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ANIMAL CANCER RESEARCH ACT

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HEARING BEFORE THE SUBCOMMITTEE ON AGRICULTURAL RESEARCH AND GENERAL LEGISLATION OF THE COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY UNITED STATES SENATE NINETY-SIXTH CONGRESS

FIRST SESSION

ON

S. 2043

TO PROVIDE FOR RESEARCH IN THE DIAGNOSIS, PREVENTION, AND CONTROL OF MALIGNANT TUMORS IN DOMESTIC ANIMALS, POULTRY, AND WILDLIFE

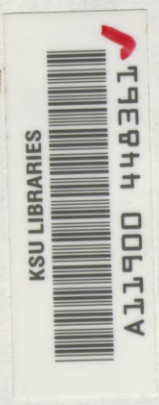
DECEMBER 10, 1979

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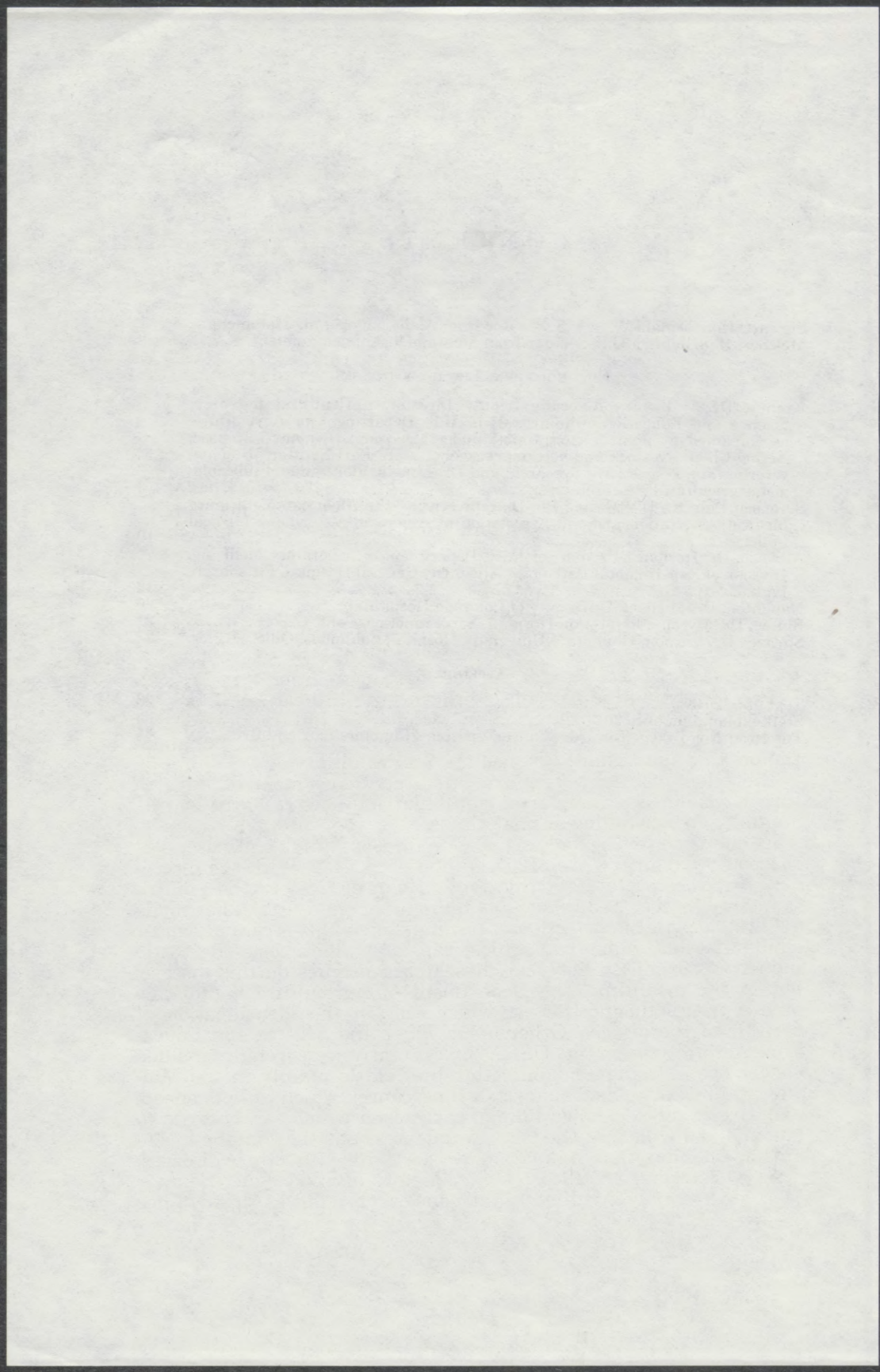
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ANIMAL CANCER RESEARCH ACT

(S. 2043)

MONDAY, DECEMBER 10, 1979

U.S. SENATE,
SUBCOMMITTEE ON AGRICULTURAL RESEARCH
AND GENERAL LEGISLATION OF THE
COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY,
Washington, D.C.

The subcommittee met, pursuant to notice, at 9:55 a.m., in room 324, Russell Senate Office Building, Hon. Donald W. Stewart (chairman of the subcommittee) presiding.

Present: Senator Stewart.

Also present: Senator Melcher.

STATEMENT OF HON. DONALD W. STEWART, A U.S. SENATOR FROM ALABAMA

Senator STEWART. We will call the meeting to order.

This subcommittee convenes this morning to hear testimony on S. 2043,¹ introduced by Senator Melcher, a bill to provide for research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife.

The scientists and veterinarians at the Department of Agriculture have made a number of vital contributions recently in preventing and controlling animal disease.

At one time, avian leukosis, also known as Marek's disease, cost the poultry industry over \$200 million each year. With the discovery of a vaccine to treat this type of cancer, loss to the poultry industry has been reduced to \$30 million per year. USDA has made great strides in the detection of bovine leukemia, a strain of cancer similar to that which can afflict man, and which costs the cattle industry \$20 million per year. Research continues on this disease, but in the meantime, the Department of Agriculture has discovered a useful diagnostic test which aids in the identification of carriers of the disease. Other areas which the Science and Education Administration at USDA is currently researching include cancer eye, a malignancy affecting beef cattle mainly in the Midwest; pulmonary adenomatosis, a lung cancer which afflicts sheep; and mycotoxins, a known human carcinogen which can be toxic to animals and which, at the least, can depress animal immune mechanisms making that animal more susceptible to other diseases.

