211	39	3.0	3.0
Ethylene chlorohydrin	71.6	-	-	< 30.0	10.0
Ethylene glycol	5300.0	3857 - 7478	2657	< 1700.0	1000.0
Merthiolate	98.0	82-117	26	< 5.0	1.0
Methyl paraben	> 500.0	-	-	-	3.5
Phenol red	> 600.0	-	-	-	1.0
Pyridine	866.0	649-1155	496	< 180.0	100.0

tolerated dose level to be used in the long-term study. Table 3 summarized the data from the first two studies.

Chronic Study:

The final study was initiated within three months after the start of the contract. Two hundred animals were used for each compound tested. These were divided into four groups containing 80, 60, 40 and 20 rats (with equal numbers of males and females in each group), to be treated with four dose levels, high to low, respectively. The dose levels for each compound, except for Methyl Paraben and Phenol Red, were separated by half log intervals. The insolubility of Methyl Paraben and Phenol Red prevented the establishment of the MTD. Therefore, a saturated solution was used as the highest dose level, and other levels were set at quarter log intervals. The treatment consisted of twice weekly injections for 52 weeks, with the dose level maintained on the mg/kg basis by adjusting the injection volumes to the animal weigths. All animals were weighed weekly throughout the study. Animals from the preliminary studies that were already on dose levels selected for the chronic study were used to supplement the corresponding groups in the chronic study. Table 4 shows the doses used and the starting dates for each compound.

Control:

Three types of controls were used: (1) vehicle controls (60 males, 60 females) received twice weekly injections of saline at 0.25 ml per injection; (2) negative controls (60 males, 60 females) received no treatment; and (3) positive controls (80 males, 80 females) received predetermined fixed doses of Nickel sulfide (Ni_3S_2). The positive controls were divided into four sub-groups: A, B, C and D of 40 animals each (20 males, 20 females). Each animal in the A and B groups received a single subcutaneous injection of 10.0 mg and 3.3 mg, respectively. Groups C and D were given the same doses of Nickel sulfide by a single intramuscular injection in the thigh. The powder was suspended in Duracilin A.S.® (Sterile procaine penicillin G, aqueous suspension, 300,000 units per cc), and administered in 0.1 ml volumes.

TABLE 4

CHRONIC STUDY DOSE LEVELS AND STARTING DATES*

Compound	Dose (mg/kg)	No. Animals Started	Starting Date
Benzethonium chloride	3.0 1.0 0.3 0.1	80 60 40 20	5-4-67
Ethylene Chlorohydrin	10.0 3.0 1.0 0.3	80 60 40 20	4-28-67
Ethylene glycol	1000.0 300.0 100.0 30.0	80 60 40 20	4-21-67
Merthiolate (thimerosol)	1.0 0.3 0.1 0.03	80 60 40	5-25-67
Methyl Paraben	3.5 2.0 1.1 0.6	80 60 40 20	5- 8-67
Phenol Red	1.0 0.56 0.32 0.18	80 60 40 20	5-22-67
Pyridine	100.0 30.0 10.0 3.0	80 60 40 20	4-20-67
Ni_3S_2 Positive control (single injection)	10.0 mg s.c. 3.3 mg s.c. 10.0 mg i.m. 3.3 mg i.m.	40 40 40 40	3-29-67
Vehicle control (saline)	0.25 ml	120	3-23-67
Negative control	None	120	3-23-67

* After 52 weeks of drug treatment the animals were kept for observation for an additional six months.

Formulation:

All compounds, with one exception (Phenol Red), were formulated fresh from the commercial product every two weeks. A stock solution of 600 mg/L of Phenol Red was prepared every six weeks, from which the biweekly dilutions were made.

Data and Records:

Animals were examined each day by the technicians and all abnormalities were reported immediately. A weekly record was kept of animal weights, injection volumes and gross observations. Formal reports reflecting the results of the initial and supplementary studies were submitted upon their completion, and status reports have been submitted monthly commencing with March, 1967. All experimental animals were necropsied after they died or were sacrificed. Organ weights were obtained and selected tissues preserved for histopathological study.

Results:

The objective of this trial was to investigate the toxicity of repeated injections of seven commonly used preservatives and to measure the degree of carcinogenicity of each compound. These objectives were carried out in that the acute, subacute and maximum tolerated doses were fairly well established for each drug tested.

Toxicity:

Only three major criteria will be considered for assaying toxicity. These are:

1. Survival time
2. Weight gains
3. Drug-related organ pathology

1. Survival time

The first criterion is met in Table 5 which details the monthly and cumulative rat mortality. It clearly shows that for the first nine months there was little mortality in any group but the positive control (where deaths were principally due to rapid tumor growth). The mortality for all other groups was less than 1% for this period. By the end of the 12-month treatment period the mortality was still very low ranging from 1.5 to 2.0%. It was during the last five months that the mortality increased. In the negative and vehicle controls the range varied between 5.8% to 8.3% while in test-drug groups it varied from 4.0% to 9.0%. Merthiolate was highest with 9.0%, while Benzethonium Chloride and Ethylene Chlorohydrin both had a mortality of 7.5%. There was a fairly even distribution of deaths except for the bronchopneumonia seen in the Merthiolate treated rats (Fuller details later).

2. Weight gains

Weekly weight determinations were made of each animal and the results of these body weight observations are summarized in Table 6 for the 12-month period and in Table 7 for the results at the end of 18 months. For the 12-month period it would appear that only three compounds caused any retardation of weight gains as compared to the untreated and vehicle controls. Benzethonium Chloride has an average retardation

TABLE 5

MONTHLY AND CUMULATIVE RAT MORTALITY

Treatment Group	MONTH OF TREATMENT												POST TREATMENT						Total Number Started	12 MONTHS		18 MONTHS	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18		Total Mortality	% Mortality	Total Mortality	% Mortality
Benzethonium Chloride					1				1		1		1	3	2		3	3	200	3	1.5	15	7.5
Ethylene Chlorohydrin	1										1	2		2	3		4	2	200	4	2.0	15	7.5
Ethylene Glycol		1									1	2		1	1	2	2		200	4	2.0	10	5.0
Merthiolate				1					1	1			1	1	1		9	3	200	3	1.5	18	9.0
Methyl Paraben			1			1			1		2		1	1	1	3		2	200	5	2.5	13	6.5
Phenol Red	1			1			1					1		2	1		4	1	200	4	2.0	12	6.0
Pyridine							1	2					1	2			1	1	200	3	1.5	8	4.0
CONTROLS Negative (no treatment)				1		1				1		1				2	1		120	4	2.0	7	5.8
CONTROLS Vehicle (saline)		2									1	1	1		1	2	2		120	4	2.0	10	8.3
CONTROLS Positive (Ni_3S_2)	1			1	2	21	10	18	24	13	12	18	12	9		3			160	120	75.0	144	90.0

- 11 -

TABLE 6

Comparative Mean Weights of the Highest Dosage Group of Test Compounds

End of Treatment (12 months)

Compound	Approx. Mean Age (wks)	Weeks on test	Mean Wt. in Grams				Final Body Wt. % Control			
			No. of Rats	Male	No. of Rats	Female	♂ NC	♂ VC	♀ NC	♀ VC
egative ontrol	59	53	49	406	50	247		96		94
ehicle ontrol	58	53	46	423	50	262	104		106	
nzethonium nloride	57	51	40	333	40	233	82	79	94	89
ylene nlorohydrin	58	52	30	454	28	265	112	107	107	101
hylene lycol	59	53	30	416	29	259	102	98	105	99
niolate	57	53	30	365	28	234	90	86	95	89
ıyl ıraben	57	51	40	423	38	264	104	100	107	101
ienol id	60	53	30	443	30	272	109	105	110	104
ridine	59	53	29	357	28	234	88	84	95	89

TABLE 7

Comparative Mean Weights of the Highest Dosage Group of Test Compound

18 Months After Start of Treatment

Compound	Approx. Mean Age (wks)	Weeks on test	Mean Wt. in Grams				Final Body Wt. % Control			
			No. of Rats	Male	No. of Rats	Female	♂ NC	♂ VC	♀ NC	♀ VC
Negative Control	84	78	47	430	46	310		101		96
Vehicle Control	84	78	46	426	44	322	99		104	
Benzethonium Chloride	84	78	19	372	19	281	87	87	91	87
Ethylene Chlorohydrin	84	78	29	439	26	331	102	103	107	103
Ethylene Glycol	84	78	28	434	28	324	101	102	105	101
Merthiolate	84	78	26	331	25	249	77	78	80	
Methyl Paraben	84	78	29	432	27	314	100	101	101	98
Phenol Red	84	78	30	421	27	305	98	99	98	95
Pyridine	84	78	29	420	28	304	98	99	98	94

of weight gained of 14% (6-21%). Pyridine averaged 11% (5-16%) while Merthiolate at its highest dose showed a decrease of 10% (5-14%). These figures were compiled only for the highest dose levels of all compounds. At lower doses the retardation of weight gains were less significant.

The 18 month compilation shown in Table 7 shows that there was a good recovery almost to normal by the animals in the Pyridine group but that the weight gains by the Merthiolate and Benzethonium groups were still retarded. Merthiolate was the most affected with weight retardation of 22% (20-23%), while Benzethonium Chloride recovered slightly to end with a weight lowering of 12% (9-13%).

3. Drug-related organ pathology

During the examination of about 2,000 rats a great variety of pathology was observed. The most frequent of these were mild changes in the liver, kidneys, heart and lungs. Only in the Merthiolate treated animals were the lesions in the lungs numerous or severe enough to warrant comment (See Table 8). Here only disease incidence in the high dose of each compound is recorded. The three compounds chosen had the highest incidence of bronchopneumonia and in comparision with the controls it is evident that Merthiolate had a damaging effect on the lung or its defense apparatus. Since the death rate in this group paralleled the deaths in the other compounds, it must be concluded that the damage was slight, continuous and perhaps cumulative. The incidence of pneumonia within the four dose levels of the Merthiolate group was dose-related.

Carcinogenicity:

The outstanding result was the occurrence of 26 sarcomas at the injection site of Benzethonium Chloride out of 200 injected animals (13%). All the other test compounds had from two to four such tumors (1% to 2%). This is strongly correlated with the high incidence of granulomatous reactions to the subcutaneous injection of the compound. This response was dose related and at the highest dose the indurations persisted for 10 to 12 months. These sarcomas were principally fibrosarcomas showing very little tendency to metastasize but grew steadily to a larger size. The majority of these tumors developed during the last 9 months of the trial.

TABLE 8

INCIDENCE OF BRONCHOPNEUMONIA
(18 Months)

(High Level of Compounds Compared with Vehicle and Negative Controls)

Treatment Group	Total Number of Animals	No. of Animals with Bronchopneumonia		Percentage of Animals with Bronchopneumonia	
		Gross Pathology	Histopathology	Gross Pathology	Histopathology
Negative Control	120	5	16	4	13
Vehicle Control	120	3	9	3	8
Benzethonium Chloride	80	2	3	3	4
Ethylene Chlorohydrin	80	3	2	4	3
Merthiolate	80	39	48	49	60

The incidence of other tumors was carefully recorded. Each animal on trial was autopsied either at 12 months or at 18 months as planned. All spontaneous deaths, moribund animals and those showing pathology or abnormal organ weights were histologically examined in addition to those chosen for routine examination. Every animal in the highest dose level was so processed. This led to the accumulation of a large number of incidental tumor findings.

Mammary fibroadenomas were encountered within each group and the incidence usually varied between 2% and 5%. Only the Methyl Paraben group showed an incidence of 8%.

Uterine polyps were encountered in many rats and the incidence varied from 4% to 11% in the test group as compared to 10% in the controls.

Pituitary adenomas occurred in many groups but only Ethylene Chlorohydrin had seven in the 100 females with none occurring in the males. Of the 18 pituitary adenomas seen in this study 15 occurred in females.

Of the eight adrenal tumors seen six occurred in males but no test group had a significant number.

Leukemias were discovered by damage to liver, and enlargement of the lymph glands and spleen. Seventeen such cases were found and 15 of these occured in females.

The tables showing the tumor types, location, size, metastases are grouped for each of the test compounds.

TABLE 9

Tumor Incidence and Location

Treatment	% of Tumor Bearing Rats* (All dose levels included)		Tumor Location ** (All dose levels included)					
			Male ***		Female			
	Male	Female	Injection Site	Other	Injection Site	Mammary	Uterine	Other
Negative Control	10	12	0/50	7/50	0/50	1/50	5/50	7/50
Vehicle Control	6	14	0/50	3/50	0/50	3/50	5/50	8/50
Benzethonium Chloride	19	18	16/100	6/100	10/100	5/100	4/100	3/100
Ethylene Chlorohydrin	3	16	2/100	1/100	0/100	3/100	6/100	13/100
Ethylene Glycol	5	12	2/100	4/100	0/100	5/100	11/100	6/100
Merthiolate	6	10	2/100	4/100	2/100	2/100	8/100	5/100
Methyl Paraben	5	17	2/100	3/100	1/100	8/100	8/100	9/100
Phenol Red	7	10	2/100	5/100	0/100	3/100	11/100	8/100
Pyridine	3	5	2/100	1/100	0/100	3/100	7/100	2/100

* Excluding - Testicular interstitial cell tumors and uterine polyps.
** Some rats had more than one tumor type.
*** Excluding testicular tumors.

TABLE 10

TUMOR INCIDENCE AND LOCATION

Compound	Pituitary (Adenoma)			Adrenal			Blood (Leukemia)		
	Male/Female		Tumor Bearing/No. of Rats	Male/Female		Tumor Bearing/No. of Rats	Male/Female		Tumor Bearing/No. of Rats
Negative Control	0	1	1/120	1	0	1/120	0	2	2/120
Vehicle Control	1	1	2/100	1	0	1/100	0	1	1/100
Benzethonium Chloride	0	0	0/200	1	0	1/200	0	1	1/200
Ethylene Chlorohydrin	0	7	7/200	0	0	0/200	1	4	5/200
Ethylene Glycol	0	0	0/200	2	1	3/200	0	2	2/200
Merthiolate	0	0	0/200	0	1	1/200	0	1	1/200
Methyl Paraben	2	2	4/200	0	0	0/200	0	1	1/200
Phenol Red	0	3	3/200	1	0	1/200	1	2	3/200
Pyridine	0	1	1/200	0	0	0/200	0	1	1/200
Totals	3	15	18/1620	6	2	8/1620	2	15	17/1620

TABLE 11

TUMOR INCIDENCE

TEST COMPOUND: NEGATIVE CONTROL

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	0	50	5	10					1	2	0	0	4	8
B	0	50			9	18					1	2	8	16
							14	14	1	1	1	1	12	12

* Excluding testicular tumors.

** Some animals had more than one tumor type.

TABLE 11A

NEGATIVE CONTROL - 100 Rats

Tumor Bearing Animals (excluding testicular tumors)

Group	Sex	Dose ml	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor Testes + or -	Other Tumors
A	♂	0	11		483	D	94	340	Adenocarcinoma	Kidney Liver	-	-	+	No	none	-	-
A	♂	0	13		537	RS	114	439	Fibrosarcoma	rt. armpit	-	4.34	-	No	none	+	Pheohromocytoma & lipoma
A	♂	0	44		537	RS	78	439	Papilloma	skin flank	2x2	1.94	-	No	keratin	+	-
A	♂	0	47		537	RS	84	479	Fibroadenoma	L. ear	3x2	-	-	No	none	+	-
A	♂	0	56		537	RS	87	370	Adenocarcinoma	Abdomen	17x13	2.26	+	No	slight	+	-
B	♀	0	62		537	RS	82	260	Adenoma, pituitary	Pituitary	Small		-	No	none		uterine polyp.
B	♀	0	65		304	D	88	154	Papilloma, bladder	Bladder	-	-	-	No	none		
B	♀	0	72		537	RS	94	251	Polyp, uterine	Uterus	-	-	-	No	none		
B	♀	0	87		537	RS	100	300	Polyp, uterus	Uterus	-	-	-	No	none		Papilloma on nose
B	♀	0	93		537	RS	100	362	Adenocarcinoma, mammary	mammae		1.2	-	No	none		-
B	♀	0	94		537	RS	94	240	Leukemia, lymphocytic	Spleen	-	-	-	No	none		-
B	♀	0	95		537	RS	90	224	Leukemia, lymphocytic	Spleen	-	-	-	No	none		uterine polyp. / bladd cance
B	♀	0	96		537	RS	92	296	Carcinoma, Squamous-skin	vagina	Small	-	-	No	none		-
B	♀	0	119		537	RS	96	335	Polyp, uterine	Uterus	Small	-	-	No	none		-

TABLE 12

TUMOR INCIDENCE

TEST COMPOUND: VEHICLE CONTROL (SALINE)

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	.25	50	3	6					0	0	0	0	3	6
B	.25	50			9	18			0	0	3	6	6	12
							12	12	0	0	3	3	9	9

* Excluding testicular tumors.

** Some animals had more than one tumor type.

TABLE 13

Tumor Bearing Animals (excluding testicular tumors)

VEHICLE CONTROL (SALINE) - 100 Rats

Group	Sex	Dose ml	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor Testes + or -	Other Tumors
A	♂	0.25	23	106	545	RS	90	437	Adenoma, lung	Lung	Small	-	-	-	none	+	
A	♂	0.25	29	106	545	RS	86	448	Pheochromocytoma	Adrenal	Small	-	-	-	none	+	-
A	♂	0.25	31	106	546	RS	78	442	Adenoma, pituitary	Pituitary	Small	-	-	-	none	+	-
B	♀	0.25	63	106	541	RS	72	302	Polyp, uterine	Uterus	Small	-	-	-	none		
B	♀	0.25	77	106	541	RS	66	396	Luteoma, ovarian	Ovary	Small	-	-	-	none		
B	♀	0.25	82	106	541	RS	69	337	Fibroadenoma, uterine	Uterus		25.28					mesothelioma lung-adenoma
B	♀	0.25	89	106	541	RS	69	350	Leukemia	Liver Spleen	-	-	+	-	none		uterine polyp.
B	♀	0.25	93	106	541	RS	78	258	Adenoma, pituitary	Pituitary	Small	-	-	-	none		
B	♀	0.25	106	106	541	RS	76	390	Fibroadenoma, mammary	rt. side mammae		12.96					
B	♀	0.25	114	106	541	RS	76	300	Fibroadenoma, mammary	lt. side flank		48.82	-	-	none		
B	♀	0.25	116	106	541	RS	78	348	Polyp., uterine	Uterus	Small	-	-	-	none		
B	♀	0.25	119	106	541	RS	78	338	Fibroadenoma, mammary	rt. side mammae		134.0	-	-	none		uterine polyp.

TABLE 14

TUMOR INCIDENCE

TEST COMPOUND: BENZETHONIUM CHLORIDE

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	3.0	80	11	28	10	25	21	26	16	20	2	3	6	8
B	1.0	60	6	20	4	13	10	17	8	13	2	3	3	5
C	0.3	40	2	10	3	15	5	13	2	5	1	3	3	8
D	0.1	20	0	0	1	10	1	5	0	0	1	5	0	0

* Excluding testicular tumors.

** Some animals had more than one tumor type.

COMPOUND: BENZETHONIUM CHLORIDE - 700 Rats

TABLE 15

Group	Sex	Dose mg/kg	Animal No.	No. of Rx	Exp. Time (days)	Fate*	BW (gms)	BW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Anat. Necropsy	Tumor Tested + or -	Other tumors
A	♂	3.0	3	105	553	RS	106	408	Adenoma	Thyroid			-	-	nonn		-
A	♂	3.0	7	105	536	RS	94	374	Fibrosarcoma (low grade)	Rt. Flank		44.62	-	+	sl.		Adrenal Adenoma
A	♂	3.0	8	105	521	D	103	308	P.M.D. (Illness or Fibrosarcinoma) no tissues sections	L. Flank	6.5x 6.5	about 28 g		+			
A	♂	3.0	15	105	536	RS	126	346	Fibrosarcoma	L. Hip		38.00	-	+	sl.	-	-
A	♂	3.0	16	105	536	RS	122	294	Fibrosarcoma	L. Flank		76.91	-	+	sl.	-	-
A	♂	3.0	19	105	536	RS	129	408	Fibrosarcoma	Rt. Flank		66.21	-	+	none	+	-
A	♂	3.0	20	105	536	RS	124	414	Fibrosarcoma	L. Flank		47.61	-	+	none	+	-
A	♂	3.0	22	105	536	RS	122	316	Fibrosarcoma	L. Flank		24.66	-	+	mod.	+	-
A	♂	3.0	24	105	486	D	110	87	Squamous Cell Carcinoma	L. Side Esoc. Throat		3.43	+	-	mod.	-	-
A	♂	3.0	33	105	536	RS	124	385	Fibrosarcoma	Rt. Hip		19.02	-	+	none	+	-
A	♂	3.0	38	105	536	RS	124	436	Fibrosarcoma	Rt. Flank		1.38	-	+	none	+	-
A	♀	3.0	47	105	536	RS	102	286	Fibrosarcoma	Rt. Flank		30.79	-	+	none		Uterine Polyp
A	♀	3.0	51	105	536	RS	93	312	Fibroadenoma, Mammary	Chest, L. Axa		17.08	-	-	none		-
A	♀	3.0	57	105	415	S-M	106	224	Fibrosarcoma	L. Flank		15.50	-	+	none		-
A	♀	3.0	62	105	536	RS	111	331	Fibrosarcoma	L. Flank	1.5x1 cm		-	+	none		Uterine Polyp
A	♀	3.0	68	105	415	RS	109	218	Fibrosarcoma	Chest		18.93	-	+	none		-
A	♀	3.0	69	105	536	RS	101	366	Fibrosarcoma	Rt. Flank		6.00	-	+	none		-
A	♀	3.0	70	105	553	RS	108	290	Fibrosarcoma	Flank		28.27	-	+	none		-
A	♀	3.0	73	105	380	D	93	252	Fibroadenoma, Mammary	Nuck		36.00	-	-	none	-	-
A	♀	3.0	74	105	512	D	103	278	Fibroma	Rt. Flank	5.5x 7.0		-	+	sl.		-
A	♀	3.0	75	105	360	RS	99	219	Adenoma	Lung			-	-	none	-	-
B	♂	1.0	85	105	536	RS	128	434	Fibrosarcoma	L. Flank		2.18	-	+	none	+	-
B	♂	1.0	86	105	536	RS	122	413	Fibrosarcoma	L. Hip		7.15	-	+	none	+	-
B	♂	1.0	89	105	519	D	103	500	Fibrosarcoma	L. Flank		287.00	-	+	mod.	-	-
B	♂	1.0	97	105	552	RS	134	470	Fibroma	Rt. Flank		2.30	-	-	none	-	-
B	♂	1.0	99	105	525	D	120	406	Lung Squamous Cell Carcinoma, (1)	Lip				-	mod.	+	Lip-papilloma
B	♂	1.0	103	105	474	D	123	432	Fibromarcoma	Lower Rt. Side		143.00	+	+	sl.	-	-
B	♀	1.0	114	105	536	RS	106	330	Fibroadenoma, Mammary	L. Chest		3.77	-		none		Uterine Polyp
B	♀	1.0	116	105	536	RS	111	370	Fibrosarcoma	Rt. Flank	2.5 x2.5	Eaten		+	mod.		-
B	♀	1.0	120	105	536	RS	98	398	Fibrosarcoma	Perioneal	2/4.5 cm			+	sl.		
B	♀	1.0	125	105	536	RS	93	282	Fibrosarcoma	Chest, Throat		103.0/	-		mod.		Uterine Fibroid
C	♂	0.3	141	105	435	M-S	242	437	Fibroma	Back		8.10	-	-	none	-	Skin papilloma
C	♂	0.3	160	105	536	RS	102	436	Fibrosarcoma	Rt. Flank		160.00		+	mod.	+	-
C	♀	0.3	164	113	576	M-S	150	375	Fibroadenoma, Mammary	Rt. Thoracic Region	3/2 cm	6.08	-	-	none		-
C	♀	0.3	173	105	469	D	94	261	Leukemia	Whole Body Involved			-	-	none	-	
C	♀	0.3	175	105	536	RS	94	295	Squamous Cell Carcinoma (Ear canal)	Perioneal Region	2.1 cm	7.29	-	+	sl.	-	-
D	♀	0.1	198	105	536	RS	101	300	Adenocarcinoma, Mammary	Rt. Perioneal	4/3 cm	11.48	-	-	mod		-

TABLE 16

TUMOR INCIDENCE

TEST COMPOUND: ETHYLENE CHLOROHYDRIN

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	10.0	80	1	3	7	18	8	10	1	1	1	1	6	8
B	3.0	60	1	3	9	30	10	17	1	2	2	3	7	12
C	1.0	40	1	5	4	20	5	13	0	0	0	0	5	13
D	0.3	20	0	0	1	10	1	5	0	0	0	0	1	5

* Excluding testicular tumors.