As a veterinarian and a U.S. Senator, my colleague, Senator Melcher is doubly qualified to introduce such a bill as this. He has

¹See p. 33 for the text of S. 2043 and staff explanation of S. 2043.

a long history of interest in the progress of cancer research in this country not only in farm animals, but in humans as well. I laud the Senator for his abiding interest and efforts in this area.

Due to a prior commitment, I will be unable to remain for the hearing today, and turn the Chair over to my able colleague from Montana. I would like to assure you, Senator Melcher, that this subcommittee will give full consideration to the views expressed here today as it considers the piece of legislation before it.

Thank you, Senator Melcher.

STATEMENT OF HON. JOHN MELCHER, A U.S. SENATOR FROM MONTANA

Senator MELCHER [presiding]. Thank you very much, Senator.

In the United States, after billions of dollars have been spent on research through the National Cancer Institute to alleviate cancer, only relatively limited results have been attained. Human cancer research has received more public funding than any other medical research being conducted by the National Institutes of Health. Yet the results from basic research in terms of prevention or cure have been very limited.

As a contrast, the research on cancer involving animals and poultry conducted by the Department of Agriculture through its Science and Education Administration with comparatively miniscule funding has yielded some positive results in the control in poultry of neurolymphomatosis gallinarum, commonly known as Marek's disease. A successful vaccine has been developed that prevents this type of cancer in poultry.

While it should be emphasized at the outset that the scientists working within the Department of Agriculture and the National Cancer Institute cooperate to the fullest extent, it is apparent that a funding disparity exists between the two, comparable to David and Goliath.

The Department of Agriculture's Science and Education Administration will testify that approximately \$6 million is being spent annually on cancer-related problems in domestic animals. In the budget process developed by the executive branch over the past several years the Department of Agriculture has not been pressing for rapid or gigantic increases in appropriations for this purpose. However, a comparison of the amounts appropriated for the basic research on cancer between the Science and Education Administration and the National Cancer Institute leads me to state emphatically that an increase in basic research work on cancer in animals should definitely be granted.

Finding the keys to unlock the puzzle of what causes cancer or how it can be prevented is related in animals and man. Successful research on man, animals, or birds will begin to unravel the unknown on cancer for all of them.

There have been complaints for several years that the National Cancer Institute has not adequately considered some basic cancer research areas. Dr. Bob Netterburg—not a researcher himself but a dentist by profession—has consistently argued over the past several years that recognition of some previous research, chorionic gonadotrophin has been ignored by the National Cancer Institute; that very little attention has been paid by the National Cancer Institute

to grant applications by researchers in this and other areas. Dr. Netterburg has documented these facts in his recent publication, "The Road Not Taken: Toward a Cancer Vaccine."¹

S. 2043 was introduced a few weeks ago to provide more emphasis through the Science and Education Administration for basic research on cancer in animals. Specifically, the bill directs emphasis on basic research on common agents found in many types of cancer such as chorionic gonadotrophin. While the Science and Education Administration has an ongoing program of researching the physiology of chorionic gonadotrophin, it has not attempted the research on the basis of its linkage as an agent with animal cancers. The bill specifically is intended to develop basic research on cancer in this area. It is a small start—a very late start—but a start that is needed immediately.

Our first witness this morning will be Dr. T. B. Kinney, Jr., Associate Deputy Director, Agricultural Research, Science and Education Administration, of the U.S. Department of Agriculture.

STATEMENT OF DR. T. B. KINNEY, JR., ASSOCIATE DEPUTY DIRECTOR, AGRICULTURAL RESEARCH, SCIENCE, AND EDUCATION ADMINISTRATION, U.S. DEPARTMENT OF AGRICULTURE, ACCOMPANIED BY JOHN VICTOR, CHIEF, BUDGET DIVISION; DR. GRAHAM PURCHASE, ACTING CHIEF, LIVESTOCK AND VETERINARY SCIENCE STAFF; DR. EARL V. SPLITTER, PRINCIPAL VETERINARIAN, COOPERATIVE RESEARCH; AND DR. DOUGLAS BOLT, ANIMAL PHYSIOLOGIST, AGRICULTURAL RESEARCH

Dr. KINNEY. Mr. Chairman and members of the subcommittee, thank you for the opportunity to testify on S. 2043, the Animal Cancer Research Act, and the research on malignant tumors which the Science and Education Administration (SEA) is conducting.

I am accompanied by Mr. John Victor, Chief, Budget Division, SEA; Dr. Graham Purchase, DVM, Ph. D., Acting Chief, Livestock and Veterinarian Science Staff, Science and Education Administration/Agricultural Research (SEA/AR); Dr. Earl J. Splitter, DVM, principal veterinarian, Science and Education Administration, Cooperative Research (SEA/CR); and Dr. Douglas Bolt, animal physiologist, SEA/AR.

The Department supports the intent of this legislation. However, the Department has adequate authorization and funding for this research, and does not believe that enactment of S. 2043 is necessary. The Department does recognize that some aspects of cancer research could possibly be more intensively reviewed. However, we are not prepared to ask for additional authorization at this time.

Losses in livestock and poultry caused by malignancies have been of continuing concern to the Department. In 1978, tumorous conditions resulted in the loss of millions of pounds of federally inspected meat animals and poultry because of condemnations at time of slaughter. This does not include the very substantial but unmeasured losses due to reduced productivity and deaths occurring from malignancies in animals on the farm.

Intensive research efforts by the Science and Education Administration (SEA) and its cooperators in the past decade have led to

¹See p. 34.

major breakthroughs in controlling several of the most important causes of malignancies in farm animals. Cancer viruses and cancer cells have been grown artificially in culture and their chemical and antigenic makeup determined. Mechanisms of virus and cell replication have been studied and compared with replication in other viruses and normal cells.

From these discoveries the mechanism of transmission has been better understood and diagnostic tests have been developed. Marek's disease of poultry—a leukemia-like malignancy—has been found to be caused by a virus.

This discovery led to the development of a vaccine which has resulted in annual losses from the disease formerly at \$200 million being reduced now to about \$30 million.