** Some animals had more than one tumor type.

Tumor Bearing Animals (excluding testicular tumors)

COMPOUND: ETHYLENE CHLOROHYDRIN - 200 Rats

TABLE 17

Group	Sex	Dose mg/kg	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor Testes + or -	Other Tumors
A	♂	10.0	30	105	552	RS	118	498	Fibroma	R. Flank	3/2 cm		-	+	none	+	
A	♀	10.0	41	113	597	RS	133	300	Polyp, uterine	Uterus	small		-	-	none		
A	♀	10.0	46	113	597	RS	162	365	Leukemia	Spleen	general		+	-	none		
A	♀	10.0	54	105	553	RS	110	355	Fibroadenoma, Mammary	Lower Abdomen		4.88	-	-	none		
A	♀	10.0	65	105	553	RS	86	284	Polyp, uterine	Uterus	small		-	-	none		
A	♀	10.0	68	105	553	RS	96	268	Adenoma, pituitary	Pituitary	small		-	-	none		
A	♀	10.0	70	105	553	RS	112	264	Adenoma, pituitary	Pituitary	small		-	-	none		
A	♀	10.0	73	105	553	RS	91	161	Adenoma, pituitary	Pituitary	moderate		-	-	none		
B	♂	3.0	97	105	504	D	135	395	Fibroma	Back		1.41	-	+	none	+	
B	♀	3.0	111	105	551	RS	91	378	Fibroadenoma, polyp	Uterus	1.x.7		-	-	none		
B	♀	3.0	113	105	460	D	114	286	Leukemia, lymphatic	Whole Body	-	-	+	-	none		
B	♀	3.0	119	105	388	D	108	222	Adenoma, pituitary	Pituitary	-	-	-	-	none		
B	♀	3.0	120	105	551	RS	97	308	Adenoma, pituitary	Pituitary	-	-	-	-	none		
B	♀	3.0	121	105	550	RS	101	298	Polyp, uterine	Uterus	-	-	-	-	none		
B	♀	3.0	127	105	551	RS	110	354	Fibroadenoma, Mammary	L. Side		13.6	-	-	none		
B	♀	3.0	128	98	341	D	106	302	Liposarcoma	Abdomen Cavity		116.	-	-	none		
B	♀	3.0	130	105	550	RS	108	364	Fibroadenoma, Mammary	L. Chest	5/4cm	28.94	-	-	none		
B	♀	3.0	135	105	550	RS	108	298	Lymphocytic Leukemia, Lymphosarcoma	Spleen Liver	general		+	-	none		
C	♂	1.0	150	105	549	RS	127	406	Lymphocytic Leukemia	Spleen	general		+	-	none	+	
C	♀	1.0	172	105	550	RS	99	322	Adenoma, Pituitary	Pituitary	small		-	-	none		
C	♀	1.0	173	105	550	RS	94	291	Adenoma, Pituitary	Pituitary	small		-	-	none		
C	♀	1.0	174	105	504	D	102	196	Lymphatic Leukemia	Limb Uterus	general		+	-	none		
C	♀	1.0	178	105	550	RS	90	314	Polyp, uterine	Uterus	small		-	-	none		
D	♀	0.3	194	105	549	RS	114	306	Polyp, uterine	Uterus	small		-	-	none		

TABLE 18

TUMOR INCIDENCE

TEST COMPOUND: ETHYLENE GLYCOL

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	1000.0	80	2	5	6	15	8	10	2	3	2	3	8	10
B	300.0	60	1	3	9	30	10	17	1	2	2	3	7	12
C	100.0	40	2	10	3	15	5	13	0	0	1	3	4	10
D	30.0	20	0	0	1	10	1	5	0	0	1	5	1	5

* Excluding testicular tumors.

** Some animals had more than one tumor type.

Tumor Bearing Animals (excluding testicular tumors)

COMPOUND: ETHYLENE GLYCOL - 200 Rats

TABLE 19

Group	Sex	Dose mg/kg	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor testes + or -	Other Tumors
A	♂	1000.0	5	113	590	RS	230	498	Fibrosarcoma	Rt. Flank		10.85	-	+	none	+	Pheochrom.
A	♂	1000.0	21	105	515	D	108	428	Fibrosarcoma	Rt. Flank				+	none	+	
A	♀	1000.0	44	105	591	RS	143	305	Fibroadenoma, Mammary	Throat, Chest		68.73	-	-	none		Uterine Polyp
A	♀	1000.0	62	105	553	RS	80	350	Squamous Epithelioma	Face		3.29	-	-	none		Uterine Polyp
A	♀	1000.0	65	105	553	RS	93	248	Leukemia	Spleen	general		+	-	none		
A	♀	1000.0	69	105	553	RS	98	264	Fibroadenoma, Mammary	Rt. Side Groin		1.65 5.66	-	-	none		Uterine Polyp
A	♀	1000.0	71	105	553	RS	82	284	Polyp, Uterine	Uterus	small		-	-	none		
A	♀	1000.0	72	105	367	RS	102	267	Papilloma, Trachea	Trachea	-	-	-	-	none		
B	♂	300.0	102	105	551	RS	106	398	Mammary Adenocarcinoma	Post-abdomen	4/3 cm		-	-	none	+	
B	♀	300.0	111	113	589	RS	135	292	Adenoma, Adrenal	Adrenals	small		-	-	sl.		
B	♀	300.0	117	105	551	RS	94	373	Polyp, Uterine	Uterus	small		-	-	none		
B	♀	300.0	119	105	551	RS	96	318	Polyp, Uterine	Uterus	small		-	-	none		
B	♀	300.0	123	101	350	D	87	240	Carcinoma, Undifferentiated	Throat		34.04	-	-	none		
B	♀	300.0	126	105	435	D	78	234	Fibrosarcoma	Ovary Bladder Uterus		82.00	+	-	none		
B	♀	300.0	128	105	551	RS	86	326	Polyp, Uterine	Uterus	small		-	-	none		
B	♀	300.0	133	105	551	RS	73	329	Polyp, Uterine	Uterus	small		-	-	none		
B	♀	300.0	137	105	551	RS	98	315	Polyp, Uterine	Uterus	small		-	-	none		
B	♀	300.0	140	105	551	RS	78	326	Fibroadenoma, Mammary	L. Cervical L. Shoulder		54.99	-	-	none		
C	♂	100.0	145	105	546	RS	102	408	Adenoma, Cortical	L. Adrenal	small		-	-	none	+	
C	♂	100.0	150	105	546	D	72	230	Mesothelioma	Lungs Pleura	0.3/ 0.2 cm		-	-	sl.	+	
C	♀	100.0	164	105	545	RS	77	374	Polyp, Uterine	Uterus	small		-	-	none		
C	♀	100.0	177	105	545	RS	98	321	Leukemia, lymphatic	Spleen	general		+	-	none		
C	♀	100.0	180	105	545	RS	88	384	Fibroadenoma, Mammary	Mammary Gland	small		-	-	none		
D	♀	30.0	198	105	545	RS	87	352	Fibroadenoma, Mammary	Post Mammary Glands	small		-	-	none		Polyp Uterine

TABLE 20

TUMOR INCIDENCE

TEST COMPOUND: MERTHIOLATE

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	1.0	80	4	10	7	18	11	14	4	5	0	0	11	14
B	0.3	60	2	7	6	20	8	13	1	2	3	5	6	10
C	0.1	40	0	0	3	15	3	8	0	0	0	0	3	8
D	.03	20	0	0	0	0	0	0	0	0	0	0	0	0

* Excluding testicular tumors.

** Some animals had more than one tumor type.

Tumor Bearing Animals (excluding testicular tumors)

COMPOUND: MERTHIOLATE - 200 Rats

TABLE 21

Group	Sex	Dose ml	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor testes + or -	Other Tumors
A	♂	1.0	4	105	431	D	116	216	Squamous Cell Carcinoma - Ear	Rt. Side Head		16.66	-	-	-	-	
A	♂	1.0	6	105	516	RS	126	327	Fibroma	Chest		10.09	-	+	-	-	
A	♂	1.0	8	105	516	MS	106	445	Fibrosarcoma	Chest, L. Armpit		23.25	-	+	-	-	
A	♂	1.0	39	105	407	RS	100	360	Adenoma	Lung	1.5 m		-	-	-	-	
A	♀	1.0	48	105	516	RS	89	250	Fibroadenoma	Uterus		1.5	-	-	-		
A	♀	1.0	53	105	516	RS	143	253	Polyp, uterine	Uterus			-	-	-		
A	♀	1.0	56	105	516	MS	108	358	Fibrosarcoma	Rt. Flank & Hip		26.95	-	+	-		
A	♀	1.0	66	105	516	RS	78	236	Polyp, uterine	Uterus	Small		-	-	-		
A	♀	1.0	71	105	516	MS	112	398	Fibroma	Skin Abdomen	12x9	216.0	-	+	-		
A	♀	1.0	73	105	516	RS	102	264	Adenoma-neuroblastoma	Adrenal		5.02	-	-	-		
A	♀	1.0	77	105	516	RS	94	232	Papilloma	Bladder	Small		-	-	-		
B	♂	0.3	82	105	516	RS	100	276	Carcinoma	Neck		10.04	-	-	-	+	
B	♂	0.3	96	105	550	RS	119	333	Lipoma	Skin Abdomen		38.86	-	-	-	+	
B	♀	0.3	111	105	516	MS	104	258	Fibrosarcoma	Abdomen		111.86	-	-	-		uterine polyp
B	♀	0.3	120	105	516	RS	88	260	Polyp, uterine	Uterus	Small		-	-	-		
B	♀	0.3	121	105	516	MS	99	318	Fibroadenoma, Mammary	L. Chest, throat		35.34	-	-			uterine polyp
B	♀	0.3	137	105	516	RS	100	328	Polyp, uterine	Uterus	Small		-	-	-		
B	♀	0.3	138	91	326	D	108	188	(not examined)	Abdomen		Eaten	-	-	-		
B	♀	0.3	140	105	547	RS	126	311	Fibroadenoma, Mammary	Pectoral		7.46	-	-			
C	♀	0.1	162	105	516	RS	90	279	Polyp, uterine	Uterus	Small		-	-	-		
C	♀	0.1	177	105	516	RS	93	272	Polyp, uterine	Uterus	Small		-	-	-		
C	♀	0.1	178	105	516	RS	83	258	Leukemia	Spleen	Generalized		+	-	-		

TABLE 22

TUMOR INCIDENCE

TEST COMPOUND: METHYL PARABEN

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	3.5	80	3	8	6	15	9	11	1	1	4	5	5	6
B	2.0	60	1	3	10	33	11	18	2	3	3	5	8	13
C	1.1	40	1	5	2	10	3	8	0	0	0	0	3	8
D	0.6	20	0	0	5	50	5	25	0	0	1	5	4	20

* Excluding testicular tumors.

** Some animals had more than one tumor type.

Tumor Bearing Animals (excluding testicular tumors)

COMPOUND: METHYL PARABEN - 200 Rats

TABLE 23

Group	Sex	Dose mg/kg	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor Testes + or -	Other Tumors
A	♂	3.5	1	105	556	RS	188	453	Lipoma	Sacrum	6x4cm	31.12	-	-	none	+	
A	♂	3.5	7	105	556	RS	170	408	Fibroma	Rt. Flank		2.64	-	+	none	+	
A	♂	3.5	37	105	556	RS	154	318	Adenoma, Pituitary	Pituitary	small		-	-	none	-	
A	♀	3.5	42	105	479	D	138	386	Mammary Adenosarcinoma	Rt. Side		18.27					
A	♀	3.5	52	105	557	RS	125	264	Adenoma, Pituitary	Pituitary	small		-	-	none		
A	♀	3.5	59	91	321	D	138	259	Mesothelioma	Abdomen or Lymph gl.		5.00	+	-	moderate		
A	♀	3.5	60	105	557	RS	123	314	Fibroadenoma, Mammary	L. Flank	3x1 1/2 cm	3.08	-	-	none		
A	♀	3.5	71	105	557	RS	121	314	Fibroadenoma, Mammary	Thoracic		9.10	-	-	none		Uterine polyp
A	♀	3.5	72	105	366	RS	123	245	Fibroadenoma, Mammary	L. Side		28.00	-	-	none		
B	♂	2.0	101	105	555	RS	182	526	Fibroma	L. Thoracic	8/6 cm	93.32	-	+	none	+	
B	♀	2.0	112	113	587	RS	148	300	Fibroma	Rt. Flank	1.7/ 1.5cm		-	+	none		
B	♀	2.0	116	70	480	D	148	264	Fibrosarcoma	Throat		52.06	-	-	none		
B	♀	2.0	117	113	587	RS	160	308	Fibroadenoma, Mammary	Mammary Gland	small		-	-	none		
B	♀	2.0	118	113	587	RS	137	294	Uterine Polyp	Uterus	small		-	-	none		
B	♀	2.0	121	113	587	RS	121	329	Lipoma	Mesentery	2/1	1.35	-	-	none		
B	♀	2.0	126	105	555	RS	115	298	Fibroadenoma, Mammary	Mammary Gland		9.12	-	-	none		
B	♀	2.0	134	109	555	RS	127	296	Uterine Polyp	Uterus	small		-	-	none		Adenoma Parathyroid
B	♀	2.0	135	105	555	RS	120	362	Carcinoma, Mammary	Rt. Thoracic	6/5	113.0	-	-	moderate		Uterine polyp
B	♀	2.0	136	105	555	RS	120	297	Uterine Polyp	Uterus	small		-	-	none		
B	♀	2.0	138	105	555	RS	125	276	Adenoma, Pituitary	Pituitary	small		-	-	none		
C	♂	1.1	153	105	554	RS	125	248	Adenoma, Pituitary	Pituitary	small		-	-	none	+	
C	♀	1.1	166	113	582	RS	140	360	Uterine Polyp	Uterus	small		-	-	none		
C	♀	1.1	169	105	550	RS	143	348	Leukemia, Lymphatic	Spleen	generalized			-	none		
D	♀	0.6	191	113	582	RS	139	312	Lipoma	Mesentery	small		-	-	none		
D	♀	0.6	194	105	550	RS	124	242	Uterine Polyp	Uterus	small		-	-	none		
D	♀	0.6	195	105	376	D	117	246	Fibroadenoma, Mammary	Neck	2.5x 2.5x 2.5cm	11.95	-	-	none		
D	♀	0.6	196	53	211	D	120	171	Papilloma	Bladder	small		-	-	none		
D	♀	0.6	200	105	550	RS	113	319	Uterine Polyp	Uterus	small		-	-	none		

TABLE 24

TUMOR INCIDENCE

TEST COMPOUND: PHENOL RED

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	1.0	80	2	5	4	10	6	8	0	0	1	1	7	9
B	0.56	60	4	13	8	27	12	20	2	3	2	3	10	17
C	0.32	40	1	5	1	5	2	5	0	0	0	0	3	8
D	0.18	20	0	0	2	20	2	10	0	0	0	0	2	10

* Excluding testicular tumors.

** Some animals had more than one tumor type.

Tumor Bearing Animals (excluding testicular tumors)

COMPOUND: PHENOL RED - 200 Rats

TABLE 25

Group	Sex	Dose mg/kg	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor Testes + or -	Other Tumors
A	♂	1.0	7	105	547	RS	242	413	Pheochromocytoma	Adrenal	-	-	-	-	none	+	
A	♂	1.0	33	105	547	RS	218	474	Leukemia, lymphatic	Liver Spleen Lymph nodes	-	-	+	-	none	+	
A	♀	1.0	42	118	604	RS	148	336	Adenocarcinoma	Uterus	-	-	-	-	none		
A	♀	1.0	66	105	548	RS	142	306	Leukemia, lymphatic	Spleen Liver	-	-	-	-	none		Pituitary adenoma
A	♀	1.0	73	105	519	MS	149	374	Fibroadenoma, Mammary	L. Thoracic		11.67	-	-	none		
A	♀	1.0	78	105	366	RS	150	303	Arrhenoblastoma	Ovary	-	.27	-	-	none		Adenoma thyroid
B	♂	0.56	83	118	603	RS	267	490	Adenocarginoma, Mammary	L. Flank	8/6 cm	62.03	-	-	none	+	
B	♂	0.56	94	105	519	MS	174	395	Fibroma	Rt. Flank		75.15	-	+	none	+	
B	♂	0.56	101	105	519	MS	247	524	Fibroma	L. Thoracic	8/4 cm	74.18	-	+	none	+	
B	♂	0.56	109	105	547	RS	226	453	Adenocarcinoma, Mammary	L. Flank	0.3/ 0.2 cm		-	-	none	+	
B	♀	0.56	111	118	602	RS	160	294	Uterine, polyps	Uterus	small		-	-	none		Pituitary adenoma
B	♀	0.56	116	118	602	RS	163	305	Uterine, polyps	Uterus	2x2		-	-	none		
B	♀	0.56	121	118	602	RS	158	280	Uterine, polyps	Uterus	small		-	-	none		
B	♀	0.56	125	105	546	RS	132	268	Adenoma, pituitary	Pituitary		120 mg	-	-	none		
B	♀	0.56	126	105	546	RS	145	328	Papilloma	Nose	small		-	-	none		
B	♀	0.56	129	105	546	RS	80	332	Uterine, polyp	Uterus		4gr	-	-	none		
B	♀	0.56	134	105	546	RS	85	314	Fibroid, uterus	Uterus	small		-	-	none		
B	♀	0.56	138	105	546	RS	90	266	Leukemia	Spleen	general		+	-	none		Uterine polyp
C	♂	0.32	160	105	543	RS	82	444	Lipoma		small			-	none	+	Uterine polyp
C	♀	0.32	169	105	543	RS	80	348	Uterine, polyps	Uterus	small		-	-	none		
D	♀	0.18	193	118	416	D	168	308	Fibrosarcoma	Uterus	9.0x 7.5x 3.5 cm		+	-	moderate		
D	♀	0.18	196	105	571	RS	148	292	Uterine, Carcinoma	Uterus	small		-	-	none		

TABLE 26

TUMOR INCIDENCE

TEST COMPOUND: PYRIDINE

Group	Dose ml or mg/kg	Animal Tested	Tumor Bearing Rats*						Tumor Types**					
			Male		Female		Both		fibroma or sarcoma		Mammary		Others	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	100.0	80	2	5	2	5	4	5	2	3	0	0	2	3
B	30.0	60	1	3	7	23	8	13	0	0	2	3	6	10
C	10.0	40	0	0	2	10	2	5	0	0	0	0	2	5
D	3.0	20	0	0	1	10	1	5	0	0	1	5	0	0

* Excluding testicular tumors.

** Some animals had more than one tumor type.

Tumor Bearing Animals (excluding testicular tumors)

COMPOUND: PYRIDINE - 200 Rats

TABLE 27

Group	Sex	Dose mg/kg	Animal No.	No. of Rx	Exp. Time (days)	Fate*	IBW (gms)	FBW (gms)	TUMOR TYPE	Tumor Site	Tumor Size	Tumor wt. (g)	Metastases + or -	Tumor at Site of Inj. + or -	Amt. Necrosis	Tumor Testes + or -	Other Tumors
A	♂	100.	3	105	542	RS	95	393	Fibrosarcoma	L. Hip		29.36	-	+	none	+	
A	♂	100.	31	105	542	RS	107	360	Fibrosarcoma	Rt. Hip	4x3 1/2	11.70	-	+	none	+	
A	♀	100.	64	105	543	RS	88	318	Polyp, uterine	Uterus	small		-	-	none		
A	♀	100.	69	105	543	RS	90	316	Polyp, uterine	Uterus	small		-	-	none		
B	♂	30.0	85	115	584	RS	210	434	Adenoma - lung	Lung	0.4x 0.3		-	-	none	+	
B	♀	30.0	111	115	583	RS	129	342	Polyp, uterine	Uterus	small		-	-	none		
B	♀	30.0	112	115	583	RS	135	341	Polyp, uterine	Uterus	small		-	-	none		
B	♀	30.0	115	115	583	RS	124	320	Fibroadenoma, Mammary	Groin	4x3cm	8.81	-	-	none		
B	♀	30.0	119	105	538	RS	103	321	Polyp, uterine	Uterus	small		-	-	none		
B	♀	30.0	125	105	531	D	92	176	Adenoma, pituitary	Pituitary	small		-	-	none		
B	♀	30.0	126	105	538	RS	90	295	Polyp, uterine	Uterus	small		-	-	none		
B	♀	30.0	131	105	539	RS	106	349	Fibroadenoma, Mammary	L. Armpit	2x2		-	-	none		
C	♀	10.0	166	105	538	RS	75	276	Leukemia, lymphatic	Spleen lymph	general			-	none		
C	♀	10.0	176	105	538	RS	102	295	Polyp, uterine	Uterus	small		-	-	none		
D	♀	3.0	196	105	537	RS	100	303	Fibroadenoma, Mammary	L. Flank	5/4cm		-	-	none		

Testicular Tumors in Fischer Rats

In a previous trial at this laboratory, under Contract PH43-63-525, Fischer rats were used in a long term carcinogen trial. Toward the end of the trial, a great deal of information was gathered on the incidence of spontaneous interstitial cell tumors in this strain of rats. Some of the results were reported by Hadidian et al., J. Nat. Cancer Inst. 41:985-1036, 1968. "Both vehicle and untreated control male rats exhibited a progressively increasing proportion of interstitial cell tumors of the testis. This lesion was diagnosed in almost all males autopsied at 600 days" (p. 998).

Incidence of interstitial cell tumors among the vehicle control (VC) and negative control animals (NC) in relation to age:

	90-410 Days		411-530 Days		531-600 Days		600 Days
	NC	VC	NC	VC	NC	VC	VC
ICT	1/25	0/52	7/19	11/45	17/45	62/115	25/26

Jacobs and Huseby (J. Nat. Cancer Inst. 39:303-309, 1967) reported on the spectrum of tumors that arose spontaneously in 102 female and 92 aged Fischer rats. They reported an incidence of 68 percent of interstitial cell tumors. These are Leydig cell tumors, of which many are androgen producing. When large, they may become hemorrhagic, sometimes cystic but rarely show massive necrosis. They make no mention of metastases but do note the ease of transplantation.

Recent Results:

Reference is made to Tables 28 & 29 which includes most of the pertinent data. The following remarks will serve to highlight the important points:

1. Interstitial cell tumors (I.C.T.) of the testis occur with high frequency in male Fischer rats older than 500 days. At 600 days more than 95% of the animals have some tumors and more than 85% have tumors bilaterally.

2. The high incidence was partially due to the method we developed to detect very small tumors macroscopically. After the testes had been fixed in formaldehyde, they were "candled" in the same fashion as egg are examined. A small point of a powerful light was arranged to come out of a 3 cm opening. The testis was then placed over the opening. In a dark room, the testis becomes translucent and very small tumor masses can be detected.

3. There were no instances of invasion of other organs by this tumor. No other tumor types were found in the testis. Occasionally the opposite testis would atrophy despite the fact that it was free of any tumor itself. The hormonal balance in these cases is open for investigation. Within each testis there might be varying degrees of atrophy which had no relation to the presence of an I.C.T. except when it got so large that it caused pressure atrophy.

4. The most outstanding feature in this set of data is the apparent dose-related inhibition of spontaneous I.C.T. by merthiolate. At the highest dose level only 4 out of 27 male rats showed any I.C.T. The incidence of 100% in the negative controls decreased to 14.8% by the methiolate treatment is certainly remarkable. As the dose of merthiolate decreases the incidence of I.C.T. rapidly increases. Even at the lowest dose there is still a significant inhibition in that many cases of I.C.T. are confined to a single testis rather than bilateral.

The inhibition of interstitial cell tumors is not an unrecognized phenomenon. Gunn, Gould and Anderson have written three papers in 1963 and 1964 showing how zinc inhibited calcium-generated interstitial cell tumors. However, this appears to be the first time that inhibition of spontaneous I.C.T. has been reported.

5. It is of great interest to note that of the other 6 compounds only benzethonium has any significant decrease in the I.C.T. incidence. Despite the more pronounced decrease of body weight during treatment, the increased number of irritating injection areas and the increased number of fibromas and fibrosarcomas produced by these compounds they did not have as great an effect on the I.C.T. incidence as did merthiolate.

TESTICULAR TUMORS (ICT) IN FISCHER RATS

588-602 DAYS OLD

Treatment Group	Dose (mg/kg)	No. of Rats	Without ICT	Interstitial Cell Tumors: Only one testes No.	%	Both testes No.	%	Only one or both No.	%
Untreated Control		47	0	6	13	41	87	47	100.0
Vehicle Control		46	1	4	9	41	89	45	97.8
Benzethonium Chl.									
A	3.0	24	5	13	54	6	25	19	79.1
B	1.0	27	6	9	33	12	44	21	77.7
C	0.3	19	2	5	26	12	63	17	89.4
D	0.1	10	0	0	0	10	100	10	100.0
Ethylene Chlorohydrin									
A	10.0	29	1	2	7	26	90	28	96.5
B	3.0	29	1	5	17	23	79	28	96.5
C	1.0	19	0	2	11	17	89	19	100.0
D	0.3	10	2	1	10	7	70	8	80.0
Ethylene Glycol									
A	1000.0	28	0	2	7	26	93	28	100.0
B	300.0	30	1	2	7	27	90	29	96.6
C	100.0	18	1	4	22	13	72	17	94.4
D	30.0	10	2	1	10	7	70	8	80.
Merthiolate									
A	1.0	27	23	3	11.1	1	3.7	4	14.8
B	0.3	28	12	13	46.4	3	10.7	16	57.1
C	0.1	19	3	12	63.1	4	21	16	84.2
D	0.03	11	2	1	9	8	73	9	81.8
Methyl Paraben									
A	3.5	29	1	2	7	26	40	28	96.5
B	2.0	29	2	3	10	24	83	27	93.1
C	1.1	18	2	5	28	11	61	16	88.8
D	0.6	10	1	0	0	9	90	9	90.0
Phenol Red									
A	1.0	30	1	2	7	27	90	29	96.6
B	0.56	27	3	9	33	15	56	24	88.8
C	0.32	19	0	7	37	12	63	19	100.0
D	0.18	10	0	1	10	9	90	10	100.0
Pyridine									
A	100.0	30	1	2	7	27	90	29	96.6
B	30.0	27	1	4	15	22	81	26	96
C	10.0	19	2	6	32	11	58	17	89.4
D	3.0	10	0	5	50	5	50	10	100.0

TABLE 29

TESTICULAR TUMOR DATA SUMMARY

Interstitial Cell Tumors in Fischer Rats

(588–602 Days Old)

Treatment	All Dose Levels Combined					High Dose Only	
	NVT*	NVL/ATR** or ATR/ATR	No. of Animals	Animals with tumors / No. Animals	% Animals with tumors	Animals with tumors / No. Animals	% Animals with tumors
NC negative control	0	0	47	47/47	100	–	100
VC vehicle control	1	1	46	45/46	97.8	–	97.8
I Benzethonium Cl.	13	2	80	67/80	83.8	19/24	79.1
II Ethylene Chlorohydrin	4	4	87	83/87	95.4	28/29	96.5
III Ethylene Glycol	4	4	86	82/86	95.3	28/28	100
IV Merthiolate	40	5	85	45/85	52.9	4/27	14.8
V Methyl paraben	6	2	86	80/86	93.0	28/29	96.5
VI Phenol Red	4	0	86	82/86	95.3	29/30	96.6
V Pyridine	4	1	86	82/86	95.3	29/30	96.6

* No. of animals with no visible tumors in either testis.

** No. of animals with either one atrophic and one NVL testis or with atrophy of both testes.

Remarks on the use of Nickel Sulfide as a positive control:

In the experimental design of this trial, 160 animals were used as positive controls for carcinogenesis. Nickel sulfide was given to these animals in a single injection at doses of 3.3 mg and 10 mg subcutaneously or intramuscularly into the thigh.

The objectives for including a positive control were as follows:

1. To determine how responsive this batch of Fischer rats were to a proven carcinogen.
2. Since previous trials with nickel sulfide had used the intramuscular route and the test drugs were to be injected subcutaneously it was considered worthwhile to have some receive the carcinogen using both routes and at two dose levels as well.
3. Nickel sulfide was chosen in preference to more commonly used carcinogens such as methylcholanthrene because it was not readily excreted in a form that would constitute a carcinogenic hazard either to the personnel or the other animals.
4. Since an untreated control was to be used as a vehicle control, it was considered that a low dose of a known carcinogen might alter the evidence rate of those tumors which arose spontaneously.

The results of the use of the positive control is shown in Tables 30-34. In summary:

(1) One hundred out of 159 animals died bearing tumors during the trial. Only three animals died without neoplasia before the end of the trial.

(2) An additional 40 of the 159 animals had to be killed because of tumor related illness or size of the tumor. All had good sized fibrosarcomas or rhabdomyosarcomas at the injection site.

(3) When the trial was terminated 553 days after the nickel sulfide injections only 15 animals remained in the four groups of positive controls. Two of these had slow growing tumors while another had leukemia but no sarcoma. Two other animals had been subjected to surgery early in the trial by removal of the original tumors. These had failed to reappear. It, therefore, left 10 animals which had not responded

to the injection of nickel sulfide. The possibility always remains as to a technical error in which some of the animals did not receive a full or proper injection.

(4) It is interesting to speculate as to the possibility of leukemia having some precursor which may have interfered with the development of the sarcoma after the nickel injection.

(5) The survival time of all the animals varied as follows:

Group	Average Survival Time in Days	Range
A	311	156-553
B	367	184-543
C	252	140-553
D	292	166-553

(6) It is unfortunate that a lower dose of nickel sulfide had not been selected, since the incidence of typical sarcomas resulting from nickel sulfide injection given by either route was between 94.8% and 97.4%.

(7) The dose relationship is brought out, however, in the figures averaging the first appearance of the tumors. The tumors appeared after 10 mg doses at an average of 131 days for the subcutaneous and 135 days for the intramuscular while at the 3.3 mg dose the averages were 242 days and 217 days. Since nickel sulfide is irritating to the tissue and this inflammatory response persists, it is understandable that the mass would be more readily and earlier recognized subcutaneously.

Conversely, the late recognition of intramuscular tumors would give rise to a shortened period between tumor recognition and death of the host.

(8) The spread of the sarcomas from the injection site is very interesting since it gives rise to such a high incidence of lung metastases. Of the 160 animals originally started, 50 lung metastases were seen. In the four groups of animals which had a tumor at the injection site from 20.5% to 44.1% had metastases to the lung. In some cases there was metastases to the regional lymph glands or even the spleen, but unrecognized or non-existent in the lung. The majority of metastatic cases involved the regional lymph glands and then the lungs. The involvement of the spleen was seen in 38 cases and in various groups, the percentages varied from 23.7% to 28.2%.

(9) It was interesting to compare the survival time of those animals that showed only a primary tumor with animals that had metastases. Group D (3.3 mg im.) was used as an example. Thirty-eight out of the 40 animals started had typical sarcomas.

Twenty-two had a tumor only at the injection site with a survival time of 268.3 days (166-378).

Sixteen had metastases (of which 13 were in the lung). The survival time averaged 325.8 days (219-468).

Metastases would seem to be more related to time in residence rather than to early spread of cells or multiple transfer and deposit of the originally injected material.

Estimates of survival time once metastases had occurred could not be made.

(10) Many of the animals that had metastases to the lung finally died of hemothorax. The erosion of the lung capillaries by the rapidly growing tumor can account for these events.

(11) A number of the sarcomas were biopsied and grew very rapidly when transferred to young Fischer rats. Primary transfer also grew very well in tissue culture. They also survived nitrogen freezing and storage and could be revived readily. Some of these cultures are still in a frozen state and are available for study.

(12) The histology of the sarcomas has been studied intensively by workers in England, Canada and the U.S. Our findings agree with these workers that the tumors are sarcomas, rhabdomyosarcomas or as fibrosarcomas. They can be classified as depending on the diligence of study and the use of histochemical techniques to demonstrate the presence of striated muscle fibers. Both have large numbers of multinucleated cells. This academic point is not considered germaine to the present investigations.

(13) Because of the high dose of nickel sulfide used and the resultant shortened survival time, the influence of the carcinogen on the appearance of spontaneous tumors could not be properly evaluated.

TABLE 30

POSITIVE CONTROL

NICKEL SULFIDE POWDER

End Points	Group/Dose (mg) and Route			
	A 10 mg s.c.	B 3.3 mg s.c.	C 10 mg i.m.	D 3.3 mg i.m.
No. of animals started	40	39	40	40
No. died during trial	25	23	30	26
No. sacrificed (Moribund)	9	14	4	13
No. sacrificed terminally	6	2	6	1
Survival time — mean days	311	367	252	292
Survival time — range in days	156-553	184-542	140-553	166-553
No. of tumors	37/40	37/39	34/40	38/39*
% of animals autopsied showing typical Fibro- or Rhabdomyosarcomas	90%	94.8	85%	97.4
Initial detection of tumors				
a. Mean days (all tumors)	131	242	135	217
b. range in days	21-512	35-518	100-202	133-364
c. survival-time after detection	155	119	60	75
Metastases Lung — Number	14	8	15	13
Metastases Lung — Percent	37.8%	20.5%	44.1%	34.2%
Metastases Spleen — Number	9	11	9	9
Metastases Spleen — Percent	24%	28.2%	26.4%	23.7%

* One animal excluded because it died 20 days after start of trial.

TABLE 31

NICKEL SULFIDE

10 mg s.c. - Single Injection

GROUP A

Rat No.	Sex	Detection and Growth of Lesions: Initial Detection Days Post Injection	Duration of First Lesion	Interval Between Injection & Tumor Formation	Survival in Days After Tumor Detection	Primary at Injection Site	Fate	Survival Time	Tumor Characterization: Metastases: Lung	Liver	Spleen	Lymph G'land	Adrenal	Hemothorax	Other	Histological Tumor Type *
1	♂	21	69	253	53	+	D	306								N.T.S.
2	♂	28	56	112	65	+	D	177				+				R
3	♂	42	53	-	-	-	D	120								-
4	♂	35	-	35	185	+	MS	264								N.T.S.
5	♂	42	-	42	191	+	D	233	+							I
6	♂	35	-	35	264	+	D	299								F
7	♂	63	-	63	257	+	D	320								R
8	♂	100	-	100	123	+	D	223	+							I
9	♂	63	-	63	93	+	D	156	+							F
10	♂	63	-	63	121	+	MS	184	+		+		+	+		F
11	♂	105	7	175	83	+	D	258								I
12	♂	56	-	56	336	+	MS	392	+		+					R
13	♂	77	77	224	112	+	D	336								I
14	♂	77	77	168	168	+	D	336	+		+					I
15	♂	112	83	217	128	+	MS	345	+		+					R
16	♂	84	-	84	222	+	D	306								N.T.S.
17	♂	105	-	105	225	+	D	330	+		+		+	+	Kidneys	R
18	♂	63	-	63	156	+	MS	219								I
19	♂	112	7	-	-	-	RS	553								-
20	♂	35	-	35	215	+	D	250							PMD	F
21	♀	35	-	35	135	+	MS	170	+		+		+	+	Abdominal cavity	-
22	♀	91	251	224	118	+	D	342	+							-
23	♀	105	-	105	114	+	MS	219	+	+		+				F
24	♀	84	77	512	-	-	RS	553								F
25	♀	56	497	-	-	-	RS	553								-
26	♀	35	518	-	-	-	RS	553								-
27	♀	343	-	343	65	+	MS	408								R
28	♀	28	7	245	36	+	D	281								F
29	♀	21	-	21	166	+	D	187			+			+	Abdominal cavity	R
30	♀	84	42	-	-	-	RS	553								-
31	♀	42	-	42	231	+	D	273							PMD	N.T.S.
32	♀	70	-	70	111	+	D	181	+					+	PMD	F
33	♀	28	28	252	44	+	D	296								I
34	♀	70	250	231	89	+	D	320							Uterus PMD	R
35	♀	56	70	221	-	-	RS	553	+	+	+	+	+	-	Leukemia	Lymphocyt Leukemia
36	♀	77	-	77	279	+	D	356	+							F
37	♀	56	-	56	198	+	D	254			+		+	+	Abdominal cavity, pancreas	I
38	♀	56	-	56	245	+	D	301								I
39	♀	56	56	175	86	+	D	261			+	+			Abdominal cavity, PMD	I
40	♀	35	-	35	184	+	MS	219	+	+		+				R

* F - Fibrosarcoma
R - Rhabdomyosarcoma
I - Intermediary
N.T.S.-No Tissue Saved

** D - Died during trial
MS-Moribund, sacrificed
RS -Routine, sacrificed at end of trial

TABLE 32

NICKEL SULFIDE

GROUP 5 — 3.3 mg i.c. - Single Injection

Rat No.	Sex	Detection and Growth of Lesions: Initial Detection Days Post Injection	Duration of First Lesion	Interval Between Injection & Tumor Formation	Survival In Days After Tumor Detection	a & Fate	Survival Time	Tumor Characterization: Primary at Injection Site	Metastases: Lung	Liver	Spleen	Lymph Gland	Adrenal	Hemothorax	Other	Histological Tumor Type
41	♂	35	126	313	83	MS	408	-								I
42	♂	35	77	237	84	D	321	+								I
43	♂	35	105	315	53	D	368	+							PMD	N.T.S.
44	♂	42	70	-	-	RS	553	+							Papilloma wt. Injection site	Papilloma
45	♂	301	-	301	97	MS	398	+	+		+	+				I
46	♂	35	7	210	33	D	243	+							PMD	N.T.S.
47	♂	35	126	217	49	MS	266	+			+					I
48	♂	56	84	245	7	D	314	+	+						PMD	I
49	♂	35	7	287	89	D	376	+	+	+		+			PMD	I
50	♂	35	-	35	292	D	327	+								F
51	♂	434	-	434	63	D	497	+	+						Tumor eaten	N.T.S.
52	♂	35	7	266	81	D	347	+	+							R
53	♂	42	49	154	244	MS	398	+			-					F
54	♂	35	119	308	100	MS	408	+	-		+				Thyroid	I
55	♂	84	56	217	125	D	343	+			+					F
56	♂	35	98	195	134	D	299	+								I
57	♂	133	7	357	51	MS	408	+							Pancreas	I
58	♂	77	7	357	51	MS	408	+								F
59	♂	35	126	217	78	D	295	-								I
60	♂	35	70	357	59	D	416	+							PMD	N.T.S.
61	♀	35	-	35	357	MS	392	+			+					I
62	♀	91	16	266	126	MS	392	+	+							R
63	♀	70	-	70	229	D	299	+							PMD	I
64	♀	63	37	237	108	MS	345	+								F
65	♀	35	147	294	104	MS	398	+								I
66	♀	56	-	56	336	MS	392	+			+					I
67	♀	35	-	35	149	D	184	-								F
68	♀	107	7	-	-	D	493	-							Abdominal Tumor	N.T.S.
69	♀	35	56	280	86	D	366	+			+					R
70	♀	35	77	210	131	D	341	+		+			+			R
71	♀	35	56	175	233	MS	408	+			+					R
72	♀	35	98	182	138	D	320	+			+					I
73	♀	35	-	-	-	RS	553									-
74	♀	42	21	106	106	D	338	+			+				PMD	R
75	♀	35	7	-	-	D	385									-
76	♀	42	70	64	64	D	295	+								I
77	♀	42	21	44	364	MS	408	+								R
78	♀	244	-	97	97	D	341	+	+	+		+		+	Sternum	R
79	♀	42	28	124	124	D	236	+								I
80	♀	35	133	50	50	D	542	+							Excessive PMD	N.T.S.

F - Fibrosarcoma
R - Rhabdomyosarcoma
I - Intermediate
N.T.S. - No Tissue Saved

** D - Died during trial
MS - Moribund, sacrificed
RS - Routine, sacrificed at end of trial

TABLE 33

NICKEL SULFIDE

GROUP C — 10 mg i.m. - Single Injection

Rat No.	Sex	Detection and Growth of Lesions: Initial Detection, Days Post Injection	Duration of First Lesion	Interval Between Injection & Tumor Formation	Survival in Days After Tumor Detection	a b Fate	Survival Time	Tumor Characterization: Primary at Injection Site	Metastases: Lung	Liver	Spleen	Lymph Gland	Adrenal	Hemothorax	Other	Histolog Tumor T
81	♂			100	100	D	200	+								N.T.
82	♂			100	77	D	177	+	+					+		R
83	♂			133	37	D	170	+	+			+		+		R
84	♂			147	40	D	187	+								N.T.
85	♂			100	73	D	173	+	+					+	PMD	N.T.
86	♂			100	130	D	230	+	+							R
87	♂			147	30	D	177	+	+					+		R
88	♂			126	85	D	211	+							PMD	N.T.
89	♂			133	7	D	140	+	+							R
90	♂			126	21	D	147	+								N.T.
91	♂			182	71	D	253	+	+			+				R
92	♂			147	34	D	181	+	+					+		N.T.
93	♂			119	29	D	148	+	+					+		F
94	♂			126	124	D	250	+								N.T.
95	♂			119	91	D	210	+								N.T.
96	♂			119	54	D	173	+	+					+	PMD	R
97	♂			175	50	D	225	+								F
98	♂			119	54	D	173	+	+		+			+		I
99	♂			202	63	MS	265	+	+		+					R
100	♂					RS	553	-								-
101	♀			126	67	D	224	+								F
102	♀			133	124	D	257	+								N.T
103	♀			133	56	D	189	+								N.T
104	♀			126	58	D	184	+								N.T
105	♀			140	79	MS	219	+	+			+				I
106	♀			126	56	D	182	+								-
107	♀			147	57	D	204	+								N.T
108	♀			147	17	MS	264	+				+				F
109	♀	126	21			RS	553	-								-
110	♀	175	7			RS	553	-								-
111	♀					RS	553	-								-
112	♀					RS	553	-								-
113	♀			126	28	D	154	+	+			+		+		N.T
114	♀					RS	553	-								-
115	♀			182	43	D	225	+								F
116	♀			147	68	D	215	+							PMD	N.T
117	♀			126	79	D	205	+								N.T
118	♀			133	56	D	189	+								N.T
119	♀			126	44	MS	170	+	+	+			+	+		I
120	♀			140	27	D	167	+								

* F - Fibrosarcoma
R - Rhabdomyosarcoma
I - Intermediary
N.T.S. - No Tissue Saved

** D - Died during trial
MS-Moribund, sacrificed
RS-Routine, sacrificed at end of trial

TABLE 34

NICKEL SULFIDE

3.3 mg i.m. - Single Injection

GROUP D

Rat No.	Sex	Detection and Growth of Lesions: Initial Detection Days Post Injection	Duration of First Lesion	Interval Between Injection & Tumor Formation	Survival in Days After Tumor Detection	** Fate	Survival Time	Tumor Characterization: Primary at Injection Site	Metastases: Lung	Liver	Spleen	Lymph Gland	Adrenal	Hemothorax	Other	Histology Tumor Ty.
121	♂	-	0	147	104	D	251	+								
122	♂	-	0	147	214	D	361	+	+		+					R
123	♂	-	0	210	56	MS	266	+								I
124	♂	-	0	182	40	D	222	+								F
125	♂	-	0	245	147	MS	392	+	+		+				Bone Marrow	R
126	♂	-	0	140	43	D	183	+								N.T.S
127	♂	-	0	210	23	D	233	+	+	+	+			+		R
128	♂	234	7	364	34	MS	398	+								I
129	♂	-	0	176	178	D	354	+							PMD	N.T.S
130	♂	-	0	126	125	D	251	+								N.T.S
131	♂	-	0	217	8	D	225	+								I
132	♂	-	0	231	29	MS	260	+								R
133	♂	-	0	224	110	D	334	+							PMD	I
134	♂	-	0	266	35	D	301	+								F
135	♂	-	0	231	65	D	296	+	+						PMD	R
136	♂	-	0	203	57	MS	260	+								
137	♂	-	0	272	72	MS	345	+	+		+					
138	♂	-	0	133	55	D	188	+								N.T.S
139	♂	-	-	-	-	D	20	-								-
140	♂	-	0	175	44	MS	219	+								I
141	♀	-	0	147	112	D	259	+								N.T.S
142	♀	147	7	280	41	D	321	+	+							R
143	♀	168	7	231	35	MS	266	+			+				Lower jaw	F
144	♀	-	0	147	112	MS	259	+	+		+				Abdomin	R
145	♀	-	0	287	60	D	347	-	+						PMD	I
146	♀	-	0	147	117	MS	264	+	+		+					R
147	♀	-	0	133	33	D	166	+							PMD	F
148	♀	140	7	329	139	D	468	+	+							I
149	♀	-	0	301	77	D	378	+								I
150	♀	-	0	182	37	MS	219	+	+							I
151	♀	-	0	224	141	D	365	+	+		+					I
152	♀	147	7	287	47	D	334	+							PMD	I
153	♀	-	0	329	74	D	404	+							PMD	N.T.S
154	♀	-	0	195	55	D	250	+							PMD	N.T.S
155	♀	-	0	175	76	D	251	+								I
156	♀	-	0	208	84	D	287	+							PMD	N.T.S
157	♀	-	0	252	91	D	343	+			+	+				I
158	♀	147	7	217	43	MS	260	+								R
159	♀	147	7	294	51	MS	345	+	+							R
160	♀	-	-	217	75	RS	553	-								-

* F - Fibrosarcoma
R - Rhabdomyosarcoma
I - Intermediary
N.T.S. - No Tissue Saved

** D - Died during trial
MS-Moribund, sacrificed
RS-Routine, sacrificed at end of trial

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e receiving vessel to drain the tips. Volume readings on burets hould be estimated to the nearest 0.01 mL for 25- and 50-mL urets, and to the nearest 0.005 mL for 5- and 10-mL burets. Pipets alibrated "to contain" are called for in special cases, generally for measuring viscous fluids like syrups; however, a volumetric flask may be substituted for a "to contain" pipet. In such cases, the pipet or flask should be washed clean, after draining, and the washings added to the measured portion.