The mechanism of the protection has been shown to be mediated by both cellular and humoral responses against new antigens that are characteristic of and appear in tumor cells.

Leukemia in cattle also has been found to be of viral origin and technology has been developed which will lead to reduction and perhaps eventual elimination of the disease. SEA research also has determined the cause and provided means for controlling the malignancy-like disease of mink known as Aleutian disease. This was a major cause of loss in the production of mink for fur.

Despite these advances, other formidable malignancy problems of livestock and poultry remain to be solved. SEA currently—fiscal year 1980—is allocating \$6 million for this research.

The Science and Education Administration in cooperation with other Federal agencies and other institutions has a significant program in basic research on cancer in animals. This includes studies on the genetics of the immune response, possible etiologic agents of different kinds of cancer, the effects of these agents on the host genetic materials that change in the process of becoming cancerous, mechanisms by which the control of cell proliferation of cancerous cells is lost, and new antigens, receptors, and other substances on the surface of cancer cells.

Other efforts by SEA and its cooperators to solve animal malignancies include studies to prevent cancer-eye in cattle and pulmonary adenomatosis in sheep. More effective methods are being sought to reduce or eliminate leukemia of cattle and Marek's disease and lymphoid leukosis of poultry. In addition, studies are in progress on mechanisms occurring in animals that affect natural and acquired immunity to malignancies. Promising substances are being evaluated that show suppressant action against the multiplication of animal tumor cells.

Another major effort is centering on the problem of mycotoxins, a group of known carcinogens for man and possible carcinogens and known toxicants for farm animals. Methods are being sought to eliminate these carcinogens from food and feeds. A portion of the basic research program on mycotoxins is related to cancer in animals including the effect of mycotoxins on the cellular and humoral immune response, the ability of animals to resist disease, the ability of animals to respond to vaccines and the effect of mycotoxins on cellular genetic components that results in cancer.

SEA has a strong program on cancer in animals and basic research on animal reproduction. These programs give high priority

to solving problems of significant economic importance in farm animals. We are not proposing to reduce any of these high priority programs.

SEA has ongoing programs on the endocrinology of reproduction involving pituitary and gonadal hormones. Chorionic gonadotrophin causes ovulation as does the pituitary luteinizing hormone which is important in farm animals. Chorionic gonadotrophin is used extensively in research as a tool, often in combination with other hormones, to regulate ovarian function.

Some of the possible research approaches are the clarification of the nature of the hormone chorionic gonadotrophin and the mechanisms of its action including its role in stimulation of cell proliferation and its possible role in the acceptance or rejection by the animal of embryo cells or cancer cells.

We agree with statements in S. 2043 that basic research on malignant tumors is essential to the health of animals; that such research may be beneficial in determining whether there are common factors which may cause malignancies in both man and animals, and that all carcinogenic agents have not been adequately identified in domestic animals.

We believe there have been and continue to be well-coordinated efforts to solve the malignancies of food animals which cause major economic losses. The health-related research programs of SEA are regularly reviewed and adjusted as necessary to assure that attention is being directed to the most important problems. The successes just referred to in this testimony in controlling Marek's disease in poultry and in solving the cause of leukemia in cattle did not result from isolated studies, but were due to well-coordinated efforts by SEA and its cooperators.

These efforts resulted in advances of substantial significance to veterinary as well as medical science. This included the first cancerous disease for which a successful, commercially applicable vaccine was ever developed and the vaccine is now applied worldwide. Another major advance included conclusive proof of the viral cause of leukemia in cattle—a question not completely resolved as yet in the similar disease of human leukemia.

In conclusion, we believe that current authorizations are adequate for continued, productive studies by SEA on malignancies of food animals; \$6 million of the \$74.4 million of SEA's fiscal 1980 appropriation for animal protection research, or more than 8 percent of that money, is currently being spent on malignancy research.

We would expect to be spending at least the same amount in fiscal year 1981. Given the basic nature of the research involved, research is being conducted in other Federal agencies directed toward these same underlying factors.

Mr. Chairman, thank you very much for the opportunity to testify before your subcommittee. My colleagues and I will be glad to answer your questions.

Senator MELCHER. Dr. Bolt, so far as the intensive research efforts by the Science and Education Administration, it has been connected with the problem of domestic animals or poultry, and in looking at that problem, and in trying to alleviate the losses on an economic basis, is that correct? Is that an accurate statement?

Dr. BOLT. Yes.

Senator MELCHER. So when you get the economic loss, you look at that problem and say: "Let's find a way to resolve it or to alleviate it or to minimize it." Then you go to basic research at that point; is that correct?

Dr. BOLT. That approach is used. However it is sometimes more efficient to first see if the applied approach might solve the problem. Then if that is not successful, go to basic research.

Senator MELCHER. For instance, in the complete leukosis problem in poultry, it is a combination, is it not, the vaccine for Marek's disease is part of it, and hygienic prevention is also a part of it?

Dr. BOLT. That is correct.

Dr. PURCHASE. That is correct

Senator MELCHER. So you come from the start, here is a problem that costs money. Let's see how we can alleviate it, minimize it.

When basic research gets into it, well and good. But if you could alleviate it without the basic research, that is about where you would stop?

Dr. BOLT. If the applied approach will solve the problem, yes.

Senator MELCHER. While the testimony dwells on the problems connected with food animals, you did mention the mink and what you call the Aleutian disease. You got into that because of an economic problem of people who produced mink for fur, which is not a food of course.

That is also a part of it, is it not?

Dr. KINNEY. Yes. I think research on fur-bearing animals comes under the purview of the Department of Agriculture insofar as fur bearing animals are raised domestically for income purposes.

Senator MELCHER. There is one obvious handicap. As far as basic research is concerned, you do not start with the basic research when you get into it. What was the term you used, applied?

Dr. BOLT. Applied approach, yes.

Senator MELCHER. While I am sure that the Science and Education Administration has been diligent on this, the bill would attempt to have you go a little bit beyond that into basic research itself.

Do you find any problem with that, if you went beyond this applied approach? There is an economic cost, let's see how we can alleviate it. Do you find any problem in the Department with, "Let's do a little broader basic research"?

Dr. BOLT. We are involved with both basic and applied research. For the most part, we use the applied approach first, and if it is not satisfactory, we proceed to a more basic approach.

Senator MELCHER. Well, the bill attempts to change that a little bit. The bill dwells on the fact that basic research is essential, that some types of basic research have not been adequately pursued, gets into coordination, and states "that significant theories of a common factor in malignant tumors, such as chorionic gonadotrophin, have not been pursued in depth."

So the bill really does not start by saying, we have a huge economic loss in certain areas. The bill starts on the premise that we are not doing enough basic research. That is a little bit of a different start for the Science and Education Administration than what you have been doing before, because you have identified the

economic loss and said, perhaps we can alleviate that by various applied means, not basic research.

Dr. BOLT. Yes, it is different. We try not to spend effort to solve a problem that does not exist.

But there are certainly many problems in the area that I am familiar with, which is reproduction, that need a basic research approach.

Dr. KINNEY. If I might interject, I think in most of our research, and particularly our research on reproduction, somewhere between 40 and 50 percent of the funds are devoted to basic research. In this case, I think approximately \$2.4 million of the \$6 million is actually what we would classify as basic research.

Senator MELCHER. The bill, first of all, identifies basic research as not being sufficient in terms of animal cancer and research, and second, authorizes funds to augment it.

One other point: You have not been given any direction in terms of wildlife. I will use that term in its broadest sense, which would include wild birds. And while the mink research you have done would relate itself to both domestic mink—I do not know if we even call them domestic.

Dr. KINNEY. I may have used that term a little broadly. I meant to refer to fur-bearing animals.

Senator MELCHER. Yes, that are in captivity and that are ranched; I think that is the best term, for income. You have not been given any direction to look at wildlife, and again, I use that term in its broadest sense, including wild birds.

Is that a problem?

Dr. KINNEY. I would ask one of my colleagues to respond. But I might say that we are not precluded from looking at wildlife insofar as it relates to vectors or reservoirs of domestic diseases or because they simply may be a good research animal.

Dr. PURCHASE, would you comment further and perhaps with respect to the fact that we do research on any animals, including those related to exotic disease transmission.

Dr. PURCHASE. That is correct; where the wildlife or vectors play an important role in domestic diseases, we are heavily involved. In our turkey-raising areas, we have found influenza infections are introduced by wild ducks, migrating ducks. And we are doing considerable work on the role of wild ducks in causing the influenza outbreaks in turkeys.

That is one of many examples.

Senator MELCHER. I am well aware that we are going to carefully husband and probably limit any basic research in wildlife. But, again, I come to the point of the basic research, not necessarily being related to anything economic, but it is the basic research for the purpose of the search for knowledge, the most basic type of research, which is not motivated necessarily at all by economic considerations, but which is only motivated by search of knowledge.

I think that that is perhaps a much broader direction than what the Science and Education Administration has had before in the Department of Agriculture. It is one that I believe we need a modest increase in, entirely in that direction.

So the bill attempts to emphasize that approach, rather than simply looking at the economics of it. In doing so, as first-named author of this bill, and the introducer of the bill, on the basis of the feeling that we are not using all our capability in basic cancer research; we are attempting to allow and to direct another branch of the Federal Government with competence to enter into cancer research on the basic level, rather than just on the basis of the economic returns involved with animals or poultry.

In regard to your grant program, about half of your \$6 million is spent on the basis of the grants to other institutions, other than within the Department of Agriculture?

Mr. VICTOR. Of the total of \$6 million, \$3.3 million is in-house in the USDA laboratories.

Senator MELCHER. Within, which would be where?

Mr. VICTOR. There is \$1.3 million in research on avian leukosis underway in Pullman, Wash., and East Lansing, Mich.

Senator MELCHER. Wait a minute; this is not in-house?

Mr. VICTOR. This is in SEA's research laboratories. There is almost a half-million dollars of research on bovine leukemia in Ames, Iowa, and Pullman, Wash. There is also better than a million and a half of work currently underway in the area of mycotoxins.

Senator MELCHER. That is in-house?

Mr. VICTOR. That is in-house. In addition, there is considerable work in the various State agricultural experimental stations.

Senator MELCHER. That would be at the land-grant colleges?

Mr. VICTOR. The major portion of the extramural program is at the land-grant colleges. A minor portion is in the area of special research grants.

So the bulk of the work is either in the SEA-owned and operated research laboratories, and/or the State experimental stations.

Senator MELCHER. What type of criteria do you have for any grants to any of the other research centers that are not within the Department of Agriculture?

Dr. SPLITTER. We have several programs that would allow research or provide for research in extramural institutions. We have a special program in animal health that provides funding for veterinary colleges as well as experiment stations.

Some of this money is being used in a special competitive grant program, which includes mycotoxin research projects, placed by competition. Some of the formula grant programs in animal health are being used for cancer research at experiment stations such as Nevada, Utah, and Texas.

So these are some of the examples of how funds are placed outside the Department by formula and by competitive means.

Senator MELCHER. When you say competitive means, how do you handle that?

Dr. SPLITTER. In the last several years, we have had specific amounts of money appropriated for animal health research. We have advisory committees that indicate the priorities in animal health research.

These priorities then are identified as eligible areas for competition by veterinary college personnel, or experiment stations, or any

university scientists who have competence in the eligible areas of research.

The availability of money is advertised in the Federal Register. Proposals are received, and then peer panels of experts in these various subject areas evaluate proposals and recommend those proposals to the Department which they feel will accomplish the most for the money; these are then funded on that basis for periods of from 1 to 5 years.

Senator MELCHER. About how much—could you give me a figure of how much is going into the grants?

Dr. SPLITTER. The total extramural program includes about \$2.7 million, of which the special research grants portion is \$127,000.

Senator MELCHER. Of the \$6 million?

Dr. SPLITTER. Yes.

Senator MELCHER. And that is mostly for work on mycotoxins?

Dr. SPLITTER. About \$2.3 million of the total extramural program is for mycotoxin research, including the \$127,000 special research grants.

Senator MELCHER. And then also cancer eye?

Dr. SPLITTER. The total extramural program is \$34,000 in cancer eye research.

Senator MELCHER. Is there another area besides the mycotoxins and cancer eye? Is that it on the grants?

Dr. SPLITTER. The extramural program includes \$268,000 on avian leukemia and there is research on bovine leukemia which is considerably less. None of this is special research grants.