Volumetric Flasks

esignated volume, mL	10	25	50	100	250	500	1000
mit of error, mL	0.02	0.03	0.05	0.08	0.12	0.15	0.30
mit of error, %	0.20	0.12	0.10	0.08	0.05	0.03	0.03

Transfer Pipets

esignated volume, mL	1	2	5	10	25	50	100
mit of error, mL	0.006	0.006	0.01	0.02	0.03	0.05	0.08
mit of error, %	0.60	0.30	0.20	0.20	0.12	0.10	0.08

Burets

signated volume, mL	10 ("micro" type)	25	50
divisions, mL	0.02	0.10	0.10
mit of error, mL	0.02	0.03	0.05

⟨41⟩ WEIGHTS AND BALANCES

The intent of this section is to bring the requirements for weights conformity with American National Standard ANSI/ASTM 7, "Laboratory Weights and Precision Mass Standards." This dard is incorporated by reference and should be consulted for descriptions and information on the tolerances and construction weights.[1]

harmacopeial tests and assays require balances that vary in ca-ty, sensitivity, and reproducibility. Unless otherwise specified, substances are to be "accurately weighed" for *Assay* the ghing is to be performed with a weighing device whose mea-ment uncertainty (random plus systematic error) does not ex-0.1% of the reading. Measurement uncertainty is satisfactory ree times the standard deviation of not less than ten replicate ghings divided by the amount weighed, does not exceed 0.001. ss otherwise specified, for titrimetric limits tests, the weighing be performed to provide the number of significant figures in weight of the analyte that corresponds to the number of signif-figures in the concentration of the titrant.

e class designations below are in order of increasing ances.

ss 1.1 weights are used for calibration of low-capacity, high-tivity balances. They are available in various denominations 1 to 500 mg. The tolerance for any denomination in this class g. They are recommended for calibration of balances using l or electrical methods for accurately weighing quantities be-0 mg.

ss 1 weights are designated as high-precision standards for ation. They may be used for weighing accurately quantities 20 mg. (For weights of 10 g or less, the requirements of 1 are met by *USP XX*/ class M.)

ss 2 weights are used as working standards for calibration, n weights for analytical balances, and laboratory weights for analytical work. (The requirements of class 2 are met by *XX*/ class S.)[2]

pies of ASTM Standard E 617-81 (Reapproved 1985) may ained from the American Society for Testing and Materials, Race Street, Philadelphia, PA 19103.

te that the designations S and P no longer designate weight but rather weight grades, that is, design limitations such as of density of materials, surface area, surface finish, corrosion nce, and hardness.

Class 3 and class 4 weights are used with moderate-precision laboratory balances. (Class 3 requirements are met by *USP XX*/ *class S-1; class 4 requirements are met by USP XX*/ class P.)[2]

A weight class is chosen so that the tolerance of the weights used does not exceed 0.1% of the amount weighed. Generally, class 2 may be used for quantities greater than 20 mg, class 3 for quantities of greater than 50 mg, and class 4 for quantities of greater than 100 mg. Weights should be calibrated periodically, preferably against an absolute standard weight.

Microbiological Tests

⟨51⟩ ANTIMICROBIAL EFFECTIVENESS TESTING

Antimicrobial preservatives are substances added to nonsterile dosage forms to protect them from microbiological growth or from microorganisms that are introduced inadvertently during or subsequent to the manufacturing process. In the case of sterile articles packaged in multiple-dose containers, antimicrobial preservatives are added to inhibit the growth of microorganisms that may be introduced from repeatedly withdrawing individual doses.

Antimicrobial preservatives should not be used as a substitute for good manufacturing practices or solely to reduce the viable microbial population of a nonsterile product or control the presterilization bioburden of multidose formulations during manufacturing. Antimicrobial preservatives in compendial dosage forms meet the requirements for *Added Substances* under *Ingredients and Processes* in the *General Notices*.

All useful antimicrobial agents are toxic substances. For maximum protection of patients, the concentration of the preservative shown to be effective in the final packaged product should be below a level that may be toxic to human beings.

U.S. Licensed Pediatric Vaccines

Product	Trade Name (first licensure)	Manufacturer	Dosage	Preservative and amount	Adjuvant	Other Additives	Mfg. Residuals
DTaP	ACEL-IMUNE (12/91)	Lederle Labs.	.5 ml	thimerosal 0.01%	$AL(OH)_3/AlPO_4$; Al 0.23mg	gelatin, tween	formaldehyde <0.02%
DTaP	Tripedia (6/92)	Aventis Pasteur Inc.	.5 ml	thimerosal 0.01%	Alum; Al 0.170mg	$NaPO_4$	formaldehyde <0.02%, tween
DTaP	Infanrix (1/97)	SKB	.5 ml	2-phenoxyethanol 2.5mg,	$Al(OH)_3$; Al ≤0.625mg		formaldehyde <0.02%, sodium chloride, tween
DTaP	Certiva (7/98)	North Amer Vaccine	.5 ml	thimerosal 0.01%,	$Al(OH)_3$; Al 0.5mg		free formald. ≤10ppm, fetuin
Haemophilus b Conj. Vaccine (Meningococcal Protein Conj.)	PedvaxHIB (12/89)	Merck & Co., Inc.	.5 ml	liquid: None lyoph: thimerosal 0.02% *	$Al(OH)_3$; Al 225mcg	liquid: no lactose, sodium chloride 0.9% lyoph: lactose 2 mg	
Haemophilus b Conj. Vaccine (Tetanus Toxoid Conj.)	ActHIB, OmniHIB (3/93)	Aventis Pasteur, SA	.5 ml	single dose: none,	None	sucrose 8.5%	
Haemophilus b Conj. Vaccine (Diphtheria CRM197 Protein Conj.)	HibTITER (6/94)	Lederle Labs.	.5 ml	single dose: none, multi dose: thimerosal 0.01%		sodium chloride 0.9%	
Haemophilus b Conj. Vaccine (Meningococcal Protein Conj.) and Hepatitis B	Comvax (10/96)	Merck & Co., Inc.	.5 ml	none	$Al(OH)_3$; Al 225mcg	sodium chloride 0.9%, sodium borate	yeast protein, formald.
Hepatitis B Vaccine (Recombinant)	RECOMBIVAX HB (7/86)	Merck & Co., Inc.	.5 ml	Two formulations (1) thimerosal 25 mcg (2) thimerosal-none	$Al(OH)_3$; Al 0.25mg	sodium chloride 0.9%,	yeast protein, formald.
Hepatitis B Vaccine (Recombinant)	Engerix-B (8/89)	SKB	.5 ml	none	$Al(OH)_3$; Al 0.25mg	sodium chloride & phosphate buffers	thimer.< 0.5 mcg mercury
M, M, and R Virus Vaccine Live	M-M-R II (4/71)	Merck & Co., Inc.	.5 ml	None	None	sorbitol, 14.5mg, neomycin 25mcg, gelatin (sucrose 1.9mg, culture medium, phosphate, glutamate)human albumin 0.3mg sodium chloride	FCS <1ppm
Pneumococcal Vaccine 7-valent Conj. Vaccine (CRM197 Protein)	Prevnar (2/00)	Lederle	.5 ml	None	$AlPO_4$, 0.125mg Al		
Poliovirus Vaccine Inactivated	IPOL (12/90)	Aventis Pasteur, SA	.5 ml	2-phenoxyethanol 0.5%, formald 0.02%	None		neomycin <5ng, streptomycin 200ng, polymyxin B, 25ng,

							calf serum protein <1ppm
Tetanus & Diphtheria Toxoids ads.	No trade name (7/70)	Lederle	.5ml	thimerosal 0.01%	$AlPO_4$, Al 0.3mg	sodium bicarbonate, physiological saline	formaldehyde <0.02%
Tetanus & Diphtheria Toxoids ads.	No trade name (1/78)	Aventis Pasteur, SA	.5ml	thimerosal 0.01%	$ALPO_4$; Al 0.28mg	sodium chloride, sodium phosphate	formaldehyde
Tetanus & Diphtheria Toxoids ads.	No trade name (7/70)	MPHBL	.5ml	thimerosal 0.01%	$AlPO_4$ 2.0mg	sodium chloride, sodium hydroxide, aluminum chloride	formaldehyde < 0.02%
Tetanus & Diphtheria Toxoids ads.	No trade name (9/70)	Wyeth	.5ml	thimerosal 0.01%	$ALPO_4$; Al 0.85mg	sodium chloride, HCL, sodium hydroxideto adjust pH	free formaldehyde 0.02%
Varicella Virus Vaccine Live	Varivax (3/95)	Merck & Co., Inc.	.5 ml	None	None	sucrose 2.5mg, glutamate 0.5mg, gelatin 12.5mg, potassium chloride 0.08mg, sodium chloride 3.2mg, sodium phosphate dibasic 0.45mg, glutamate 0.5mg potassium phosphate monobasic 0.06mg	neomycin, EDTA, FBS sodium phosphate monobasic cellular DNA/protein
* No longer manufactured							

DEPARTMENT OF HEALTH AND HUMAN SERVICES

21 CFR Part 333

[Docket No. 75N-0183]

Mercury-Containing Drug Products for Topical Antimicrobial Over-the-Counter Human Use; Establishment of a Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Advance notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration [FDA] is issuing an advance notice of a proposed rulemaking that would classify over-the-counter (OTC) mercury-containing drug products for topical antimicrobial use as not generally recognized as safe and effective and as being misbranded. This notice related to the development of a monograph for topical antimicrobial drug products in general, which is part of the ongoing review of OTC drug products conducted by FDA. This notice also reopens the administrative record for OTC topical antimicrobial drug products to allow for consideration of recommendations on mercury-containing drug products that have been received from the Advisory Review Panel on OTC Miscellaneous External Drug Products.

DATES: Written comments by April 5, 1982, and reply comments by May 5, 1982.

ADDRESS: Written comments to the Dockets Management Branch (formerly the Hearing Clerk's Office) (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Bureau of Drugs (HFD-510), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In accordance with Part 330 [21 CFR Part 330], FDA received on October 6, 1980 a report on OTC mercury-containing drug products for topical antimicrobial use from the Advisory Review Panel on OTC Miscellaneous External Drug Products. FDA regulations [21 CFR 330.10(a)(6)] provide that the agency issue in the Federal Register a proposed rule containing (1) the monograph recommended by the Panel, which established conditions under which OTC mercury-containing drug products for topical antimicrobial use are generally recognized as safe and effective and not misbranded; (2) a statement of the conditions excluded from the monograph because the Panel determined that they would result in the drugs' not being generally recognized as safe and effective or would result in misbranding; (3) a statement of the conditions excluded from the monograph because the Panel determined that the available data are insufficient to classify these conditions under either (1) or (2) above; and (4) the conclusions and recommendations of the Panel.

Because mercurial ingredients are marketed in OTC drug products for topical antimicrobial use, FDA has determined that the Miscellaneous External Panel's recommendations on OTC mercury-containing drug products should be included as part of the proposed rulemaking for topical antimicrobial drug products. Development of this rulemaking has been ongoing for some time.

In the Federal Register of September 13, 1974 (39 FR 33103), FDA issued an advance notice of proposed rulemaking to establish the monograph for OTC topical antimicrobial drug products. In the Federal Register of January 6, 1978 (43 FR 1210), FDA issued a tentative final monograph (notice of proposed rulemaking) for OTC topical antimicrobial drug products. In the Federal Register of March 9, 1979 (44 FR 13041) FDA reopened the administrative record and announced its intent to publish an updated (amended) tentative final monograph (amended notice of proposed rulemaking) for OTC topical antimicrobial drug products. FDA advises that it is again reopening the administrative record for OTC topical antimicrobial drug products in order to allow for the consideration of the Miscellaneous External Panel's recommendations on mercury-containing drug products. An amended tentative final monograph (amended notice of proposed rulemaking) will be published in a future issue of the Federal Register. At that time, comments received on this advance notice of proposed rulemaking concerning mercury-containing drug products will be addressed. Also, the proceeding to develop a monograph for mercury-containing drug products will be merged with the general proceeding to establish a monograph for OTC topical antimicrobial drug products. Because the Panel has recommended that mercury-containing drug products be classified in Category II, no new sections to Part 333 are being included in this advance notice of proposed rulemaking.

The unaltered conclusions and recommendations of the Panel relating to OTC mercury-containing drug products for topical antimicrobial use are issued to stimulate discussion, evaluation, and comment on the full sweep of the Panel's deliberations. The statement has been prepared independently of FDA, and the agency has not yet fully evaluated the Panel's recommendations. The Panel's findings appear in this document to obtain public comment before the agency reaches any decision on the Panel's recommendations. This document represents the best scientific judgment of the Panel members, but does not necessarily reflect the agency's position on any particular matter contained in it.

After reviewing all comments submitted in response to this document, FDA will issue in the Federal Register an amended tentative final monograph for OTC topical antimicrobial drug products, including mercury-containing drug products, as an amended notice of proposed rulemaking. Under the OTC drug review procedures, the agency's position and proposal are first stated in the tentative final monograph, which has the status of a proposed rule. Final agency action occurs in the final monograph, which has the status of a final rule.

The agency's position on OTC topical antimicrobial drug products will be restated when the amended tentative final monograph is published in the Federal Register as an amended notice of proposed rulemaking. In that amended notice of proposed rulemaking, the agency also will announce its initial determination whether the proposed rule is a major rule under Executive Order 12291 and will consider the requirements of the Regulatory Flexibility Act (5 U.S.C. 601-612). The present notice is referred to as an advance notice of proposed rulemaking to reflect its actual status and to clarify that the requirements of the Executive Order and the Regulatory Flexibility Act will be considered in the amended notice of proposed rulemaking. At that time FDA also will consider whether the proposed rule has a significant impact on the human environment under 21 CFR Part (proposed in the Federal Register of December 11, 1979; 44 FR 71742).

The agency invites public comment regarding any impact that this rulemaking would have on OTC mercury-containing drug products for topical antimicrobial use. Types of impact may include, but are not limited to, the following: Increased costs due to relabeling, repackaging, or

reformulating; removal of unsafe or ineffective products form the OTC market; and testing necessary, if any, to elevate Category III conditions to Category I. Comments regarding the impact of this rulemaking on OTC mercury-containing drug products for topical antimicrobial use should be accompanied by appropriate documentation. Comments will not be accepted at this time on any portion of the OTC topical antimicrobial rulemaking other than that relating to mercury-containing drug products.

In accordance with § 330.10(a)(2), the Panel and FDA have held as confidential all information concerning OTC mercury-containing drug products for topical antimicrobial use submitted for consideration by the Panel. All the submitted information will be put on public display in the Dockets Management Branch, Food and Drug Administration, after February 4, 1982, except to the extent that the person submitting it demonstrates that it falls within the confidentiality provisions of 18 U.S.C. 1905 or section 301(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(j)). Requests for confidentiality should be submitted to William E. Gilbertson, Bureau of Drugs (HFD-510) (address above).

FDA published in the Federal Register of September 29, 1981 (46 FR 47730) a final rule revising the OTC procedural regulations to conform to the decision in *Cutler v. Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). The Court in *Cutler* held that the OTC drug review regulations (21 CFR 330.10) were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph has been established. Accordingly, this provision is now deleted from the regulations. The regulations now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph.

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I," "Category II," and "Category III" at the final monograph stage in favor of the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and II). This document retains the concepts of Categories I, II, and III because that was the framework in which the Panel conducted its evaluation of the data.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 6 months after the date of publication of the final monograph in the Federal Register. On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e., conditions which would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce. Further, any OTC drug products subjects to this monograph which are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

Statement of the Advisory Review Panel on OTC Miscellaneous External Drug Products on Mercury-Containing Drug Products for Topical Antimicrobial Use.

A proposed review of the safety, effectiveness, and labeling of all OTC drugs by independent advisory review panels was announced in the Federal Register of January 5, 1972 (37 FR 85). The final regulations providing for this OTC drug review under § 330.10 were published and made effective in the Federal Register of May 11, 1972 (37 FR 9464). In accordance with these regulations, a request for data and information on all active ingredients used in OTC miscellaneous external drug products was issued in the Federal Register on November 16, 1973 (38 FR 31697). (In making their categorizations with respect to "active" and "inactive" ingredients, the advisory review panels relied on their expertise and understanding of these terms. FDA has defined "active ingredient" in its current good manufacturing practice regulations (§ 210.3(b)(7), (21 CFR 210.3(b)(7))) , as "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure of any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect." An "inactive ingredient" is defined in § 210.3(b)(8) as "any component other than an 'active ingredient.' ") In the Federal Register of August 27, 1975 (40 FR 38179) a notice supplemented the original notice with a detailed, but not necessarily all inclusive, list of ingredients in miscellaneous external drug products to be considered in the OTC drug review. The list, which included ingredients described as "mercurials," was provided to give guidance on the kinds of active ingredients for which data should be submitted. The notices of November 16, 1973, and August 27, 1975, informed OTC drug product manufacturers of their opportunity to submit data to the review at that time and of the applicability of the monographs from the OTC drug review to all OTC drug products.

Under § 330.10(a)(1) and (5) the Commissioner of Food and Drugs appointed the following Panel to review the information submitted and to prepare a report on the safety, effectiveness, and labeling of the active ingredients in these OTC miscellaneous external drug products:

William E. Lotterhos, M.D., Chairman

Rose Dagirmanjian, Ph. D.

Vincent J. Derbes, M.D. (resigned July 1976)

George C. Cypress, M.D. (resigned November 1978)

Yelva L. Lynfield, M.D. (appointed October 1977)

Harry E. Morton, Sc. D.

Marianne N. O'Donoghue, M.D.

Chester L. Rossi, D.P.M.

J. Robert Newson, M.D. (appointed September 1978)

Representatives of consumer and industry interests served as nonvoting members of the Panel. Marvin M. Lipman, M.D., of Consumers Union served as the consumer liaison. Gavin Hildick-Smith, M.D., served as industry liaison from January until August 1975, followed by Bruce Semple, M.D., until February 1978. Both were nominate by the Proprietary Association. Saul A. Bell, Pharm. D., nominated by the Cosmetic, Toiletry, and Fragrance Association, also served as an industry liaison since June 1975.

Two nonvoting consultants, Albert A. Belmonte, Ph. D., and Jon J. Tanja, R.Ph., M.S., have provided assistance to the Panel since February 1977.

The following FDA employees assisted the Panel: John M. Davitt served as Executive Secretary until August 1977, followed by Arthur Auer until September 1978, followed by John T. McElroy, J.D. Thomas D. DeCillis, R.Ph., served as Panel Administrator until April 1976, followed by Michael D. Kennedy until January 1978, followed by

John T. McElroy, J.D. Joseph Hussion, R. Ph., served as Drug Information Analyst until April 1976, followed by Victor H. Lindmark, Pharm. D., until March 1978, followed by Thomas J. McGinnis, R.Ph.

The Advisory Review Panel on OTC Miscellaneous External Drug Products was charged with the review of many categories of drugs. Due to the large number of ingredients and varied labeling claims, the Panel decided to review and publish its findings separately for several drug categories and individual drug products. The Panel presents in this document its conclusions and recommendations on OTC mercury-containing drug products for topical antimicrobial use. The Panel's findings on other categories of miscellaneous external drug products are being published periodically in the Federal Register.

The Panel was first convened on January 13, 1975 in an organizational meeting. Working meetings which dealt with the topic in this document were held on: January 27 and 28, March 7 and 8, April 20 and 21, June 22 and 23, August 3 and 4, and October 5 and 6, 1980.

The minutes of the Panel meetings are on public display in the Dockets Management Branch (HFA-305) Food and Drug Administration (address above).

No individuals requested to appear before the Panel to discuss mercury-containing drug products for topical antimicrobial use, nor was any individual requested to appear by the Panel.

The Panel has thoroughly reviewed the literature and data submissions, and has considered all pertinent information submitted through October 6, 1980 in arriving at its conclusions and recommendations.

In accordance with the OTC drug review regulations set forth in § 330.10, the Panel reviewed OTC mercury-containing drug products for topical antimicrobial use with respect to the following three categories:

Category I. Conditions under which OTC mercury-containing drug products for topical antimicrobial use are generally recognized as safe and effective and are not misbranded.

Category II. Conditions under which OTC mercury-containing drug products for topical antimicrobial use are not generally recognized as safe and effective or are misbranded.

Category III. Conditions for which the available data are insufficient to permit final classification at this time.

The Panel reviewed 18 active ingredients in OTC mercury-containing drug products for topical antimicrobial use and classified all 18 in Category II.

I. Submissions of Data and Information

In an attempt to make this review as extensive as possible and to aid manufacturers and other interested persons, the agency compiled a list of ingredients recognized, either through historical use or in marketed products, as mercurial active ingredients. Fourteen ingredients were identified as follows: Ammoniated mercury, bichloride of mercury, calomel, mercuric salicylate, mercuric sulfide, mercurochrome, mercury, mercury chloride, mercury oleate, nitromersol, *para*-chloromercuriphenol, vitromersol, yellow mercuric oxide, and zyloxin. Notices were published in the Federal Register of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179) requesting the submission of data and information on these ingredients or any other ingredients used in OTC mercurial drug products. In addition, in the Federal Register of September 13, 1974 (39 FR 33103), the following ingredients were deferred from the OTC Antimicrobial I Panel to the Miscellaneous Topical Panel (later renamed the Advisory Review Panel on OTC Miscellaneous External Drug Products) for review: mercuric chloride (also included in the call-for-data as bichloride of mercury), *ortho*-chloromercuriphenol, and *ortho*-hydroxyphenylmercuric chloride.

A. Submissions.

Pursuant to the above notices, the following submissions were received:

Firms and Marketed Products

Becton, Dickinson and Co., Rochelle Park, NJ 07662—Mercurochrome.

Bowman Pharmaceuticals, Inc., Canton, OH 44702—Merphol, Mercuronate, Ointment.

Corona Manufacturing Co., Atlanta, GA 30301—Corona Ointment.

Eli Lilly and Co., Indianapolis, IN 46206—Merthiolate.

Marion Health and Safety, Inc., Rockford, IL 61101—Kip Ointment, Merthiolate Swabs, Mercurochrome Swabs.

Whitehall Laboratories, New York, NY 10017—Sperti.

B. Ingredients Reviewed by the Panel.

1. *Labeled ingredients contained in marketed products submitted to the Panel.*

Ammoniated mercury
Merbromin
Orthohydroxyphenylmercuric chloride
Phenylmercuric nitrate
Thimerosal

2. *Other ingredients reviewed by the Panel.*

Calomel (mercurous chloride)
Mercuric chloride (bichloride of mercury)
Mercuric salicylate
Mercuric sulfide
Mercury
Mercury chloride
Mercury oleate
Nitromersol
Ortho-chloromercuriphenol
Para-chloromercuriphenol
Vitromersol
Yellow mercuric oxide
Zyloxin

C. Classification of Ingredients.

1. *Active ingredients.*

Calomel (mercurous chloride)
Merbromin
Mercuric chloride (bichloride of mercury)
Mercury, ammoniated (ammoniated mercury)
Ortho-hydroxyphenylmercuric chloride
Phenylmercuric nitrate
Thimerosal

2. *Inactive ingredients.*

None.

3. *Other ingredients.* Mercury oleate was submitted to this Panel for the treatment of psoriasis only and will be included in the Panel's recommendations on dandruff, seborrheic dermatitis, and psoriasis drug products to be published in a future issue of the Federal Register.

Mercuric oxide, yellow (yellow mercuric oxide) was reviewed as an ophthalmic anti-infective by the Advisory Review Panel on OTC Ophthalmic Drug Products in its report published in the Federal Register of May 8, 1980 (45 FR 30002).

The Panel was not able to locate nor is it aware of data demonstrating the safety and effectiveness of the following ingredients when used as OTC mercurial topical antimicrobial active ingredients. The Panel, therefore, classifies these ingredients as Category II, not generally recognized as safe and effective for this use, and they will not be discussed further in this document.

Mercuric oxide, yellow (yellow mercuric oxide)
Mercuric salicylate
Mercuric sulfide, red (mercuric sulfide)
Mercury
Mercury chloride
Mercury oleate
Nitromersol
Ortho-chloromercuriphenol
Para-chloromercuriphenol
Vitromersol
Zyloxin

D. Referenced OTC Volumes.

The "OTC Volumes" cited in this document include submissions made by interested persons in response to the call-for-data notices published in the Federal Register of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179). All of the information included in

these volumes, except for those deletions which are made in accordance with the confidentiality provisions set forth in § 330.10(a)(2), will be put on public display after February 4, 1982, in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

II. General Discussion

Mercury is a silver-white, heavy, liquid metal with an atomic weight of 200.59. It forms alloys with most metals except iron and combines with sulfur at ordinary temperatures.

Mercury has been known to humans perhaps longer than any other metal, and humans have used it in various ways for treating illness. With the advent of the science of chemistry, new compounds of mercury were developed and used in treatment of different pathological conditions. With the advent of the science of bacteriology, mercury compounds were among the preparations chosen for antimicrobial therapy.

It has been the general course of events that, whenever a mercury compound has been tried for a particular therapeutic function, it has been used enthusiastically at first, only to be replaced eventually by a safer or more effective drug.

Elemental mercury, especially when vaporized, is toxic and readily absorbed through intact skin, the respiratory tract, and the gastrointestinal tract (Ref. *1*). The mercury compounds exhibit varying degrees of toxicity, and sensitivity to these compounds is not unusual. The literature includes a number of cases of sensitivity to mercury-containing preparations ranging from topical salves and solutions to amalgam tooth fillings (Refs. *2* and *3*). Both organic and inorganic mercury compounds produce allergic contact dermatitis, and cross-sensitivity has been noted (Ref. *3*).

The decline in the importance of mercury in antimicrobial therapy since midcentury can be attributed more to the discovery of its lack of effectiveness for this purpose than lack of safety, however. Work done in the field of enzyme chemistry clarifying the mode of action of mercury against bacterial and fungal cells has shown that mercury compounds as a class are of dubious value for antimicrobial use (Ref. *4*).

Mercuric ions combine with free sulfhydryl groups in the bacterial cells and thus deprive the cells of these sulfhydryl groups which are necessary to insure that metabolism and growth take place. The action of mercury is primarily bacteriostatic, but it may act slowly as a bactericide (Ref. *5*). That is to say, mercury inhibits the growth of bacteria, but does not act swiftly to kill them (Ref. *6*).

In late 1939 and early 1940, important discoveries were made showing that the bacteriostatic action of mercury can be reversed by many types of sulfur-containing compounds. Brewer (Refs. *7* and *8*) formulated a culture medium, thioglycollate, which allowed the growth of anaerobic microorganisms by the use of aerobic techniques. Marshall, Gunnison, and Luxen (Ref. *9*) demonstrated that the thioglycollate medium was capable of inactivating the bacteriostatic action of thimerosal and supported the growth of contaminants. Morton, North, and Engley (Refs. *10* and *11*) demonstrated that inhibited bacteria are not completely killed by mercury-containing compounds. When these inhibited bacteria are cultured in sodium thioglycollate solution, growth resumes because the solution chemically removes the mercury and eliminates any residual bacteriostatic activity (Ref. *12*). Intraperitoneal injections of the sodium thioglycollate culture proved fatal to mice and hemolytic streptococci were isolated from the heart's blood after death of the mice (Ref. *11*). These discoveries made it necessary to reexamine all previous reports in the literature claiming a killing activity for mercurial compounds.

It has been found that, if mercury is first allowed to combine with the sulfhydryl groups in bacterial cells, growth is inhibited, but the introduction of additional sulfhydryl groups to the cell-mercury complex neutralizes this action, and growth again takes place (Ref. *6*). Brewer (Ref. *13*) examined a hospital's stock of sutures, some of which had been stored for up to 10 years. Some of the sutures were nonsterile even though they had been stored in a solution containing a high concentration of mercury. Viable *Staphylococcus aureus* were recovered from sodium thioglycollate solution after exposure to a phenylmercuric nitrate preparation for 24 hours (Ref. *14*).

The presence of serum has also been shown to reduce the antibacterial action of mercury compounds. Three hundred times more mercuric chloride, 800 times more merbromin, and 14,000 times more thimerosal were required to inactivate half the *Salmonella typhosa* cells suspended in 10 mL of an 80-percent serum solution than were required to achieve comparable results in the same period of time when the microorganisms were suspended in a salt solution (Ref. *15*). Thus, the activity of mercury preparations as topical antimicrobial agents would be markedly affected if the microorganisms on the skin or the surface of a wound were in contact with serum, pus, or other body fluids.

In 1933 Birkhaug (Ref. *16*) calculated extremely high phenol coefficients (measurements of the killing power of a compound compared to that of phenol) for mercury compounds. The method of measurement, however, was imprecise so that one could not distinguish between the bacteriostatic and bactericidal activity. Today, measurement techniques for bactericidal activity have demonstrated that the phenol coefficient for OTC mercury-containing topical antimicrobial preparations is nonexistent when their bacteriostatic action is neutralized. This has been demonstrated by Morton, North, and Engley (Ref. *11*) in studies demonstrating the effect of merbromin and thimerosal on *Streptococcus pyogenes* and by Engley (Ref. *17*) in additional studies of the effect of mercuric chloride, phenylmercuric borate, and other mercurial compounds on this strain of bacteria.

After reviewing all data and information submitted on mercury-containing products for which topical antimicrobial activity is claimed, and after a careful review of the literature, the Panel concludes that some mercury-containing preparations are not effective and others are not safe and effective for OTC topical antimicrobial use. A bacteriostatic action that is capable of being reversed by contact with body fluids and other organic matter does not constitute an effective topical antimicrobial action, and the Panel has therefore placed all mercury compounds in Category II for topical antimicrobial use.

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III. Categorization of Data

A. Category I Conditions.

These are conditions under which active ingredients used as OTC mercury-containing drug products for topical antimicrobial use are generally recognized as safe and effective and are not misbranded. This document contains no Category I conditions.

B. Category II Conditions.

These are conditions under which active ingredients used as OTC mercury-containing drug products for topical antimicrobial use are not generally recognized as safe and effective or are misbranded.

1. *Category II ingredients.*

Inorganic mercury compounds:
Calomel
Mercuric chloride
Mercury, ammoniated
Organic mercury compounds:
Merbromin
Thimerosal
Ortho-hydroxyphenylmercuric chloride
Phenylmercuric nitrate

a. *Inorganic mercury compounds*—(i) *Calomel.* Calomel (mercurous chloride) is practically insoluble in water and therefore relatively nonpoisonous for humans unless it remains in the body for a long enough time to be oxidized. Once oxidized to mercuric chloride, it is highly toxic (Ref. *1*). It has been used in the past by inunction (rubbing into the skin) as a prophylactic against venereal disease and internally as a cathartic. The Panel concludes calomel may be safe as a topical antimicrobial agent, but is not effective for this purpose.

(ii) *Mercuric chloride.* Mercuric chloride (bichloride of mercury) is a bivalent mercury salt that exhibits a high toxicity for tissue cells, a low lethal action for microorganisms, and an inability to protect against infection (Ref. *1*). The Panel concludes that mercuric chloride is not safe and not effective as a topical antimicrobial agent.

(iii) *Mercury, ammoniated.* Ammoniated mercury is insoluble in water and alcohol, but readily soluble in warm hydrochloric, nitric, and acetic acids. If ingested, it causes epigastric pain, nausea, and purging.

Ammoniated mercury has been used topically in the treatment of impetigo, ringworm, psoriasis, pruritus ani, pinworm, and infestations with pubic lice (Refs. *2* and *3*). Prolonged use may cause chronic mercury poisoning, local pigmentation of skin and eyelids (Ref. *4*), and/or hypersensitivity to mercury (Ref. *5*).

Of 70 patients treated for psoriasis with ammoniated mercury, 33 showed signs of mercury poisoning (Ref. *6*). The Panel concludes that ammoniated mercury is not safe for use as a topical antimicrobial agent.

b. *Organic mercury compounds.* Organic mercury compounds were first synthesized in an attempt to decrease the toxicity of the mercuric ion. That the attempt was not wholly successful is shown by the fact that, while merbromin and phenylmercuric nitrate have been found to be less toxic than bichloride of mercury for human epithelial cells in vitro, thimerosal was found to be more toxic (Ref. *7*). The toxicities of these compounds were not in proportion to their mercury content.

Some microorganisms have exhibited a tolerance to organic mercury compounds. For example, a strain of *Penicillium roqueforti* resistant to phenylmercuric acetate was shown to incorporate mercury in its hyphae, thus reducing the amount of biologically active mercury in its environment and permitting other microorganisms to grow that would have been inhibited by the mercury (Ref. *8*).

(i) *Merbromin.* Merbromin is soluble in water and alcohol but practically insoluble in acetone, chloroform, and ether. This compound produces a carmine red solution that stains the skin a deep red, not a desirable property for an antimicrobial agent, as this can mask inflammation, and inflammation is a warning sign of infection.

In a 1928 study Simmons (Ref. *9*) pointed out that most of the killing action of merbromin in an alcohol-acetone vehicle was due to the vehicle. Aqueous merbromin, 2 percent, failed to kill two strains of *Staphylococcus aureus* in an exposure of 10 minutes and one strain of hemolytic streptococci in an exposure of 5 minutes. The cultures were killed under similar conditions by merbromin, 2 percent, in an alcohol-acetone vehicle and by the alcohol-acetone vehicle alone, which was included as a control. It was shown in 1942 that a 1:20 dilution of merbromin failed to kill *Staphylococcus aureus* and *Escherichia coli* during an exposure of 10 minutes at room temperature (Ref. *10*). A 1:20 dilution is two and one-half times more concentrated than the 2-percent aqueous solution of merbromin that is marketed OTC for topical antimicrobial use.

The Panel concludes that merbromin is safe for topical use but lacks a bactericidal action and is not an effective topical antimicrobial active ingredient.

(ii) *Thimerosal.* Thimerosal is a cream-colored crystalline powder that is stable in air, but not in sunlight. One gram (g) is soluble in approximately 1 milliliter (mL) water and in 8 mL alcohol, but is practically insoluble in ether and benzene. At the cellular level, thimerosal has been found to be more toxic for human epithelial cells in vitro than mercuric chloride, phenylmercuric nitrate, and merbromin (Ref. *7*). It was found to be 35.3 times more toxic for embryonic chick heart tissue than for *Staphylococcus aureus* (Ref. *11*).

Moller and Trofast (Ref. *12*) demonstrated that 10 of 20 guinea pigs sensitized to thimerosal developed a delayed hypersensitivity. This production of a hypersensitivity condition in 50 percent of laboratory animals demonstrates that the substance is very allergenic and it is reasonable to expect that thimerosal will act similarly in humans.

In Sweden, where thimerosal is used mainly as a preservative in vaccines and test materials and is not sold as an OTC skin disinfectant, Moller (Ref. *13*) reported a mean frequency of thimerosal allergy of 3.7 percent among dermatologic patients throughout a 5-year period during which 600 to 800 patients were treated for contact allergy each year. Moller classified thimerosal a medium stong allergen in comparison to nickel and balsam of Peru, which showed an incidence of reactions of 9 percent and 7 percent, respectively. Moller also found that among healthy subjects 10 percent of school children, 16 percent of military recruits, 18 percent of twins, and 26 percent of medical students had hypersensitivity to thimerosal. He concluded that the periodic tuberculin testing of individuals in Sweden with vaccines containing thimerosal as a preservative affords an opportunity for the development of delayed hypersensitivity to thimerosal in this population.

Underwood et al. (Ref. *14*) patch tested over 400 patients in which 160 patients (40 percent) showed a positive reaction to one or more of the remedies which had been applied before an initial visit to a dermatologist. Of the 160 patients, 56 (35 percent) reacted to a mercury compound, and thimerosal was responsible for 90 percent of these reactions. The North American Contact Dermatitis Group (Ref. *15*) tested 1,200 subjects with 16 allergens. Thimerosal produced an incidence of 8 percent reactions and ranked third highest of the 16 allergens. Epstein, Rees, and Maibach (Ref. *16*) tested a group of private dermatological patients in the western United States with 26 substances. Thimerosal had a 13.4-percent incidence of sensitivity, which was the third highest incidence of sensitivity.

It has been suggested that hypersensitivity to thimerosal may be due to the thiosalicylate portion of the molecule and not the mercury (Ref. *5*); however, this has not been confirmed. Based on the above data, the Panel concludes that thimerosal is very allergenic.

A comprehensive study of several mercury compounds in 1950 (Ref. *1*) showed that these compounds were bacteriostatic rather than bactericidal and that thimerosal was no better than water in protecting mice from potential fatal streptococcal infection under the conditions of the study. The streptococcal culture was added to the various mercury antimicrobial preparations; the mixture held at the temperature of skin (32° to 34° C) for 10 minutes; subcultured into dextrose broth, dextrose broth with 0.1 percent thioglycollate, and dextrose broth with 10 percent blood serum; and then injected intraperitoneally into mice. The latter two culture media neutralized the bacteriostatic action of the mercury compounds (Ref. *1*).

The Panel concludes that thimersal is not safe for OTC topical use because of its potential for cell damage if applied to broken skin and its allergy potential. It is not effective as a topical antimicrobial because its bacteriostatic action can be reversed.

(iii) *Ortho-hydroxyphenylmercuric chloride.* Ortho-hydroxyphenylmercuric chloride occurs as white to faint pink feathery crystals that are soluble in water, alcohol, and benzene (Ref. *2*). It is used in burn preparations. The Panel concludes that this compound is safe for topical use in the concentration marketed for OTC use (0.056 percent). However, as a topical antimicrobial, this compound is not effective because its action is bacteriostatic rather than bactericidal (Ref. *17*).

(iv) *Phenylmercuric nitrate.* Phenylmercuric nitrate occurs as pearly, lustrous scales that are soluble in water (1 part to about 1,250 parts water) and slightly soluble in alcohol. Against human epithelial cells in vitro, phenylmercuric nitrate was found to be less toxic than bichloride of mercury and thimerosal, but it was still very toxic (Ref. *7*). Solutions of phenylmercuric salts in concentrations of 1:1,500 and greater tend to cause blistering of human skin and may act as primary skin irritants and allergens (Ref. *18*). The Panel finds phenylmercuric nitrate in the concentration submitted (1:10,000) (Ref. *19*) safe for topical application, but there is no evidence that this compound is an effective topical antimicrobial at this concentration.

2. *Category II labeling.* The Panel concludes that labeling of any OTC mercury-containing product for topical antimicrobial use is Category II because all mercury ingredients are placed in Category II.

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(19) OTC Volume 180271.

C. Category III Conditions.

These are conditions for which the available data are insufficient to permit final classification at this time. This document contains no Category III conditions.

Interested persons may, on or before April 5, 1982, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments on this advance

notice of proposed rulemaking. Three copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Comments replying to comments may also be submitted on or before May 5, 1982. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: September 23, 1981.

Arthur Hull Hayes, Jr.,

Commissioner of Food and Drugs.

Dated: December 17, 1981.

Richard S. Schweiker,

Secretary of Health and Human Services.

[FR Doc. 82-7 Filed 1-4-82; 8:45 am]

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Mercurials as Disinfectants

Evaluation of mercurial antimicrobic action and comparative toxicity for skin tissue cells.

By Frank B. Engley, Jr.*
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THE PROBLEMS involving the use of chemicals as antibacterial agents have been of particular interest to me as a bacteriologist (or should we say microbiologist since because of these chemicals taking care of many of the bacteria we have had to reach out for more organisms to work with). My first experience with them in laboratory work was some 18 years ago running, if you will pardon the expression, "phenol coefficient tests." Since that time I have been associated with problems involving antiseptics, disinfectants, preservatives, antibiotics, gaseous sterilization—in other words antibacterial agents.

Some ten years or more ago with Morton and North we were asked to carry out a study on mercurials for the Council on Pharmacy and Chemistry of the American Medical Association which was published in its journal in 1948. (1) This report suggested that mercurials did not fulfill all the conditions expected of antiseptics. The report had its desired result in that it stimulated considerable thinking, discussions, research and perhaps some controversy in the field. Unlike the theatrical or political figure who once said that it didn't matter what was written about him so long as they wrote something and spelled his name correctly—we in the field of scientific investigation would rather be quoted correctly than not at all. In this regard the report might not be the most misquoted or maligned report from certain quarters (not quaternaries) but it is in there with the best or the worst depending upon your point of view or the source of your income. In any regard, stimulation of thinking, discussion, research and perhaps some controversy (as they say in the business world) is good for any field—and what is good for any field is good for the country or vice-versa.

At this point it would be best to stress that testing of chemical antibacterial activity and evaluation of these tests is not a simple thing. Each test has its advantages and disadvantages—factors such as time, temperature concentration of drug, number of organisms, types of organisms, plus the investigator's own minor variations on the technique which defy putting in print or were cut out by the editor of a journal as superfluous, all affecting the findings.

So it is true that each test has its good and bad points, drawbacks, its pros and cons, and each chemical has its own special characteristics to suit it for some special use. There are people who argue one side or the other as to the relative merits of a test-tube test vs. an animal test vs. a "use" test. And then too, we have some who argue all sides for the sake of argument, or their chemical or just to becloud the whole issue.

Efficacy of Mercurials

WITH this background then let's come to the subject of the moment: Mercurials. I would like to present some evidence which raises questions in my mind as to the efficacy of mercurials as antiseptics, preservatives or antibacterial agents. These are very real, serious questions and doubts which I want to pass on to you for serious consideration.

Mercurial compounds have been used as disinfectants, antiseptics and preservatives for many years. It was probably the work of Koch (2) in 1881, some 75 years ago, that first stimulated the use of mercuric chloride by many workers as an antibacterial agent. His work with anthrax spores suggested that high dilutions of $HgCl_2$ would kill the spores of the organisms considered to be the most resistant of pathogenic bacteria. His work was with dried organisms and indicated that alcohol was poor in comparison. Both findings have been clarified considerably since then, as you well know, with bichloride shown to be highly bacteriostatic not cidal and alcohol to be fairly effective against spores in the wet stage.

In considering a chemical as an antibacterial agent, I personally feel that in the final analysis each chemical or group of chemicals

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* Based in part on studies with Dr. Tom Wynn, present address Cook County Hospital, Chicago, and Dr. C. M. Pomerat, The University of Texas Medical Branch, Galveston. Paper presented May 21, 1954 at 42nd midyear meeting, Chemical Specialties Manufacturers Association, Chicago.

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should be put to every possible test. Then impartial groups should decide on the basis of all the tests whether the chemicals in question really do what is claimed for and expected of them. I am not recommending here that anyone screening drugs should do a thesis problem on each and every chemical. However, those chemicals brought to the fore as potential commercial antibacterial agents should face a battery of tests to see how they show up under a variety of conditions. Don't use any one tailor-made test that one knows the chemical will pass or fail. Any chemical can be shown to be good or bad depending on the test employed.

So, back to mercurials. The early work by Koch established that bichloride of mercury could keep anthrax spores from growing out even in very high dilutions in the routine testing media.

Along these lines it would be best to look first at the "phenol coefficients" of various representative mercurials. Using *Staphylococcus aureus* as the test organism and taking the highest dilution of disinfectant killing microorganisms after 10 minutes but not after five minutes contact at 37°C. we find the following: With phenol active at a 1:85 dilution the following phenol coefficients were calculated. (McCulloch. (3)

Compound	Dilution Active	Phenol Coef.
Mercuric chloride	16,000	189
Mercurochrome	180	1.8
Merthiolate	120,000	1412
Metaphen	140,000	1647
Phenylmercuric nitrate (After Birkhaug, (4) 1933)	192,000	2259
Iodine	....	22.3
Hexylresorcinol	....	66.6

These figures lead us to bring out a very important point. This test as carried out with the usual nutrient medium reveals the chemicals' ability only to inhibit growth. By using dilution and/or preferably neutralizing substances in the recovering media one can differentiate between bacteriostasis and bactericidal activity in such a test-tube test. In the case of mercurials, fortunately or unfortunately, depending upon your point of view, both synthetic, purified and naturally occurring neutralizing substances are readily available. It is because of these neutralizing substances containing available, —SH (sulfhydryl) groups that so much controversy has developed. It would only be of perhaps academic interest that cystine, glutathione, ammonium sulfide, thioglycollate and a number of other compounds could neutralize or, if you prefer, reverse the action of mercurials on organisms after exposure, except for the fact that body fluids and tissues contain neutralizers—the skin, perspiration, urine, blood, serum, tissue exudates and all. Thus it is of practical importance. Some chemicals may have their antibacterial action reduced or neutralized only by some weird chemical such as "itchigummi acid" which does not occur naturally or in the field of use; therefore, while of academic and scientific interest in studying mode of action or kinetics of the drug activity, the fact that the drug antibacterial action may be neutralized or reversed is not of significance in its utilization. This is not the case with mercurials. The neutralizers are found everywhere. As early as 1889 (Geppert) (5) showed that such was the case.

Thus our pretty phenol coefficient values given above do not mean anything unless we add a neutralizer to the recovery medium such as thioglycollate or preferably serum. The phenol coefficients drop precipitously with the mercurials tested in this manner, revealing little antibacterial action. The same is true if serum is added to the test medium. Bichloride of mercury turns out with negligible activity as do the organic mercurials. Discussions with certain individuals suggested that this might not be too important but let me remind you that even though this is known many still use bichloride as a supposedly trusted antibacterial agent especially in hospitals for so-called "sterilizing" of thermometers. In a survey we carried out in the past two years in one large hospital in a medical center—the nursing service tested thermometer glasses on various wards and at various times isolating staphylococci, streptococci and others, as well as our friend Escherichicoli "from the other side of the tracks." The original preparation may have some activity but continuing standing and accumulation of sputum and "crud" rapidly reduces any activity. This data does not include the story about a glass of bichloride that one of the patients drank thinking it was the ice water although it might have left him a little cold.

In the course of our studies (6) we applied the paper disc assay technique to the study of mercurials using exacting and standard methods for accurate determinations. Table 1 lists some of the representative compounds tested giving proprietary name and chem-

Table 1. Mercurials Tested

Name	Manufacturer	Chemical name	Conc. of use (per cent)
Merbak	Schieffelin	2-acetoxymercuri-4-diisobutyl phenol	0.1
Mercurobolide	Upjohn	orthohydroxyphenylmercuric chloride	0.1
Mercresin	Upjohn	orthohydroxyphenylmercuric chloride + secondary-amyl tricresols	0.1
Mercuric chloride*	—	mercuric chloride	0.1
Mercuric iodide*	—	mercuric iodide	0.1
Mercurochrome	H W D †	disodium 2, 7-dibromo-4-hydroxymercuri fluorescein	2.0
Mercurophen	Sharpe & Dohme	sodium oxymercury cresol sphenolate	0.1
Merodicein	H W D †	monohydroxymercuridiodoxyacetanilide phthalate	0.2
Merthiolate	Lilly	sodium ethyl mercuri thiosalicylate	0.1
Metaphen	Abbott	anhydride of 4-nitro-3-hydroxymercuri ortho-cresol	0.2
Phenyl mercuric borate*	—	Phenyl mercuric borate	0.1

* Not proprietary.
† Hynson, Westcott & Dunning.