Senator MELCHER. Those four areas then?

Dr. SPLITTER. Yes.

Senator MELCHER. Now, Dr. Bolt, on the physiology of chorionic gonadotrophin, where is that work being done?

Dr. BOLT. Let me clarify. I don't know of research in the Department where chorionic gonadotrophin is the central focus of a research problem. Chorionic gonadotrophin is used widely by many researchers, particularly in reproduction, as a research tool, because of its biologic properties.

For the most part, it is used because it has important biologic properties that mimic those of pituitary hormones. The pituitary hormone is much less available.

Chorionic gonadotrophin (HCG) can be extracted from the urine of pregnant women. The basic research on chorionic gonadotrophin has been conducted, not because we are studying exactly what does chorionic gonadotrophin do, but we are studying the basic actions of the hormone; the goal being to understand the mechanisms responsible for the stimulation and production of progesterone, the hormone necessary to maintain pregnancy.

HCG is used where one needs to mimic the biologic action of luteinizing hormones. It is quite commonly used experimentally to ovulate sows at a precise time. Such a procedure certainly may have an economic advantage.

HCG is used to cause ovulation in cattle, and to aid in estrogen synchronization programs, or efforts to increase the number of ovulations animals might have.

Senator MELCHER. Referring to this sentence on the bottom of page 2, second from the bottom paragraph:

Some of the research problems are in the clarification of the nature of the hormone, chorionic gonadotrophin, and the mechanisms of its action, including its role in the stimulation of cell proliferation and its possible role in the acceptance or rejection by the animal of embryo cells or cancer cells.

Dr. BOLT. I cannot speak for the entire Department as to what is going on, but I can speak to some of that, particularly the mechanisms of action, and the role of stimulating cells to proliferate.

One of the actions of chorionic gonadotrophin, as well as luteinizing hormone, is to transfer a follicle into a corpus luteum, a process called luteinization.

I really can't address that last part of the question because I have not studied cancer. Absence of rejection of embryo cells implies the maintenance of pregnancy or the maintenance of a condition that is necessary for pregnancy, which chorionic gonadotrophin certainly has this function in humans, and a similar action can be demonstrated as in normal animals.

This has been studied in an effort to reveal the mechanisms responsible for maintenance of pregnancies. We try to answer questions such as, how does the female actually know she is pregnant? This mechanism is not really known.

Dr. PURCHASE. The paragraph was intended to show some of the problems that could be approached using our technology, our research, and our expertise.

Senator MELCHER. In other words, that is intended to show that——

Dr. PURCHASE. These are some of the research problems.

Senator MELCHER. Which you could go beyond, into which you are not now in.

Dr. PURCHASE. That is correct.

Senator MELCHER. That is one of the attempts of the bill, basically to authorize additional funds so that is possible.

I do recognize that none of the work you are now doing you want to see decreased; in other words, taking some of the \$6 million and taking it away from what you are now doing to pursue something that might be required if this bill is passed.

Thank you all very much. I appreciate your testimony.

The next witness will be Dr. Dale K. Sorensen, representing the American Veterinary Medical Association, and the Association of American Veterinary Medical Colleges.

STATEMENT OF DALE K. SORESENSEN, D.V.M. AND PH. D., REPRESENTING THE AMERICAN VETERINARY MEDICAL ASSOCIATION AND THE ASSOCIATION OF AMERICAN VETERINARY MEDICAL COLLEGES

Dr. SORESENSEN. Mr. Chairman and members of the subcommittee, the American Veterinary Medical Association and the Association of American Veterinary Medical Colleges appreciate this opportunity to appear before the subcommittee in support of S. 2043.

I am a member of the American Veterinary Medical Association's Council on Research, and I am chairman of the Department of Large Animal Clinical Sciences, College of Veterinary Medicine, at the University of Minnesota.

I speak for the American Veterinary Medical Association, which represents about 32,000 member veterinarians and the Association

of American Veterinary Medical Colleges, which represents the 23 colleges of veterinary medicine and the departments of veterinary science of the colleges of agriculture in the United States.

It is a pleasure for me to present a brief summary of cancer in animals, and the impact that this problem has in the United States.

Cancer is a disease not unique to man. It knows no species barriers, affecting all species of domestic animals, wildlife, and poultry.

Various types of tumors have been encountered in many vertebrate species, including mammals, birds, and reptiles. Fish are also susceptible to this disease.

There is a greater concern of cancer in the domestic species of animals than in the nondomesticated since it has a greater impact on man and our quality of life. Cancer in animals and poultry affects the food supply of the Nation, as affected animals or birds cannot be utilized for human consumption.

Malignant tumors in companion animals or pets cause disruption to family life as well as cost consumers considerable expense for veterinary medical care to manage the ill patient. The potential public health hazard of animal neoplasia is of concern and needs greater definition.

There is an urgent need to increase the emphasis of cancer research on domestic animals and poultry. The primary basis for this need is to develop better methods for the diagnosis, control, and prevention of cancer in food producing animals and poultry.

There is also a need for improved diagnostic and therapeutic methods for cancer of companion animals. Companion animals play an extremely important role in maintaining the mental health of millions of Americans. Pets are essential members of families and necessary for happiness and a high quality of life for many people. It is also well recognized that animals provide excellent models for biomedical research in oncology. Increased knowledge of animal oncology will lead to a greater utilization of animals in solving human cancer problems.

A better understanding of the needs for additional funds to conduct research on neoplasia may be gained by reviewing some data.

Prevalence of neoplasms in food animals and poultry: Reliable data are available on the prevalence of neoplasms in food producing animals and poultry from the Federal meat and poultry inspection program, Food Safety and Quality Service, U.S. Department of Agriculture. Animals and birds sent to slaughter are subjected to ante mortem and post mortem inspection to ensure wholesomeness for human consumption. The following tables provide data on the prevalence of animal neoplasms for 1978.

I will not go through the tables, but just note that in cattle we have the most neoplasms, and the three big disease problems are carcinoma, epithelioma, leukosis and sarcoma.