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Table 2. Comparison of Antibacterial Activity of Mercurial Antiseptics by Paper Disc Assay Method (20 ML. Plate)

Compound	Dilution of use (per cent)	Nutrient agar inhibition zone (in mm.)
Phenyl mercuric borate	0.1	33
Mercresin	0.1	32
Mercurbaloide	0.1	32
Merthiolate	0.1	32
Mercurophen	0.1	29
Mercuric Iodide	0.1	28
Metaphen	0.2	25
Mercurochrome	2.0	24
Merbak	0.1	23
Merodicin	0.2	18
Mercuric chloride	0.1	10

ical name. Hereafter they will be called by proprietary name so that all will recognize the substance – you realize the difficulties of referring to Merodicrin, for example, each time as monohydroxymercuridiodo-resorcinsulfonphthalein. particular chart has been copied and quoted elsewhere but means nothing as it stands alone – like the phenol coefficient test data without neutralizer. With serum added to the medium, the same mercurial giving the large zone shows negligence no antibacterial activity under this method of test.

Table 3. Comparison of Antibacterial Activity of Mercurials Using Neutralizers by Paper Disc Method

Compound	Dilution of use (%)	Nutrient agar inhibition zone (in mm.)	Nutrient agar + 0.5% thioglycollate	50% Serum agar
Phenyl mercuric borate	0.1	32	—	—
Mercresin	0.1	32	—	—
Mercurbaloide	0.1	32	—	—
Merthiolate	0.1	32	—	—
Mercurophen	0.1	29	—	—
Mercuric Iodide	0.1	28	—	—
Metaphen	0.2	25	—	—
Mercurochrome	2.0	24	—	—
Merbak	0.1	23	—	—
Merodicrin	0.2	18	—	—
Mercuric chloride	0.1	10	—	—

— = no inhibition zone.

Table 2 shows the zones of inhibition. The diameters of these zones were compared as shown using the dilution of use against *Staphylococcus aureus*. It indicates the relative activity of the various mercurials by this test. Tincture preparations gave the same data. This particular chart has been copied and quoted elsewhere but means nothing as it stands alone – like the phenol coefficient test data without neutralizer. With serum added to the medium, the same mercurial giving the large zone shows negligible activity. The table which should have been borrowed from our publication to give a more realistic picture would have been the next, (Table 3) which shows in each case with thioglycollate or with serum added no inhibition zones are present – meaning in essence no antibacterial activity under this method of test.

Table 4. Results of In Vivo Testing of Antiseptics

Authors	Disinfectant		Organism	Animals Inoc.	Animals % Dead
Nungester, Kempf 1942	Tinc. iodine	2.0%	streptococcus	29	48
	Tinc. mercresin	0.1%		31	94
	Tinc. merthiolate	0.1%		39	36
	Tinc. phenerol	0.1%		31	80
	Tinc. iodine	2.0%	pneumococcus	15	0
	Tinc. mercresin	0.1%		48	23
	Tinc. merthiolate	0.1%		40	55
	Tinc. phenerol	0.1%		52	67
	Tinc. phenerol	0.2%		56	16
	Tinc. vehicle			47	66

From "An 'Infection-Prevention' Test for the Evaluation of Skin Disinfectants," W. J. Nungester and Alice N. Kempf, J. Infec. Dis., 71:174, 1942.

In Vivo Tests

THE methods described above, the phenol coefficient and the paper disc assay procedures, are strictly test-tube tests. They have been criticized since they are not *in vivo* tests. At this time then let us examine some data on "*in vivo*" tests. In the literature as far back as 1923 Rodwald (7), with a vegetative Salmonella test organism, showed that bichloride of mercury prevented its growth in subcultures but did not prevent this organism from killing mice when injections were made. More recent studies with the mouse-tail techniques, Nungester and Kempf (8) in 1942 (Table 4) revealed the mercurials to be less effective than iodine against the fairly resistant streptococcus. Slightly better results were obtained against the pneumococcus. The pneumonococcus data perhaps should receive less attention here since it is, not primarily a skin pathogen.

In our studies (Table 5) shown here with studies by Pierce and Tilden we strove to develop a combination *in vitro–in vivo* test with a known human pathogen also infectious for mice. We used a technique similar to a phenol coefficient test, but in addition to inoculating appropriate media following exposure of organisms to the chemicals, mice were injected with the mixture of chemical in its dilution of use and the organisms. The findings on a typical experiment are shown here and in Table 6 the significance is pointed out. Here are shown the death in mice and the lack or growth in a nutrient dextrose broth. If the broth findings above were taken as the true indicator, the chemicals would appear as good antibacterial preparations. However, the broth with neutralizers thioglycollate and serum allow the organism to grow out. This is in direct correlation with the findings in the animal test where the mice die from streptococcus infection. These preparations

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Table 5. Results of In Vivo Testing of Antiseptics

Authors	Disinfectant		Organism	Animals Inoc.	Animals % Dead
Pierce-Tilden 1945	Tinc. "D.C.-12"	0.1%	pneumococcus	120	42
	Tinc. metaphen	0.1%		34	85
	Tinc. merthiolate			34	97
	NaCl	0.85%		143	94
Morton, North, Engley 1948	Mercurochrome	2.0%	streptococcus	8	63
	Metaphen	0.2%		8	25
	Merthiolate	0.1%		6	66
	Phenol	1.0%		4	0

From "Evaluation of Antimicrobial Activity" in M. E. Pierce and E. B. Tilden, J. Dis. Res., 74:65, Oct. 1945. "The Bacteriostatic and Bactericidal Action of Some Mercurial Compounds on Hemolytic Streptococci." E. Morton et al., J.A.M.A., 136:37, Jan. 8, 1948.

Table 6. Comparison of In Vivo and In Vitro Methods of Evaluating Mercurial Antiseptic Activity

Compound	Conc. of Use (%) Mice	Mice Dead Mice Injected*	Dextrose Broth	Dextrose Broth + 0.1% thioglycollate	Dextrose Broth + 10% serum
Phenyl mercuric borate	0.1	8/10		+	+
Merbak	0.1	9/10		+	+
Merthiolate	0.1	10/10	—	+	+
Mercurophen	0.1	9/10	—	+	+
Mercuric iodide	0.1	8/10	—	+	+
Mercurbiolide	0.1	8/10	—	+	+
Metadicein	0.2	10/10	—	+	+
Metaphen	0.2	7/10	—	+	+
Mercurochrome	2.0	10/10	—	+	+
Mercuric chloride	0.1	10/10	—	+	+
Water		10/10	+		
				+	+

* Mice injected and tubes inoculated with 0.1 ml. of a 1:2 dilution of the Streptococcus—mercurial mixture after a ten minute exposure at 32.34°C.

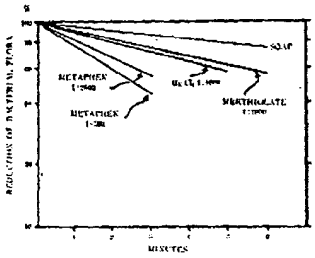
under this test do not do what an antiseptic should do—prevent infection.

The *in vivo* methods described above have been criticized not because they are not test tube tests but because they are not "use" tests. Some state that these *in vivo* and *in vitro* tests do not simulate actual usage. The major proponent of the use test Dr. Price (9) has suggested that while such tests are important procedures—the *in vitro* and *in vivo* tests are perhaps more accurate and quantitative then when using human subjects. His data using the hand washing—basin technique are of interest to us in this report. Graph 7 indicates the reduction of bacterial flora of the skin plotted against time with aqueous preparations and in Graph 8 a comparison of alcoholic preparations. The latter are more effective than water preparations but it should be noted that the solvent removes organisms faster alone than with the mercurials added. He further more suggests that the mercurials combine with skin forming a layer over the organisms neither killing nor preventing them from growing.

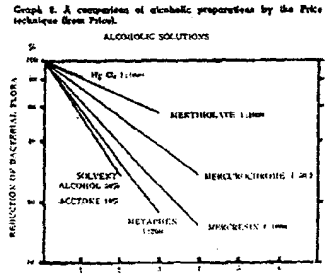
The use of mercurials as preservatives in vaccines and antisera is of considerable interest. These chemicals are added to protect against the introduction of organisms in multi-use containers in particular. We have always wondered about their efficacy in that both vaccines and antisera contain reactive groups to tie up these compounds. In a series of continuing experiments over the past several years we have begun to evaluate various preservatives in serum and vaccines under conditions of use. Employing stock vaccines and serum with and without preservatives and stored at varying lengths of time a contaminating dose of representative sporeformer (*Bacillus subtilis*) in the spore stage gram negative rod (*E. coli*) and gram positive coccus (*S. aureus*) were added. While the mercurial preservatives had good activity on initial addition, after storage of three, six or more months decreasingly

(*Turn to Page 223*)

Graph 7. A comparison of aqueous preparations tested by Price technique (from Price).



Graph 8. A comparison of alcoholic preparations by the Price technique (from Price).



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Mercurials as Disinfectants

(From Page 203)

less to negligible residual activity appeared to be left, indicating that the chemical was tied up by the protein of the biological or otherwise inactivated. A check on a series of over one thousand bottles of various biologicals from clinics obtained after use revealed that up to five percent contained microorganisms. This would suggest that once these biologicals are in the hands of the users a problem still exists.

Regarding preservatives, one of the real problems existing in hospitals and clinics is the need for good preservatives in the routine eye dilators and nasal preparations of the decongestant type. Routine checks of these indicate a high percentage of contaminated solutions. In one instance we had direct evidence of upper respiratory cross-infection from the use of a common nasal dropper preparation in a clinic.

The toxicity of chemicals used as drugs on or in the body has been of considerable interest since man first began exposing himself to various chemicals many years ago. Unfortunately there have not been good techniques for toxicity determinations of certain types of chemicals which might be really indicative of toxicity for humans.

In the past, various techniques have been employed for testing the toxicity of skin antiseptics with more or less success. These tests have included toxicity tests in and on animals such as mice, in embryonic eggs, on leukocytes and in embryonic chick tissue culture using heart or spleen(6). Each of these tests have had advantages and disadvantages. The obvious one enjoyed by all is that they are not a true test of toxicity of the chemical for human skin tissue cells. Recently the opportunity offered itself for perhaps a more significant test procedure.

A few years ago in the tissue culture laboratory of the University of Texas Medical Branch, Dr. C. M. Pomerat and co-workers found that skin from grafting procedures produced epithelial sheets *in vitro* (in tissue culture). This offered a possible method for evaluating the toxicity of a number of chemicals such as local anaesthetics, antihistamines and antiseptics on the one test material of importance – skin itself. Some of these studies have been reported from these laboratories. In this report we wish to stress studies on mercurial compounds in particular and to compare their toxicity with representative antibiotics, phenolic derivatives, quaternary ammonium compounds and furans.

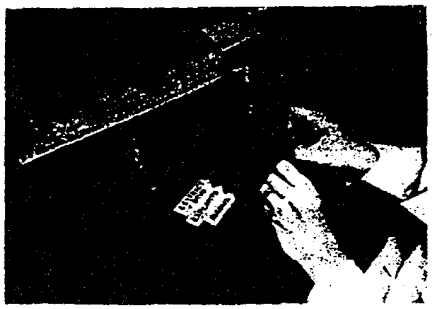
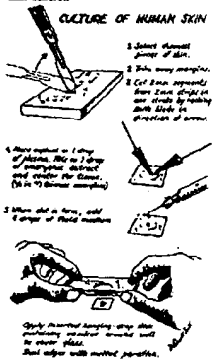


Figure 9. Preparation of serial dilutions in embryonic extract.

Figure 10. Steps in preparation of human skin cultures.



The technique used here consisted of the following: Serial dilutions of the chemicals under test were prepared in embryonic extract as shown in Figure 9. Thin slices of human skin were removed with sterile instruments and the tissue cut into fragments approximately 2mm square (Figure 10). Each explant was placed on a cover slip in plasma, and embryonic extract containing the drug dilutions was added. The tissue was centered on the cover slip and after a clot forms, the preparation was sealed onto a depression slide and incubated at 37°C for eight to ten days. Cultures were examined microscopically for growth at daily intervals and compared in growth with control skin tissue without chemicals added. Figure 11 shows a highly magnified view of some of the outgrowth from the skin. As will be noted it is pure epithelial cell growth not the fibroblasts such as the chick heart growth produces. Migration of epithelial cells usually began after 48-72 hours of incubation. Outgrowth from the edge of the explant was graded by quantitating the amount of the low power field it covered (at the 8th

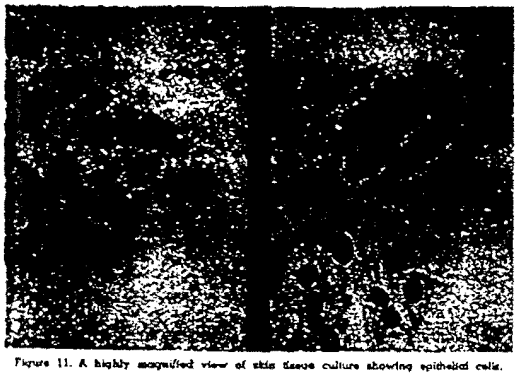


Figure 11. A highly magnified view of skin tissue culture showing epithelial cells.



Figure 12. Magnified views of skin tissue culture showing 4+, 3+, 1+ and negative growth from top left to lower right.

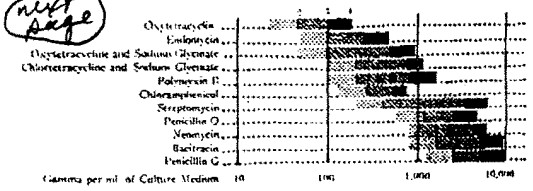
day). Figure 12 indicates the negative 1+, 3+ and 4+ outgrowth. From this data two values were determined, one the MID or minimal inhibiting dose—the smallest amount of chemical required to produce total inhibition of outgrowth and the second the LID the least injurious dose (the quantity of drug giving the slightest amount of injury as compared with the untreated control cultures). Thus we can set up a range of toxicity for any given drug. All drug concentrations given here are in gammas per ml of culture media.

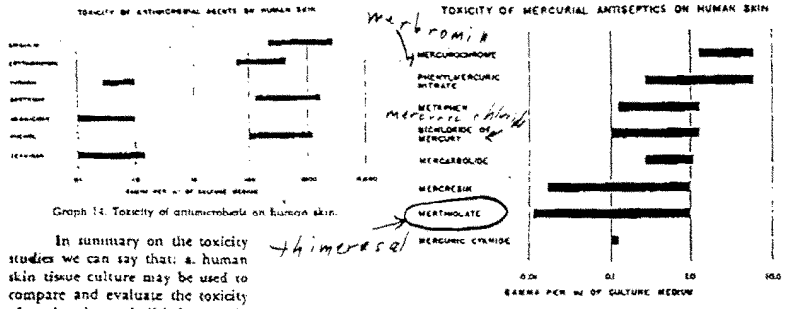
In Fig. 13 are shown some of the early studies carried out by Dr. Pouerat's laboratory (in conjunction with the dermatology department under Clarence Livingood[10]), with antibiotics and shown here for comparison purposes. For reference if you wish (10,000 gammas = one percent). It is of interest to note the low level of toxicity that we might expect for penicillin. Bacitracin, one of those considered dangerous parenterally, is not toxic for the skin and it is used frequently as a local antibiotic without apparent difficulty. The same is true of neomycin. The cycline antibiotics here show an increased or high toxicity for the skin tissue cells. In Graph 14 note that our concentration showing toxicity is dropping. Another list of materials is shown here showing varying toxicity. As we progress from right to left increasing toxicity is demonstrated. Of particular interest here is phenol to use as a guide. It is usually used as a five percent preparation which is fairly toxic for skin. Here we show that 1000 gammas per ml. (0.1 percent) is toxic for the cells. We might point out here some recent data which is not shown in the graph. That is the data on iodine. We have found the MID to be between 853-416 micrograms per ml and the LID between 13 and 7.5 micrograms per ml. It should be noted that furacin shows up to be quite toxic—as has been shown by experience. A representative quaternary ammonium compound (Zephiran) appears highly toxic. Graph 15 compares mercurial compounds and shows how they fit in with other compounds in toxicity. It should be noted that furacin, gramicidin and Zephiran are in the same general range. Mercurochrome appears to be the least toxic running down through merthiolate. It should be kept in mind that its combination of use is two percent while the others are usually 1:1000. One point should be made here. Bichloride of mercury has always been pointed out as an extremely toxic mercurial and the organic mercurials were supposed to be much less toxic but according to these data we find bichloride right in the middle of the organic mercurials in regard to cell toxicity.

In the course of these studies the question arose as to how this test on skin compared with the use of other tissues. Was skin as sensitive or less sensitive in a test. Graph 16 compares bichloride of mercury on several other tissues with skin. Here it is shown that skin is more sensitive than cord, heart or spleen tissue cells.

next page

Figure 13. Toxicity of antibiotics on human skin.





Graph 15. Toxicity of mercurial antiseptics on human skin.

Graph 14. Toxicity of antimicrobials on human skin.

In summary on the toxicity studies we can say that: a. human skin tissue culture may be used to compare and evaluate the toxicity of antiseptics and disinfectants in the test tube. b. mercurial antiseptics proved to be more toxic than the antibiotics in common usage but in the same range of toxicity as representative furan derivatives and quaternary ammonium (detergent) antiseptics. c. bichloride of mercury appears no more toxic by this test than organic mercurials. d. the procedure offers a better index of toxicity than testing on animals, animal tissues, chick embryos, white blood cells or other procedures now available.

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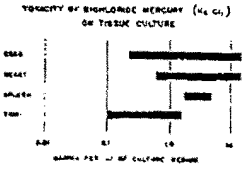
Graph 16. Toxicity of bichloride mercury ($HgCl_2$) on tissue culture.



Wax from South Africa

(*From Page* 185)

structure conventional paraffin waxes made from petroleum. Other points of resemblance are white color, brittleness, and low viscosity when melted.

The product differs from conventional paraffin waxes in high temperature characteristics and in crystal size. Crystals are much finer and more like those of petroleum-derived microcrystalline waxes than of paraffin. Melting point is 215°F, compared with 150°F for the upper limit of paraffin waxes. Hardness at elevated temperatures is one of the characteristics exhibited by "Paraflint." Moore & Munger's modified Abraham consistometer, measures the product's hardness at 75 at room temperature, against 92 for carnauba, 72 for tank bottom wax, and 43 for refined paraffin (m.p. 150). At 130°F, "Paraflint" exhibits hardness of 49, compared with 62 for carnauba, 40 for tank bottom wax, and 28 for paraffin.

"Paraflint's" good hardness characteristics and the ability to take a high shine and buff makes it suitable for incorporation in polish formulations. In addition it is said to lend itself to oxidation in the production of emulsifiable waxes.

Typical physical data on "Paraflint" are as follows:

Melting Point	215°
Needle Penetration at 77°F.	1.0
Oil Content	less than 1.0%
Average Molecular	750 (approximate)
Acid, Saponification, Bromine Numbers	Nil
Ash Content	less than .01%
Color	White
Viscosity at 250°F.	9.5 centipoises
Specific Gravity at 77°F.	0.93/.95

Essentially odorless

—*—

Carbide Assigns Four

Four technical representatives have been assigned to sales offices of Carbide and Carbon Chemical Co., New York, after completing a six-week training course at the Mellon Institute of Industrial Research, Pittsburgh, it was announced recently. The assignments follow: N. R. Carbone, Los Angeles district office; J. R. Conaway, general sales office, New York; J. A. Francis, St. Louis district office; and A. F. Murray, Pittsburgh district office.

Prevention of Surface Bacterial Contamination of Donor Corneas

Kenneth N. Goldman, MD; Yvelisa Centifanti, PhD; Herbert E. Kaufman, MD; Thomas E. Sleppey

• A simple method has been developed to reduce contamination in postmortem donor human eyes in anticipation of corneal transplantation. In vivo investigation of albino rabbits demonstrates that vigorous saline solution irrigation is extremely effective in decreasing the surface bacterial counts of the postmortem eye. In vitro and in vivo studies show that Neosporin kills bacteria at room temperature and further show that a tenfold increase in the thimerosal concentration of the Neosporin will kill fungus. Postmortem eyes contaminated by pathogenic organisms can be effectively cleaned by a combination of saline solution irrigation and the new Neosporin-Thimerosal solution. No substantial damage of the donor tissue was noted by scanning electron microscopy. Human eyes cultured before this procedure were all contaminated, but after cleaning and immersion, no bacterial or fungal growth occurred.

(*Arch Ophthalmol* 96:2277-2280, 1978)

After any intraocular surgical procedure, the occurrence of endophthalmitis is a devastating complication. In corneal transplantation, there is one additional source of possible bacterial contamination of the eye, ie, the corneal donor button itself. To avoid this possible route of infection, we have investigated methods to provide for surface sterilization of the donor tissue whether it be subsequently stored in a moist chamber or in McCarey-Kaufman medium.

Accepted for publication Feb 2, 1978.

From the Department of Ophthalmology, University of Florida College of Medicine, Gainesville. Dr Goldman is now at Montefiore Hospital, New York. Drs Centifanto and Kaufman are with the Louisiana State University Medical Center, New Orleans. Mr Sleppey is with the Southern Eye Bank, New Orleans.

Reprint requests to Department of Ophthalmology, Louisiana State University Medical Center, 136 S Basnan St, New Orleans, LA 70112 (Dr Kaufman).

MATERIALS AND METHODS

Pathogenic Organisms

Pseudomonas aeruginosa, *Staphylococcus epidermidis*, *S aureus*, *Proteus mirabilis*, *Streptococcus viridens*, and *Escherichia coli* bacterial strains were used as bacterial test organisms. Stock suspensions were grown overnight in trypticase soy broth. The suspensions were diluted in phosphate buffered saline solution (PBS) (pH 7.2). Several log dilutions were made, and 0.2 ml of these dilutions were plated on blood agar plates to quantify the inoculum. The concentration of the final bacterial inoculum was approximately 10^6 to 10^7 bacteria per milliliter. The fungus *Candida albicans* was initially grown in Sabouraud's agar in a 60-ml bottle, kept refrigerated, and used as the source of *Candida* in this investigation. The *Candida* inoculum was quantified in the same manner as that for the bacteria.

Drugs

The ophthalmic solution we used (Neosporin) contains polymyxin B sulfate (Aerosporin) (5,000 units), neomycin sulfate (2.5 mg), gramicidin (0.025 mg), 0.5% ethyl alcohol, and 0.001% thimerosal per milliliter; the mixture was selected because it is most commonly used by eye banks. To increase the concentration of thimerosal in the Neosporin solution, a thimerosal solution was made of 10 mg/ml in twice-distilled water. This stock solution was then filtered through a 0.45 mμ Millipore filter. The stock was kept refrigerated and was prepared fresh at one-month intervals. An aliquot of 0.1 ml of this solution was then added to 10 ml of the Neosporin solution to bring the final concentration of thimerosal to 0.01%.

Animal Experiments

Two 2- to 3-kg albino rabbits were used for in vivo experiments for each concentration of each organism tested.

The rabbit was killed with a lethal injection of barbital sodium. Immediately following death, 0.1 ml of a quantitated bacterial suspension was placed on the dome of the cornea. The lids were closed and gently massaged to distribute the bacteria. The lids were then sewn closed with a double-arm 4-0, black, silk, mattress suture. After an hour's incubation in the conjunctival sac of the killed animal, the lids were opened and the eye was enucleated using sterile technique. The eyes were then subjected to different sterilizing preparations and programs (to be discussed with each individual experiment), after which the corneas were cultured.

Human Experiments

Twenty human corneas were cultured for bacteria and fungi when initially obtained. They were then recultured after vigorous irrigation and immersion of the intact globe for five minutes in Neosporin with 0.01% thimerosal. Cultures were done by thoroughly swabbing the cornea and scleral rim with a thioglycollate-moistened swab, putting the swab in 1 ml of thioglycollate broth and placing 0.2 ml on each of blood agar and Sabouraud's agar plates.

Cornea Culture Technique

To culture the corneas and quantitate bacterial contamination, the cornea was excised from the eye using sterile technique. The anterior chamber was entered with a dissecting blade and then using curved corneal scissors, the whole cornea was excised. The cornea was then placed in 1 ml of thioglycollate broth to neutralize any remaining thimerosal on the cornea.

Following this, 0.2 ml of thioglycollate was placed in blood agar plates for quantitation of the corneal bacterial count.

Experiments

Experiment 1.—Irrigation.—On four separate occasions, an animal was killed and an inoculum of quantitated *Pseudomonas* was placed in the conjunctival sac of both eyes and left for one hour. The paired eyes were then enucleated in sterile fashion and subjected to one of two procedures. One eye of the pair was vigorously irrigated with a jet of 20 ml of normal saline solution using a syringe and 20-gauge hypodermic needle. The eye was then fully immersed in 10 ml of normal saline solution. The other eye was not irrigated, but was directly immersed in 10 ml of normal saline solution. After 30 minutes, the corneas were excised and cultured.

Experiment 2.—Neosporin Effect at Room Temperature (25 °C).—Using a tuberculin syringe, 0.1 ml of a quantitated pathogen suspension was injected into 1 ml of Neosporin solution and likewise into 1 ml of the prepared PBS-thimerosal-alcohol solution (0.01% thimerosal and 0.05% alcohol) and left at room temperature. At the appropriate times, 0.1 ml of each mixture was inoculated into 0.9 ml of thioglycollate broth (this neutralized thimerosal). Then, 0.2 ml of this broth was plated onto individual blood agar plates. To prevent a Neosporin carry-over effect (a "prozone") in the case of the *Staphylococcus epidermidis*, several dilutions of the 0.2 ml of inoculated thioglycollate broth were made, and each dilution was plated out. The figures in Table 1 represent a 1:100 dilution. The carry-over effect of the Neosporin is negligible. The three pathogens used in this experiment were inocula of 10^8 bacteria per milliliter of *Proteus*, *Staphylococcus epidermidis*, and *Candida*.

Experiment 3.—Combined Irrigation and Neosporin.—An in vivo model of a donor eye setting was prepared. Briefly, the animals were killed, large quantities of a specific pathogen were inoculated into the conjunctival sac and left for one hour, and the globes were enucleated (as in experiment 1). One eye of a pair was irrigated by a strong jet of normal saline solution from a 20-gauge hypodermic needle. The eye was then immersed for five minutes in 10 ml of the Neosporin 0.01% thimerosal.

The other eye was not treated or irrigated but was immediately immersed in 10 ml of normal saline solution for five minutes. The corneas of both eyes were excised and cultured. The 10 ml saline depositary of the untreated (control) eye was also cultured and quantitated to establish a control bacteria count for the globes (after enucleation) themselves.

Experiment 4.—Morphologic Examination of Treated Eyes.—The eyes of an albino rabbit that weighed 2 to 3 kg were enucleated and then subjected to the treatment of irrigation and Neosporin-thimerosal solution bath for five minutes (see experiment 3). The endothelium and epithelium were then examined by scanning electron microscopy.

Tissue for scanning electron microscopy was first fixed in 2.5% glutaraldehyde in Millonig buffer for one hour. The tissue was then rinsed in buffer and postfixed in 1% osmium tetroxide that was also in Millonig buffer for 90 minutes. Both fixations were done in cold temperatures.

After fixation, the tissue was dehydrated in increasing concentrations of ethanol. Final dehydration was performed in an apparatus with carbon dioxide.

The tissue was then coated with palladium-gold and viewed with an electron microscope.

Table 1.—Neosporin Effect at Room Temperature on *Staphylococcus epidermidis**

Time, min	Average Counts Organism per Blood Agar Plate: Neosporin (With Preservatives)	Average Counts Organism per Blood Agar Plate: 0.01% Thimerosal + 0.5% Ethyl Alcohol
5	1,147	TNTC†
10	586	TNTC
15	755	TNTC

*Inoculum, 10^8 bacteria per milliliter; 30-minute percent kill, 99.9%.
†TNTC, too numerous to count.

Table 2.—Effect of Irrigation on Bacterial Counts

Initial *Pseudomonas* Inoculum, Bacteria per Milliliter	Final Bacterial Counts of Excised Cornea, Average Bacteria Count per Plate: Irrigation of Globe	Final Bacterial Counts of Excised Cornea, Average Bacteria Count per Plate: No Irrigation
4.05×10^8	0	Confluent
2.20×10^8	15	286
1.70×10^8	1	50
6.05×10^8	1	15

Table 3.—Neosporin Effect at Room Temperature on *Proteus**

Time, min	Average Counts Organism per Blood Agar Plate: Neosporin (With Preservatives)	Average Counts Organism per Blood Agar Plate: 0.01% Thimerosal + 0.5% Ethyl Alcohol
0	TNTC†	TNTC
15	261	TNTC
30	135	TNTC

*Inoculum, 10^8 bacteria per milliliter; 30-minute percent kill, 92.4%.
†TNTC, too numerous to count.

Table 4.—Neosporin Effect at Room Temperature on *Candida**

Time, min	Average Counts Organism per Blood Agar Plate: Neosporin (With Preservatives)	Average Counts Organism per Blood Agar Plate: 0.01% Thimerosal + 0.5% Ethyl Alcohol
15	878	370
30	580	133
45	397	42

*Inoculum, 10^8 fungi per milliliter; 30-minute percent kill of 0.01% thimerosal, 83%; 45-minute percent kill of 0.01% thimerosal, 97.6%.

RESULTS

Animal Studies

Experiment 1.—Vigorous irrigation alone can substantially clear bacteria from a contaminated globe (Table 2).

Experiment 2.—At room temperature, Neosporin is an effective bactericidal agent. At room temperature, a tenfold increased concentration of thimerosal is an effective fungicidal agent, whereas Neosporin alone is not. (Using a *t* test and the kill rates determined by measuring the slope of the line best fitting the data, the 0.01% thimerosal was significantly more effective against *Candida*, with a confidence of >95%) (Tables 1, 3, and 4).

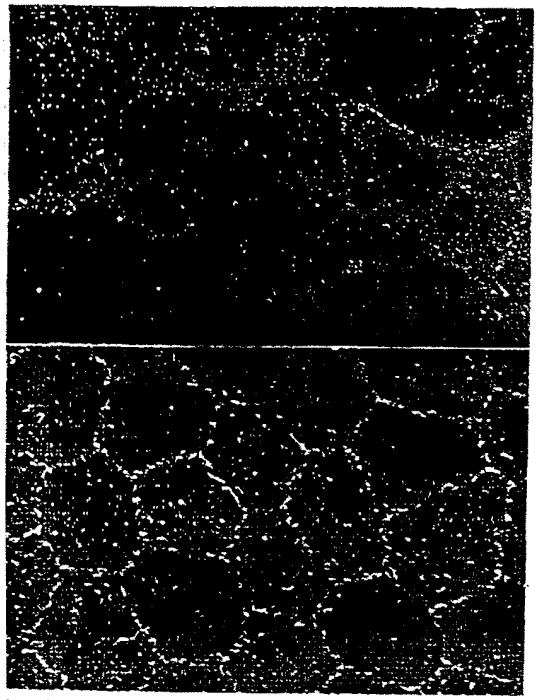
Experiment 3.—The combination of forceful jet stream irrigation of the globe and five minutes immersion into Neosporin-0.01% thimerosal solution gave a kill rate of more than 95% of bacterial contamination despite massive inocula (Table 5).

Experiment 4.—No notable damage

Table 5.—Effect of Irrigation and Neosporin-0.01% Thimerosal

Organism	*Staphylococcus epidermis*	*S aureus*	*Proteus*	*Escherichia coli*	*Pseudomonas*	*Streptococcus*	*Candida*
Initial inoculum into conjunctival sac	1.0×10^6	1.05×10^6	3.5×10^5	2.8×10^6	6.8×10^6	3.1×10^6	2.0×10^6
Organisms recovered from treated cornea (irrigation and Neosporin-0.01% thimerosal)	395	80	85	842	245	250	180
Organisms recovered from untreated cornea	390	4,362	1,260	1,715	2,480	2,175	36
Organisms in 10 ml saline depository of untreated cornea	8,400	8,870	59,400	TNTC*	42,550	74,200	5,450
Total organisms from control globe (untreated)	8,790	14,332	60,650	TNTC	45,010	78,375	5,486
Percent kill with treatment							
Compared with initial inoculum	96.1	99.3	88.8	98.9	99.8	98.8	99.8
Compared with control globe	85.5	89.9	99.8	...	99.5	98.7	98.7

*TNTC, too numerous to count.



Rabbit donor cornea after vigorous irrigation and five-minute immersion into Neosporin-0.01% thimerosal solution showing essentially normal epithelium with no damage from thimerosal. Top, Epithelium (×1,750). Bottom, Endothelium (×1,500).

or morphologic change was observed in corneas treated with irrigation and immersion into Neosporin-0.01% thimerosal solution (Figure).

Human Studies

Experiment 5.—Swab cultures taken before cleansing were all positive for bacterial contamination. Quantitation was not attempted since growth was often profuse. *Staphylococcus pyogenes* and *S epidermis* were most common, but *S aureus*, *Pneumococcus* sp, *Pseudomonas* sp, and occasionally, *Proteus* sp were seen. Following the cleansing procedure, all cultures for bacteria and fungi were negative.

COMMENT

This investigation was undertaken to minimize the risk of the donor corneal button being a possible source of contamination in corneal transplantation. Other investigators have reported that the surface of 50% to 100% of all donor eyes enucleated is bacterially contaminated.[1-3] Numerous methods have been suggested for decreasing bacterial counts in donor tissue. Neosporin has long been used for this purpose and has been suggested by numerous authors to be effective in diminishing the bacterial contamination of the donor eye.[2-4] Mechanical clearing of bacteria both by irrigation[2,4] and by removal of the donor corneal epithelium[3] have also been suggested as adjuncts in preparing bacteria-free donor tissue. In the present study, we have attempted to quantitate the effects of both mechanical and pharmacologic clearing of pathogens. By this approach we have tried to develop a simple, safe, and rational method of decreasing pathogen contamination of donor tissue.

The results of experiment 1 show

that there is a notable effect of vigorous mechanical irrigation alone. It may very well be that irrigation and washing of the globe is the single most important factor in diminishing bacterial contamination.

The purpose of experiment 2 was to observe the relative effectiveness of Neosporin with its normal preservative constitution (0.001% thimerosal and 0.5% alcohol) and a solution of increased concentration of thimerosal (0.01%) without antibiotic as bacteriocidal and fungicidal agents. The experiment was designed to prevent any carry over of the Neosporin onto the culture plates. The in vitro study demonstrated that Neosporin clearly had a bacteriocidal effect at room temperature. However, *Candida sp* was not cleared by Neosporin with its present preservative level (0.001% thimerosal, 0.5% alcohol). Therefore the increased concentration thimerosal solution was prepared and tested primarily to observe its effect on fungus. Topical thimerosal of up to 2% concentration has no deleterious effects on corneal epithelium or endothelium.[3] The results show that the increased thimerosal concentration of 0.01% indeed had fungicidal properties well in excess of Neosporin alone.

Taking cognizance of the bacteriocidal effect of Neosporin and the fungicidal effect of 0.01% thimerosal, experiment 3 was devised to test a method of producing bacteria-free corneas by using the combined actions of saline solution irrigation and immersion into a Neosporin-0.01% thimerosal solution. In experiment 3, an in vivo study was designed to simulate conditions found when obtaining human donor material. A very large bacterial inoculum was used in this experiment, far in excess of what may be found in any inapparent eye infection. The choice of bacteria used was based on those bacteria considered to be the most frequent pathogens of donor eyes.[2] A combination of jet-stream saline solution irrigation and immersion into a Neosporin-0.01% thimerosal solution was found to be highly effective in clearing of the pathogens. However, the inocula used were massive and would likely occur in the human situation only in the presence of frank, obvious infection. Despite the large numbers of organisms in the inocula and those infecting the globes, the method used herein of clearing pathogens was 90% effective in most of the tests, and the method was never below 95% effective.

The results of experiment 4 show that the integrity of donor corneal tissue (endothelium and epithelium) is maintained with the proposed regimen of sterilization. This is in agreement with another report[5] in which concentrations of thimerosal up to 2% had no harmful effect on the cornea as shown by light microscopy; however, neither that study nor the present study utilized transmission electron microscopy on the corneas.

There is now evidence that vigorous saline solution irrigation of the globe—the importance of which must be underscored—and the immersion of the globe in a solution of Neosporin with increased thimerosal concentration—which has potent bacteriocidal and fungicidal properties at room temperature—seems effective in cleansing the surface of donor corneal tissue with the concentrations of organisms that might reasonably be expected. This procedure is now being used by the North Florida Eye Bank. Studies of 20 donor eyes showed contamination before this cleansing procedure, but all cultures for bacteria and fungi were negative afterward.

This investigation was supported in part by grants EY-00156 and EY-00266 from the National Eye Institute, and the North Florida Lions Eye Bank for Restoring Sight Inc.

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The comparative toxicology of ethyl- and methylmercury

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Abstract. Neurotoxicity and renotoxicity were compared in rats given by gastric gavage five daily doses of 8.0 mg Hg/kg methyl- or ethylmercuric chloride or 9.6 mg Hg/kg ethylmercuric chloride. Three or 10 days after the last treatment day rats treated with either 8.0 or 9.6 mg Hg/kg ethylmercury had higher total or organic mercury concentrations in blood and lower concentrations in kidneys and brain than methylmercury-treated rats. In each of these tissues the inorganic mercury concentration was higher after ethyl- than after methylmercury.

Weight loss relative to the expected body weight and renal damage was higher in ethylmercury-treated rats than in rats given equimolar doses of methylmercury. These effects became more severe when the dose of ethylmercury was increased by 20%. Thus in renotoxicity the renal concentration of inorganic mercury seems to be more important than the concentration of organic or total mercury. In methylmercury-treated rats damage and inorganic mercury deposits were restricted to the P_2 region of the proximal tubules, while in ethylmercury-treated rats the distribution of mercury and damage was more widespread.

There was little difference in the neurotoxicities of methylmercury and ethylmercury when effects on the dorsal root ganglia or coordination disorders were compared. Based on both criteria, an equimolar dose of ethylmercury was less neurotoxic than methylmercury, but a 20% increase in the dose of ethylmercury was enough to raise the sum of coordination disorder scores slightly and ganglion damage significantly above those in methylmercury-treated rats.

In spite of the higher inorganic mercury concentration in the brain of ethylmercury- than in the brain of methylmercury-treated rats, the granular layer damage in the cerebellum was widespread only in the methylmercury-treated rats. Thus inorganic mercury or dealkylation cannot be responsible for granular layer damage in alkylmercury intoxication. Moreover, histochemistry demonstrated no inorganic mercury deposits in the granular layer.

Key words: Methylmercury – Ethylmercury – Neurotoxicity – Renotoxicity – Decomposition

Introduction

The neurological signs and symptoms of methyl- and ethylmercury intoxication are identical, but epidemiological-clinical studies from Iraq (Jalili and Abbasi 1961; Damluji 1962; Bakir et al. 1973) indicate that renal function is affected only by ethylmercury. The reason for this may be the faster renal accumulation and/or decomposition of ethylmercury. Thus it has been shown by Suzuki et al. (1963) that the kidneys of mice accumulated more mercury after the administration of ethylmercury than after methylmercury and by Fang and Fallin (1974) that in tissue slices incubated with these alkylmercurials the decomposition of ethylmercury was more noticeable. If this difference in decomposition is present in vivo, the comparative study of their metabolism and toxicity may be a valuable approach to investigate the role of decomposition not only in renal but also in neurotoxicity. It has been proposed by Jacobs et al. (1975) that the lipophilic methylated mercury allows the delivery of mercury to the central nervous system, where damage is caused by the cleaved Hg^{2+}, and by Ganther (1978) that cleavage through free radical formation is responsible for the neurotoxicity of methylmercury.

The purpose of the present study was to compare total and inorganic mercury concentrations in selected tissues, including the brain, after the daily administration of methylmercury or ethylmercury and to relate these findings to damage in brain and kidney.

It was planned that the effects of five daily doses of ethylmercury would be compared at two dose levels with those of 8.0 mg Hg/kg methylmercury, namely when the ethylmercury dose is equimolar with the dose of methylmercury and when the dose gives approximately the same total mercury concentration in brain as found in rats treated with 8.0 mg Hg/kg methylmercury. However, in preliminary experiments it was found that rats can tolerate 9.6 mg Hg/kg ethylmercury, while a further increase in dose to 11.2 mg Hg/kg caused high mortality within 3 days.

Material and methods

Porton Wistar male and female rats were given by gastric gavage five daily doses of 8.0 mg Hg/kg as methylmercuric chloride or 8.0 or 9.6 mg Hg/kg as ethylmercuric chloride (Pierce and Warriner Ltd.) in a volume of 2.0 ml/kg glycerol formol (Fluka A. G.). Animals were kept on MRC 41B diet during the whole experimental period with food and water freely available. The range of initial body weights was 181–231 g for males and 180–220 g for females with 210 g and 196 g means, respectively.

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A. Body weight. Body weights of 24 male and 18 female rats per treatment group were measured five times per week from the 1st treatment day. Because of respiratory problems (wheezing) three male rats had to be sacrificed before schedule and were omitted from comparison. As daily weight gains depend on initial body weight and sex, body weights on 0, 5 and 10 days after the last treatment were related to the normal weight curves supplied by our animal house. A substantial decrease in the standard error of means justified this approach.

B. Coordination disorders. Flailing reflex and hind leg crossing were scored from the last treatment day as described previously (Magos et al. 1978).

C. Histology and histochemistry. All animals were killed by decapitation, with the exception of those perfused for the histological examination of brain and dorsal root ganglia. After decapitation blood was collected in a weighed beaker and stored together with brain and kidneys at −4 °C until assay. Kidneys for histology and kidneys and brain for the histochemical demonstration of mercury were fixed in buffered formalin for 14 days. Slices between 3 and 5 mm thickness were processed and embedded in paraffin wax blocks. From these blocks 5 μm thick sections were cut and either stained with haemotoxylin and eosin or developed for the demonstration of mercury by the method of Danscher and Schroder (1979) with slight modifications. Thus the developer contained 20 ml buffer, 60 ml hydroquinone and 20 g Acacia with 1 ml silver nitrate added immediately before use. The sections were developed for 10 min at room temperature and after development they were rinsed with distilled water, fixed in 5% sodium thiosulphate for 5 min, washed in tap water for 10 min and counterstained with light haematoxylin and eosin. The presence of mercury in the tissue is demonstrated by the granular deposition of a silver-mercury complex. With this method no mercury could be demonstrated in the kidneys when rats were killed 3 h after a single dose of methylmercury, though their kidneys contained significant amounts of methylmercury. Thus in alkylmercury-treated rats this method shows only inorganic mercury (cleaved in vivo from the carbon bond). For brain and renal histochemistry, one male and one female animal per treatment group was killed 10–12 days after the last of five daily doses. In addition to these six rats, renal histochemistry was also carried out on the kidneys of 12 male rats (four per dose group) sacrificed 3 days after a single treatment.

For the histological examination of brain and dorsal root ganglia rats were perfused through the heart into the aorta with formol-acetic acid (10% formalin, 2% acetic acid) under deep ether anaesthesia. The brain and vertebral column were dissected after a delay of at least 2 h and stored in fixative for 5–7 days. The hind-brain, including the brain stem and cerebellum, was divided in the mid-sagittal plane and both halves embedded in paraffin wax for 5 μm step-serial sectioning. The vertebral column was placed in Gooding and Stewart's decalcifying solution for 2 weeks with three changes. Transverse slices (2 mm thick) were made of the vertebral column to include the cervical (C_4–C_8) and lumbar (T_{13}–L_4) cord enlargements. These were embedded in paraffin wax as composite blocks of the two regions. Step-serial sections (5 μm) were cut to ensure the presence of dorsal ganglia. Brain and spinal cord sections were stained with haematoxylin and eosin, Luxol fast blue and cresyl fast violet.

The severity of granular layer lesions in the depths and crests of the ten cerebellar lobules were scored separately according to a 4-point scale: 1+, few (<2%) pyknotic nuclei; 2+, several (2–10%) pyknotic nuclei; 3+, many (10–50%) pyknotic nuclei 4+, >50% pyknotic nuclei. The degeneration of dorsal root ganglia was also scored on a 3-point scale: 1+ few degenerating cells and Nageotte bodies: 2+, as 1+ but with chromatolytic changes and an increase in the number of satellite cells; 3+, many degenerating cells, large number of Nageotte bodies and satellite cells, with interstitial oedema and cell loss.

D. Assay for organic and inorganic mercury. Total and inorganic mercury and, by difference, organic mercury concentrations were determined by the selective atomic absorption method of Magos (1971) modified to prevent the decomposition of ethylmercury during assay. This was achieved by the reduction of the amount of $SnCl_2$ added to each sample, from 100 mg to 50 μg. Instead of adding $SnCl_2$ in 1 ml suspension to the reaction vessel, it was dissolved in and added with 10 ml 16 N H_2SO_4.

At this concentration the reducing power of tin is not stable and therefore the solution (5.0 mg $SnCl_2$ in 1000 ml 16 NH_2SO_4) must be prepared daily. When standard solutions of methyl- and ethylmercuric chloride were estimated for inorganic mercury by the modified method, methylmercury did not release inorganic mercury at all and the peak given by ethylmercury was 1.0% of the total mercury peak. This 1.0% was probably inorganic mercury contamination. Selected samples in four concentrations ranges were also analysed with a slightly modified version of the liquid gas chromatographic method of Cappon and Smith (1977), and results were compared with the selective atomic absorption method. Table 1 shows that means for organic mercury were slightly but not significantly higher than those given by gas chromatography. Consequently, it is unlikely that the atomic absorption method underestimated organic mercury concentration and consequently could not have over-estimated inorganic mercury concentration.

E. Statistics. The effects of ethylmercury at the two dose levels were compared with the effects of 8.0 mg/kg/day methylmercury. Two tailed multiple comparison procedure (Dunnett 1955) was used to evaluate significant differences ($p<0.05$) in relation to weight loss and mercury concentration, and two-tailed chi-square test or Fisher exact probability test was used to evaluate differences in coordination disorder and histology scores. Scores were arranged in 2×2 contingency tables so that the difference

Table 1. Comparison of the gas chromatographic and atomic absorption determination of organic mercury concentration in brain and blood after the administration of ethylmercury

Sample	Conc. range μg/g	No.	μg Hg/g (mean ± SEM)	
			A.A.	G.C.
Brain	< 12	8	9.8 ± 0.56	9.1 ± 0.7
Brain	12–18	8	15.4 ± 0.61	13.6 ± 0.74
Blood	60–70	8	65.8 ± 1.57	65.4 ± 2.15
Blood	200–400	8	316 ± 19.3	307 ± 19.1

Table 2. Differences between expected body weights (without treatment) and the actual body weights of methyl- and ethylmercuric chloride-treated rats at 0, 5 and 10 days after the last of five daily doses

Compound	Dose in mg Hg/kg	Sex	No.	Relative weight loss in % of expected body weight (mean ± SEM)		
				0 day	5th day	10th day
MeHgCl	8.0	M	24	10.4 ± 0.46	16.3 ± 0.89	18.5 ± 1.34
EtHgCl	8.0	M	22	12.6 ± 0.35*	20.9 ± 0.69*	24.6 ± 1.61*
EtHgCl	9.6	M	23	13.9 ± 0.43*	27.3 ± 0.93*	36.0 ± 1.49*
MeHgCl	8.0	F	18	7.8 ± 0.46	13.8 ± 0.86	20.0 ± 1.34
EtHgCl	8.0	F	18	9.6 ± 0.46*	16.6 ± 1.15	20.8 ± 2.22
EtHgCl	9.6	F	18	9.8 ± 0.45*	19.4 ± 0.98*	28.6 ± 1.74*

* Significantly different from the corresponding MeHgCl-treated groups with the Dunnett t test, $p < 0.05$

between horizontal (or vertical) sums should be as small as possible. The formula used for calculation incorporated correction for continuity (Siegel 1956).