TABLE 1.—NUMBER OF ANIMAL CARCASSES CONDEMNED FOR NEOPLASIA IN 1978

Neoplasm	Species				
	Cattle	Calves	Sheep	Swine	Horses
Carcinoma.....	3,303	7	31	444	36
Epithelioma.....	16,833	38	3	104	3
Leukosis (leukemia).....	7,945	128	42	1,316	15
Sarcoma.....	325	10	8	835	119
Miscellaneous.....	316	16	7	632	41
Total.....	29,222	199	91	3,331	214

We also have to keep in mind that any carcass which has neoplasia is condemned, not fit for human consumption. And on table 2 we have listed the number of animal carcasses with parts removed due to neoplasia, where only parts of animal carcasses are not utilized for human consumption.

TABLE 2.—NUMBER OF ANIMAL CARCASSES WITH PARTS REMOVED DUE TO NEOPLASIA

Neoplasm	Species				
	Cattle	Calves	Sheep	Swine	Horses
Epithelioma.....	75,267	328	190	295	3
Miscellaneous.....	2,059	23	5	994	64
Total.....	77,326	351	195	1,289	67

The biggest neoplasm is epithelioma. We have also listed on table 3 the number of birds and percent condemned for neoplasia for calendar year 1978.

As one can note from the table, the largest category is young chickens, where approximately 1 percent of the total birds slaughtered in calendar year 1978 were condemned for this particular disease.

TABLE 3.—NUMBER OF BIRDS AND PERCENT CONDEMNED FOR NEOPLASIA DURING CALENDAR YEAR 1978

Class of poultry	Leukosis	
	Number	Percent of total
Young chickens.....	3,633,324	0.10
Mature chickens.....	308,375	.16
Fryer/roaster turkeys.....	253	(¹)
Young turkeys.....	2,425	(¹)
Old turkeys.....	112	.01
Ducks.....	286	(¹)
Other poultry.....	11	(¹)
Total.....	3,944,786	

¹ Less than one-hundredth of 1 percent—Fourth leading cause of poultry condemnations.

The data presented in these three tables provide some useful information on the importance of neoplastic diseases in food producing animals and poultry in the United States. It should also be

kept in mind that this represents only the animals and birds that were processed through federally inspected plants in the United States. The percent of animals and birds slaughtered in federally inspected plants varies with each animal species and ranges from approximately 86 to 96 percent.

I would like to comment that we have many thousands of birds and animals which die from various melanomas that are not sent to federally inspected plants. Many go to rendering plants or are disposed of in other fashion.

For example, we recently conducted a study on leukosis cases in Minnesota and what percent went to inspected plants and what percent were disposed of using other channels. Approximately 50 percent of these animals were disposed of other than through meat processing plants.

So it is difficult to say other than this represents some fairly conservative estimate of the total numbers of these tumors that occur each year.

The economic loss due to cancer in food animals and poultry can be estimated utilizing meat and poultry inspection service data on the number of animal carcasses or parts of carcasses condemned for neoplasms. It is also necessary to include the economic loss associated with veterinary medical services for a portion of these animals.

For example, many livestock producers will have utilized veterinary medical services to diagnose the animal's disease problem. In the case of squamous cell carcinoma of the eye, the most prevalent neoplastic disease of cattle, surgical treatment is frequently employed. There is also an indirect loss associated with premature or unscheduled loss of animals from the breeding herd as it may reduce potential productivity of the herd.

I should add that there are losses of economic activity, prior to the time the animal is lost from the herd, through loss of milk production or failure to gain weight—so if we look at these 3 years, and estimate the economic loss, I have come up with a conservative estimate. It is approximately \$17,500,000 of loss due to contamination of animal carcasses or parts; \$4,500,000 in loss due to condemnation of poultry; \$2 million of loss associated with decreased productivity; and \$2 million of loss associated with veterinary medical care, for a total of \$26 million.

This figure represents a conservative assessment of the annual economic loss associated with cancer of food producing animals and poultry. It is recognized that the carcasses condemned are utilized for other nonhuman products, but all carcasses condemned represent a direct total loss to the producer and, ultimately, to the consumer in higher prices for the product.

In food producing animals and poultry there are three economically important neoplastic diseases. In cattle, the two important diseases are bovine leukosis—leukemia—and squamous cell carcinoma of the eye. The prevalence of squamous cell carcinoma in adult Hereford cattle may be as high as 20 to 30 percent, and it represents the leading cause of condemnations at slaughter. In the case of bovine leukosis—leukemia—serologic studies suggest that approximately 20 percent of adult dairy cattle are infected with the

leukemia virus necessary for the disease to develop. Meat inspection data show that this is the second leading neoplastic disease.

Another cause of economic loss is associated with the export of purebred cattle. In 1978, the United States exported 122,000 breeding cattle with a value of \$94 million. Some potential importing countries, for example Yugoslavia, prohibit the import of U.S. cattle due to the presence of bovine leukemia virus infection in dairy herds. In the future, we may be unable to export breeding cattle to foreign countries with control programs for leukosis unless we have a similar level of control.

Both of these diseases are very prevalent diseases by any standard used for comparison.

In the case of poultry, the most common neoplastic disease is Marek's disease. Prior to the development and use of a vaccine, Marek's disease constituted an extremely serious economic threat to the poultry industry. Losses were estimated to be in excess of \$150 million annually in the United States. Losses still occur because the vaccines are not 100 percent effective, and there is concern about the emergence of more pathogenic strains of the virus.

Neoplasms in companion animals: Companion animals such as dogs and cats frequently develop cancer. In fact, the prevalence is greater in companion animals than in food producing animals because the life span of farm animals is shorter than for pets, and there is less time for diseases of old age, such as neoplasms, to be expressed.

The occurrence of cancer in dogs and cats is similar to that in man with some species differences. The prevalence of tumors in dogs and cats has been subjected to several studies. The occurrence of tumors in dogs and cats hospitalized in veterinary teaching hospitals in 12 veterinary colleges in the United States was reported for a 5-year period—1964 to 1969. This study revealed a 5.5 percent incidence of tumors in over 100,000 hospitalized canine patients. Malignancy is one of the most important causes of death in dogs.

There is an urgent need for research to develop improved methods in cancer diagnosis and therapy. Veterinary oncology is just developing and needs research findings to improve the quality of care for patients and for the control of these diseases. One cannot assess an economic value on the problem of cancer in companion animals or the cost of providing veterinary medical care for these animals, but it certainly involves several millions of dollars annually.

I would like to add that it is difficult to get research funds to do any research on the whole issue of cancer in companion animals unless one can demonstrate a human health relatedness to it. So this restricts and limits the amount of funds which is available for research in this particular area.

Cancer in zoo animals, wildlife and fish: Neoplasia have been reported in virtually all animal phyla. The incidence rates of tumors encountered in this broad range of species has not been studied. There is little information available except for reports of various tumors in the many species of mammals, birds, reptiles, and fish. Funds are needed for research to provide more informa-

tion on the extent of neoplasms in this group and to develop approaches for cancer therapy in zoo animals.

Human health hazards of animal cancer: There is no evidence as yet that the bovine leukemia virus poses any danger to man. This virus infects sheep and goats, and it is oncogenic in sheep. Investigators have not found antibodies to bovine leukemia virus in the sera of cancer patients or of normal humans from high risk groups. At the present, bovine leukemia virus is an adulterant in our meat and milk which could be prevented if additional technology were known. The virus can be propagated in mammalian cells and non-human primates. This has caused concern in the scientific community. There has been similar concern with Marek's disease. There is no evidence linking this disease with human infection or cancer, but further studies are probably warranted.

Role of animal cancer for biomedical research: Animals with spontaneous neoplasms can and do play an important role in the total cancer research program. They serve as models for investigations that cannot be carried out in man. Increased knowledge and understanding of cancer in animals will increase the use of animals as models for the study of cancer in man.

In summary, we believe that there is a need for providing funds for research on cancer problems in domestic animals, poultry, and wildlife. We believe that an urgent need exists from both economic and humanitarian viewpoints. We believe that it will be a good investment and that future cost-benefit analysis will be able to demonstrate it in the area of food producing animals and poultry.

Certainly, the cost-benefit ratio of Marek's disease is an excellent example of the potential that may exist.

We have some concern that the level of funding proposed in the bill is not adequate to really provide for the level of thrust intended in the Animal Cancer Research Act. We are in total support of this bill to provide for research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife.

There is a great concern among veterinary colleges and veterinary research departments of the lack of research funds to conduct research on cancer problems in animals. Currently, in general, there are only two major potential Federal sources of support to fund such research. The National Cancer Institute provides support for projects on animal cancer demonstrating either a potential human health hazard or an animal model of a similar type of cancer in man. This severely limits the type of oncogenic research which is eligible for NCI funding. The other source is the Science and Education Administration (SEA), of the U.S. Department of Agriculture. They have supported research on economically important neoplastic diseases of animals and poultry in the past and indicate continued support for economically important cancer programs. Funding levels for animal health research and disease priorities restrict and limit the cancer disease problems that are eligible for funding from SEA. In assessing the situation there is no Federal granting agency that is supporting research on cancer in animals or birds with emphasis on protecting the health of domestic animals, poultry, and wildlife. It is believed that basic research on animal cancer will also lead to a better understanding of all

types of cancer. The potential benefit of this type of research to assist in solving the human cancer problem would be greatly increased.

We thank you for the opportunity to express our views.

Senator MELCHER. Dr. Sorensen, you touched on a significant point, I believe, the motivation for this bill, when you were talking about companion animals, that you cannot assess an economic value on the problem of cancer in companion animals.

What is their life worth? For the person who has companion animals, there is no way of assessing economic value to that life, and you add it is difficult to receive funds for this because you cannot link it to an economic cost, and cannot link it to whether it is a hazard to human health.

I think that is a good point. We do not know if cancer in these companion animals can somehow be linked to human health. We ought to find out, because they are with us, in setting aside the sentimental feelings for the animals, setting that aside, the other aspect of whether or not it is related to human health is extremely important, because we are exposed to them every day.

That is what we would like to do in this bill, start looking not just at economic matters, look first of all at basic research to see—what we can find out for the sake of knowledge, and if what we find out in basic research can lead us to a prevention and cure of any of these various types of cancer, we would be that much enhanced.

A lot of our great breakthroughs have occurred through our knowledge of animals. Jenner, didn't he develop the smallpox vaccine after he found out that milkmaids in England had a protection against it, and then linked that unknown protection against smallpox from the fact that they were milking cows that often had cowpox and developed an immunity. Is that the way?

Dr. SORENSEN. Yes; that is an excellent example of the role animal cancer has played. It was the first viral vaccine. It was the result of an observation made in animal cancer.

I sincerely believe that there is just a wealth of resource material out there if we would start looking at the animal cancers and investigate them just for the basic knowledge and information that can be generated, that can be applicable to human neoplasias.

There are many of these animal cancers that do not appear to be models of human cancers because of differences. But I think that it would be a very fruitful approach to cancer research.

There is a good deal of emphasis in cancer research in the area of immunology. So I think we also have to take a look at the immune systems of animals and how they might be utilized in the prevention and control of cancer.

So I think it even goes beyond the area of animal neoplasia per se.

Senator MELCHER. Specifically with Marek's disease and poultry, by finding the presence of a virus and developing a vaccine where the bird developed an immunology, an immune condition against the virus, then that type of leukosis in poultry is inhibited, as you correctly stated.

It does not necessarily guarantee 100 percent immunity, but it is greatly reduced down to a fraction. Then you say that there is no

evidence of linking this disease with human infection of cancer, but further studies are probably warranted.

I certainly agree. While the Department of Agriculture, through the Science and Education Administration, has played the leading role in this particular disease, in the development of that vaccine, it is obvious that their funding is very limited.

It is never a surprise to me when one of the agencies come up and testifies and says, "We have x number of dollars," in this case specifically \$6 million, "that we are utilizing for this type of research, and this type of work, and we think that is adequate."

It is no mystery to me, because through the budget process, no matter who is President, that is what they always have to testify.

So the Office of Management and Budget assesses, or makes a determination, of how much funds are going into the agency, and whenever the testimony before Congress is given by the agency, it is always the testimony really of the Office of Management and Budget, which balances out all of what they do as most significant needs of the Federal funds and where it should be utilized.

Obviously, in your judgment and my judgment, more work is needed. Yet we get that type of testimony from the people we are hoping to direct to do more work and therefore expend more Federal funds for this particular purpose.

I very much agree, doctor, with your summary, and particularly with the point that you express as a concern, that the level of funding proposed in the bill is not adequate to really provide the level of thrust intended in the Animal Cancer Research Act.