Results

It has been well documented that one of the first toxic effects of methylmercury in rats is depressed weight gain or even weight loss. Table 2 compares weight loss relative to the expected body weight. It can be seen that, based on this criteria, ethylmercury proved to be more toxic than methylmercury. Compared with methylmercury, equimolar doses of ethylmercury caused a significantly larger relative weight loss in male rats at the three selected times, and in female rats at the last treatment day. The higher dose of ethylmercury resulted in consistently greater weight loss in both sexes.

The concentrations of total mercury (the sum of organic and inorganic mercury) and organic mercury was consistently higher in the blood of ethylmercury-treated rats (see Fig. 1) and in the brain (see Fig. 2) and kidneys (see Fig. 3) of methylmercury-treated rats. In blood and brain, but not in kidneys, an increase in the dose of ethylmercury from 8.0 to 9.6 mg Hg/kg/day increased the concentrations of both organic and inorganic mercury. The lack of a consistent increase in the kidney concentration of mercury with dose seems to indicate renotoxicity resulting in a loss of mercury with desquamated cells.

Figures 1–3 also show that in ethylmercury-treated rats inorganic mercury formed a larger proportion of total mercury than in methylmercury-treated rats, but even in the kidneys the concentration of organic mercury remained higher than that of inorganic mercury.

Contrary to weight loss, equimolar doses of ethylmercury caused less severe coordination disorders than methylmercury, though the sum of flailing and crossing scores was significantly less only at 5 days in male and 10 days in female rats (see Fig. 4). This difference was caused by significantly lower flailing scores. Increase in the dose of ethylmercury by 8.0 mg to 9.6 mg Hg/kg/day almost doubled the sum of scores in male, and trebled it in female rats 10 days after treatment when the crossing scores of females were significantly higher than in methylmercury-treated rats.

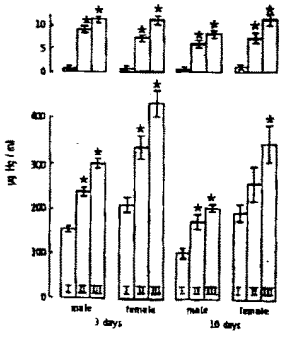

Fig. 1. The blood concentrations of organic *(lower columns)* and inorganic mercury (upper columns) 3 and 10 days after five daily doses of 8.0 mg Hg/kg given as methylmercuric chloride *(Group I)* or ethylmercuric chloride *(Group II)* and 9.6 mg Hg/kg ethylmercuric chloride *(Group III)*. *Asterisks* indicate significant difference (two-tailed Dunnett test, $p < 0.05$) from the methylmercury-treated group

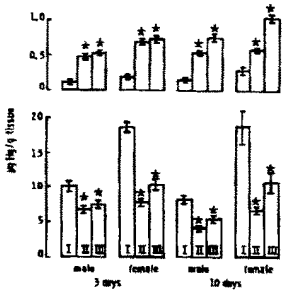

Fig. 2. Brain concentrations of organic and inorganic mercury after five daily treatments with methyl- or ethyl-mercuric chloride. For details see the legend of Fig. 1. Values were corrected to 1.1% blood content (Brown et al. 1976).

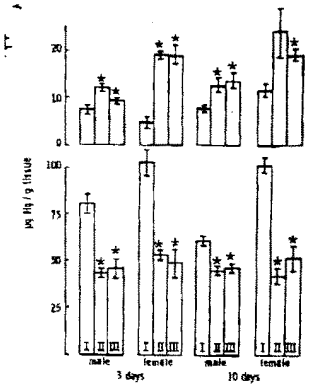

Fig. 3. The kidney concentrations of organic or inorganic mercury after five daily treatments with methyl- or ethylmercuric chloride. For details see the legend of Fig. 1.

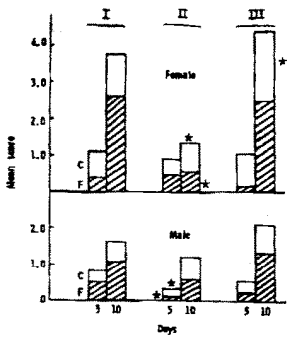

Fig. 4. Coordination disorder scores of male and female rats 5 and 10 days after the last of five daily doses of methyl- or ethylmercuric chloride. *Hatched columns:* flailing reflex; *open columns:* crossing of hind legs. Roman numerals denote the same groups as in Fig. 1. The number of rats are 19 males and 14 females *(Group I)*, 17 males and 14 females *(Group II)*, 19 males and 14 females *(Group III)*. *Asterisks* beside the hatched or open columns indicate significant difference (chi-square test, $p<0.05$) from the corresponding methylmercury mean score, and *asterisks* above columns indicate significant difference for the sum of scores

Table 3 shows that ethylmercuric chloride given in a dose of 8.0 mg Hg/kg/day for 5 days did not damage the granular cells of the cerebellum, while equimolar doses of methylmercury caused granular cell necrosis in six of nine males and in all of the female rats. Some granular cell necrosis was caused by 9.6 mg Hg/kg/day ethylmercury, but the damage was significantly less extensive than in rats given 8.0 mg Hg/kg/day methylmercury. The histochemical test for inorganic mercury did not demonstrate silver-mercury deposits in the granular layer in either methyl- or ethylmercury treated animals but deposits were consistently present in cerebellar roof nuclei and to a smaller extent in Purkinje neurones (see Fig. 5A). In neither the cerebellum nor the brain stem was there any noticeable difference in the density of silver-mercury deposits between animals, with the exception of the male rats treated with methylmercury which had less deposits than the others. Figure 5B shows an area from the brain stem. Contrary to the brain stem and cerebellum, the telencephalon and diencephalon of methylmercury-treated rats had no silver-mercury granules, while in ethylmercury-treated rats the same regions invariably contained mercury, the thalamus more than any other region.

Table 4 shows that both alkylmercurials damaged the dorsal root ganglia and 9.6 mg Hg/kg/day ethylmercury caused more damage than 8.0 mg Hg/kg/day methylmercury.

Ethylmercury was more renotoxic than methylmercury. Though animals were killed 10–12 days after the last dose, vacuolation and tubular dilation were frequently present, mostly in the P_3 region. Regeneration was also

Table 3. The extent and degree of cerebellar granular layer damage 10–12 days after the last of five daily doses of methyl- or ethyl-mercuric chloride

Compound	Dose in mg Hg per kg	Sex	No. of rats	No. of affected rats	Sum of lobular scores per group[a]							
					depth				crests			
					0	1+	2+	3+	0	1+	2+	3+
MeHgCl	8.0	M	9	6	56	26	8	0	78	12	0	0
EtHgCl	8.0	M	9	0[b]	90	0	0	0[b]	90	0	0	0[b]
EtHgCl	9.6	M	9	3	76	14	0	0[b]	76	14	0	0[b]
MeHgCl	8.0	F	9	9	7	31	47	5	28	42	19	1
EtHgCl	8.0	F	9	0[b]	90	0	0	0[b]	90	0	0	0[b]
EtHgCl	9.6	F	9	3[b]	71	19	0	0[b]	82	8	0	0[b]

[a] Granular cells in the depths and the crests of each of the ten cerebellar lobules were scored separately in each rat

[b] The number of affected rats or the number of affected lobules are significantly different from the corresponding methylmercury-treated group with the chi-square test

264

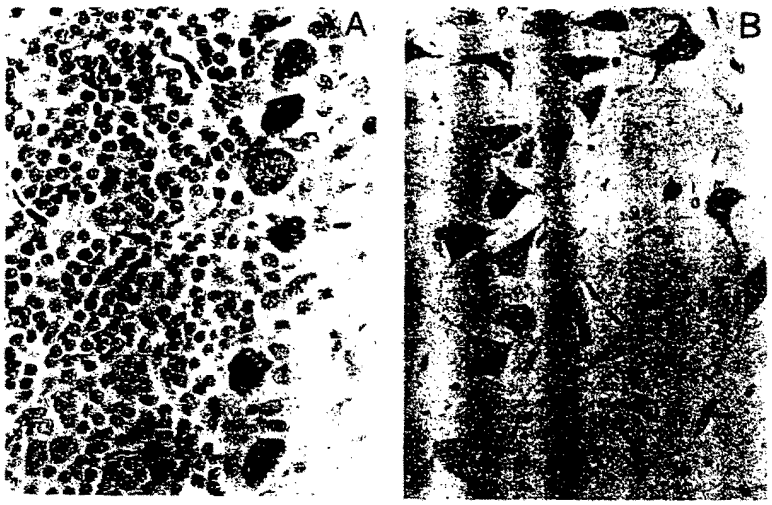

Fig. 5. Silver-mercury deposits in the cerebellum (A) and in the nucleus of facial nerve VII (B) of an ethylmercury-treated (5 x 8.0 mg Hg/kg) rat killed 10 days after the last treatment day. A deposits are in the large Purkinje neurones *(right)* but are absent in the granular layer *(left)*. B there are heavy silver-mercury deposits in the neuronal cytoplasm. x 560

present at this time. As Table 5 shows, pathological abnormalities were more frequent and more often extended to P_1 or P_3 regions in ethylmercury-treated than in methylmercury-treated rats. Table 5 also shows that with the exception of male rats treated with 8.0 mg Hg/kg/day ethylmercury, the ethylmercury-treated groups showed more extensive regeneration than methylmercury-treated ones. Fibrosis was seen in only one female rat treated with the higher and in one male rat treated with lower dose of ethylmercury. Metachromasia, pyknotic nuclei and cellular infiltration were seen only in ethylmercury-treated male rats. The extension of damage from P_2 to other regions in ethylmercury-treated rats was in agreement with the presence of the silver-mercury deposits. Both 10–12 days after the last of five daily doses and 72 h after a single dose in ethylmercury-, but not in methylmercury-treated rats, silver-mercury deposits were present not only in the P_2 but also in the P_1 and P_3 region. However, there was no correlation between severity of damage and the density of silver-mercury deposits, because in ethylmercury-treated rats, unlike damage, the localisation of deposits was predominantly in the P_3 region (Fig. 6).

Table 4. Damage in the dorsal root ganglia after the last of five daily doses of methyl- or ethyl-mercuric chloride

Compound	Dose in mg Hg/kg	Days after last dose	Degeneration scores											
			Males $N = 3$				Females $N = 3$				Both sexes $N = 6$			
			0	1+	2+	3+	0	1+	2+	3+	0	1+	2+	3+
MeHgCl	8.0	3–5	1	2	0	0	1	1	1	0	2	3	1	0
EtHgCl	8.0	3–5	2	1	0	0	1	1	1	0	3	2	1	0
EtHgCl	9.6	3–5	0	1	1	1	0	1	1	1	0	2	2	2
MeHgCl	8.0	10–12	0	2	1	0	0	0	1	2	0	2	2	2
EtHgCl	8.0	10–12	1	1	1	0	0	1	0	2	1	2	1	2
EtHgCl	9.6	10–12	0	0	0	3	0	0	0	3	0	0	0	6*

* Significantly different ($P < 0.05$) from the methylmercury-treated group with Fisher exact probability test

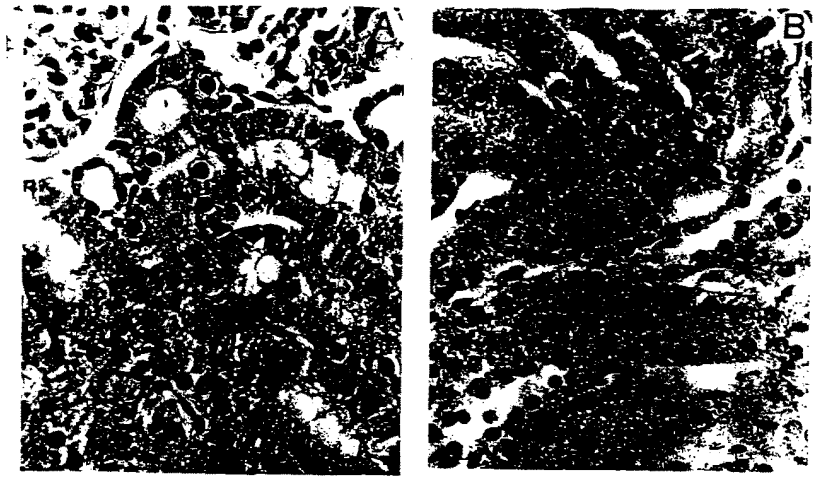

Fig. 6. Silver-mercury deposits in the kidney of an ethylmercury-treated rat 72 h after a single dose of ethylmercury (8.0 mg Hg/kg). A light deposits in the P_2 region of the proximal tubules. B heavy deposits in the P_3 region (pars recta) of the proximal tubules. × 560

Discussion

The brain accumulates less and kidneys more mercury from ethylmercury than from methylmercury treatment (Suzuki et al. 1963). However, with the prolongation of the exposure period, the difference in the kidney concentration of mercury between the two groups declines (Ulfvarson 1962), indicating that in ethylmercury-treated rats the faster renal accumulation is followed by faster depletion. In fact, as early as 3 days after the last treatment day the kidneys of ethylmercury-treated rats contained less total or organic mercury, though more inorganic mercury, than the kidneys of methylmercury-treated rats. Besides the faster renal depletion of ethylmercury, it is probable that mercury is lost with sloughed tubular cells (Magos 1982a) and the faster decomposition of the ethyl to mercury bond contributed to the difference in organic and inorganic mercury concentrations between ethyl- and methylmercury-treated rats. Increased loss of mercury with more severe renal damage may explain the lack of correlation between the renal concentrations of organic and inorganic mercury and the dose of ethylmercury.

Pathological changes observed in the kidneys 10–12 days after the last treatment day were characterized by the

Table 5. Abnormalities (vacuolation, dilation and regeneration) in the proximal tubular cells 10–12 days after the last of five daily doses of methyl- or ethylmercuric chloride

Compound	Dose in mg/kg/day	Sex	No.	No. of rats with damage		No. of rats with regeneration		
				P_2 region	+ P_1 and/or P_3 region	Slight	Moderate	Extensive
MeHgCl	8.0	M	6	4	1	1	1	1
EtHgCl	8.0	M	6	6	4	1	0	1
EtHgCl	9.6	M	6	6	6[a]	1	2	2
MeHgCl	8.0	F	6	4	0	2	0	0
EtHgCl	8.0	F	6	6	3	0	3	1[a]
EtHgCl	9.6	F	6	6	4[a]	0	2	4[a]

[a] The frequency of abnormalities outside the P_2 region or the frequency of moderate to severe regeneration is significantly different ($P < 0.05$) from the corresponding methylmercury-treated group with the Fisher exact probability test

concurrent presence of vacuolation, dilation, metachromasia, pyknotic nuclei, regenerating cells and fibrosis. Many of these changes are reminiscent of those seen in rats fed on diet containing inorganic mercury or rapidly decomposing phenylmercury (Fitzhugh et al. 1950), and contradict the possibility of acute tubular necrosis followed by postexposure regeneration. The importance of inorganic mercury in these renal abnormalities is indicated by the distribution of damage and inorganic mercury deposits. Mercury deposits, like damage, were principally restricted to the P_2 region in methylmercury-treated rats, whereas both damage and mercury deposits were more widely spread in ethylmercury-treated rats.

In methylmercury-treated rats anorexia resulting in depressed weight gain or weight loss is an indicator of neurotoxicity (Hunter et al. 1949; Magos 1982b). However, when the toxic agent can affect more than one target it is reasonable to suppose that injury to the second target also has a bearing on body weight. In fact, the order of relative weight loss in the three treatment groups, both in males and females, was the same as the order of neurotoxicity, whereas the severity of coordination disorders or dorsal root ganglion damage indicated marginally, and granular layer damage significantly higher toxicities for methylmercury than for ethylmercury. However, in the development of coordination disorders, weight loss may have influenced the direct neurotoxic effect. It has been shown previously that lactation moderated the effect of methylmercury on weight loss and coordination disorders but had no effect on dorsal root ganglion or granular layer damage (Magos et al. 1980). In the present experiments, absolute weight loss was always less in male than in female rats. There was no absolute weight loss in male rats treated with 8.0 mg Hg/kg/day methylmercury or ethylmercury, but the initial body weights of female rats decreased by an average of 21.0 g. In male rats dosed with 9.6 mg Hg/kg/day ethylmercury the 36% relative weight loss was equivalent to an average 23.0 g decline in initial body weight, while in female rats the 28% relative weight loss amounted to 38.0 g weight loss. Thus the contribution of weight loss relative to direct neurotoxic effect had to be more important in female than in male rats, and within the same sex more important in ethylmercury-than in methylmercury-treated rats. Another factor may be that, at least in female rats, dorsal root ganglia were damaged by 9.6 mg Hg/kg/day ethylmercury more than by 8.0 mg/kg/day methylmercury. In the present experiments, mercury concentrations were not measured in ganglion cells, but published data indicate that prolonged treatment with $HgCl_2$ can cause focal changes in dorsal root ganglia but, in contrast to methylmercury-treated animals, there is no progression to cell death (Chang and Hartman 1972; Jacobs et al. 1975). Thus mercuric mercury formed extraneously from alkylmercury can contribute to the injury of ganglion cells.

Contrary to dorsal root ganglion damage, the slow decomposition of lipophilic alkylmercurials to inorganic mercury cannot be the cause of neurotoxicity. All ethylmercury-treated rats had more inorganic mercury in their brain than methylmercury ones, but they either had no cerebellar damage (8.0 mg Hg/kg/day) or less damage (9.6 mg Hg/kg/day) than rats given methylmercury (8.0 mg Hg/kg/day). On the contrary, when treatment groups are arranged according to organic or total mercury concentrations, the order of brain mercury concentrations and the order of cerebellar damage are identical. Moreover, the histochemical visualization of inorganic mercury showed no silver-mercury deposits in the granular layer, where the cerebellar damage was largely localized.

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U.S. Licensed Pediatric Vaccines								
Product	**Trade Name (first licensure**	**Manufacturer**	**Dosage**	**Preservative and amount**	**Adjuvant**	**Other Additives**	**Mfg. Residuals**
DTaP	ACEL-IMUNE (12/91)	Lederle Labs.	5 ml	thimerosal 0.01%	$AL(OH)_3/AlPO_4$, Al 0.23mg	gelatin, tween	formaldehyde <0.02%
DTaP	Tripedia (8/92)	Aventis Pasteur Inc.	5 ml	thimerosal 0.01%	Alum; Al 0.170mg	$NaPO_4$	formaldehyde <0.02%; tween
DTaP	Infanrix (1/97)	SKB	5 ml	2-phenoxyethanol 2.5mg.	$Al(OH)_3$ Al ≤0.625mg		formaldehyde <0.02%, sodium chloride, tween
DTaP	Certiva (7/98)	North Amer Vaccine	5 ml	thimerosal 0.01%.	$Al(OH)_3$ Al 0.5mg		free formald. ≤10ppm, fetuin
Haemophilus b Conj. Vaccine (Meningococcal Protein Conj.)	Pedvax-HIB (12/89)	Merck & Co., Inc.	5 ml	liquid: None lyoph: thimerosal 0.02% *	$Al(OH)_3$ Al 225mcg	liquid: no lactose, sodium chloride 0.9% lyoph: lactose 2 mg	
Haemophilus b Conj. Vaccine (Tetanus Toxoid Conj.)	ActHIB, OmniHiB (3/93)	Aventis Pasteur, SA	5 ml	single dose: none,	None	sucrose 8.5%	
Haemophilus b Conj. Vaccine (Diphtheria CRM197 Protein Conj.)	HibTITER (6/94)	Lederle Labs.	5 ml	single dose: none, multi dose: thimerosal 0.01%		sodium chloride 0.9%	
Haemophilus b Conj. Vaccine (Meningococcal Protein Conj.) and Hepatitis B	Comvax (10/96)	Merck & Co., Inc.	5 ml	none	$Al(OH)_3$ Al 225mcg	sodium chloride 0.9%, sodium borate	yeast protein, formald.
Hepatitis B Vaccine (Recombinant)	RECOMBIVAX -HB (7/86)	Merck & Co., Inc.	5 ml	Two formulations (1) thimerosal 25 mcg (2) thimerosal-none	$Al(OH)_3$ Al 0.25mg	sodium chloride 0.9%.	yeast protein, formald.
Hepatitis B Vaccine (Recombinant)	Engerix-B (8/89)	SKB	5 ml	none	$Al(OH)_3$ Al 0.25mg	sodium chloride & phosphate buffers	thimer.< 0.5 mcg mercury
M, M, and R Virus Vaccine Live	M-M-R II (4/71)	Merck & Co., Inc.	5 ml	None	None	sorbitol, 14.5mg; neomycin 25mcg, gelatin (sucrose 1.9mg, culture medium, phosphate, glutamate)human albumin 0.3mg sodium chloride	FCS <1ppm
Pneumococcal Vaccine 7-valent Conj. Vaccine (CRM197 Protein)	Prevnar (2/00)	Lederle	5 ml	None	$AlPO_4$ 0.125mg Al		
...ilovirus Vaccine Inactivated	IPOL (12/90)	Aventis Pasteur, SA	5 ml	2-phenoxyetlanol 0.5%, formald 0.02%	None		neomycin <5ng, streptomycin 200ng, polymyxin B .25ng

Tetanus & Diphtheria Toxoids ads.	No trade name (7/70)	Lederle	.5ml	thimerosal 0.01%	$AlPO_4$, Al 0.3mg	sodium bicarbonate, physiological saline	formaldehyde <0.02%	
Tetanus & Diphtheria Toxoids ads.	No trade name (1/78)	Aventis Pasteur, SA	.5ml	thimerosal 0.01%	$ALPO_4$, Al 0.28mg	sodium chloride, sodium phosphate	formaldehyde	
Tetanus & Diphtheria Toxoids ads.	No trade name (7/70)	MPHBL	.5ml	thimerosal 0.01%	$AlPO_4$, 2.0mg	sodium chloride, sodium hydroxide, aluminum chloride	formaldehyde < 0.02%	
Tetanus & Diphtheria Toxoids ads.	No trade name (8/70)	Wyeth	.5ml	thimerosal 0.01%	$ALPO_4$, Al 0.85mg	sodium chloride, HCL, sodium hydroxidetio adjust pH	1mm formaldehyde 0.02%	
Varicella Virus Vaccine Live	Varivax (3/95)	Merck & Co., Inc.	.5 ml	None	None	sucrose 2.5mg, glutamate 0.5mg, gelatin 12.5mg, potassium chloride 0.08mg, sodium chloride 3.2mg, sodium phosphate dibasic 0.45mg, glutamate 0.5mg, potassium phosphate monobasic 0.06mg	neomycin, EDTA, FBS sodium phosphate monobasic cellular DNA/protein	
* No longer manufactured								

1 Note: Vaccines listed may not be currently distributed in the U.S.

Table 1 - Influenza Vaccine Dosage by Age Group
1999-2000 Season

Age Group	Vaccine**	Dosage	No. of Doses	
6-35 months	split virus only	0.25 mL	1 or 2*	
3-8 years	split virus only	0.50 mL	1 or 2*	
9-12 years	split virus only	0.50 mL		1
>12 years	whole or split virus	0.50 mL		1

Because of the lower potential for causing febrile reactions, only split-virus (subvirion) vaccines should be used for children. Immunogenicity and side effects of split- and whole-virus vaccines are similar among adults when vaccines are administered at the recommended dosage.

* Two doses administered at least one month apart are recommended for children less than 9 years of age who are receiving influenza vaccine for the first time.