It is not the level of funding that I would like to have. It is not enough, but at least it is a start, and if we can have the start, based on the thrust that more basic research is needed, that this is an area that is underfunded, that is, the animal cancer research area is underfunded, and that we can provide more funds very prudently where it is needed for basic research with animals or wildlife, then I think we can perhaps go on from there and build on it.

I certainly agree with your summary, and I want to thank you very much for testifying today and giving us some very excellent testimony for our record.

Dr. SORENSEN. Could I make another observation?

Senator MELCHER. Certainly.

Dr. SORENSEN. You mentioned that additional legislation was needed to provide funds; I agree with that. I am cognizant of the fact that before the animal health research bill there was legislation available to appropriate funds for animal health research, but it just did not get done.

Even though the mechanism exists today for additional animal health research funds, I think there is a lot of merit in Congress specifically targeting funds for animal health research, because then I think something will happen.

It is very difficult to get some of the animal cancer diseases high enough on a priority list so the funds will be directed under the existing mechanism.

Senator MELCHER. That is exactly true, doctor. The argument is made, well; we have an unbalanced Federal budget. The Federal

deficits are high, and inflation is worsened because of deficit Federal spending; and therefore we have to have less spending.

That is well and good, but your testimony further—getting away from the basic research aspects of it, just for the purpose of gaining knowledge—your testimony further demonstrates that part of the cost of food is because of the loss of the animals or birds or partial loss caused by the animal not doing well and not producing milk or not gaining weight prior to the time of slaughtering the animal.

Through those losses, we are feeding inflation also. Your testimony has very graphically demonstrated that that is a bigger factor in how we are generating higher prices for animals and birds than a very modest amount annually would be to try to alleviate those losses.

I do not think we do enough to alleviate those losses, nor do I think we do enough from the basic research aspect of it, just to gain knowledge.

I think we are on very sound ground and very defensible grounds and very prudent grounds, to spend more money here where we know there is not an adequate job being done.

Simply to list four areas of major significance, four or five or six of major significance, that the Science and Education Administration is addressing in their research on animal cancer, poultry cancer, is simply not enough. That in itself is testimony that we are not doing nearly enough.

If we were doing more, these limited benefits we have received so far would be greatly enhanced.

Thank you very much, doctor.

Now we have a panel we are anxious to hear from.

It consists of Dr. Hernan Acevedo, Dr. Michael Naughton, Dr. Myron Blume, and Dr. Vernon Stevens.

**STATEMENT OF DR. HERNAN F. ACEVEDO, SENIOR SCIENTIST,
DEPARTMENT OF LABORATORY MEDICINE, DIVISION OF EX-
PERIMENTAL PATHOLOGY, ALLEGHENY GENERAL HOSPITAL,
PITTSBURGH, PA.**

Dr. ACEVEDO. My main comments here in respect to the bill is in what it refers to in part (d). I was very interested in hearing what my colleagues at the Department of Agriculture research group have been doing. And the main aspect is that the problem of human chorionic gonadotrophin, this material that is also called choriogonadotrophin or CG. We have developed through observations and research here in the United States and in other countries, the concept, since there is enough evidence now that we are dealing with something that we could call a common denominator in respect to the process of malignant transformation occurring in cells of human beings and animals.

Chorionic gonadotrophin is recognized as the hormone of life. It was thought that it was only produced in the human trophoblast. It happens that through investigations at different levels, it appears that this protein is a little bit more ubiquitous, because we have been finding it in cells that are undergoing the process of malignant transformation in different species. Moreover, one of the most important facets of these findings, this material is associated with the cell membrane of the malignant cell. I want to stress again

that this does not occur only in human cancers, but also in animal cancers. Perhaps if the chairman permits me, I will give a few slides showing a small part of the research, and after those slides the rest of the panel can make comments.

Senator MELCHER. Certainly.

[Slide presentation.]

Senator MELCHER. Doctor, do I understand that the cells themselves synthesize chorionic gonadotrophin—

Dr. ACEVEDO. Yes; the cells synthesize it for the very simple reason that all the microphotographs that I presented correspond to isolated cell systems, cells in tissue culture.

I did not show slides demonstrating its presence in tissues, because if you show it in tissues, you still can argue about the possibility that the cells from that particular tissue from an entire animal may be taken and/or attaching the material to the cell membranes, that is, the material may have come from other places. Being this tissue culture, we are absolutely sure that the only place where the material can come is from the cell itself, since there is nothing in the culture media analysis performed in the culture media totally negative for the presence of CG-like material.

Therefore, unless the material comes flying in the air, we do not know by which other way it can be present.

Senator MELCHER. Those are cancer cells that you showed, which cells normally would synthesize chorionic gonadotrophin?

Dr. ACEVEDO. The two cells that normally synthesize chorionic gonadotrophin and fix it in their membranes, like the cancer cells, the only two that we know, that we have found are the trophoblasts, of course, and the spermatozoa.

Senator MELCHER. Just those two normally?

Dr. ACEVEDO. Yes. Work done in Texas has corroborated our findings in the spermatozoa. On the other hand, the ovum does not show synthesis; even it has to have the information to synthesize it.

Senator MELCHER. How can you be sure that what you showed on the border of those cells was chorionic gonadotrophin?

Dr. ACEVEDO. Because we are using very specific antibodies against the hormone. The possibility that the reaction could be due to the other product is ruled out because we are dealing with an antibody created to the part of the molecule that is different from luteinizing hormone.

Senator MELCHER. What is your purpose in showing—and I suspect it is—you mentioned the snake cell. Was your purpose to show from snakes or hamsters or other mammals that there is a common agent between mammalian and nonmammalian cancer types of cells?

Dr. ACEVEDO. Yes. It appears that we have in front of us what I would call a common denominator. If we have a common denominator of this type, it looks like we would have to change several aspects in respect to what we think of cancer.

If we have thought that cancer is 300 different diseases, and if we have to make a vaccine out of everyone of those diseases that are being induced by different ways, like viruses, chemical compounds and so on, it makes the investigation very expensive and the work very difficult.

But if we have a common compound that is at the level of the cell membrane that have the same immunological activity of chorionic gonadotrophin, and moreover, this compound appears to be a protein of this type, we can think that we have the possibility that we are dealing with one disease that is expressed in 300 different ways.

Senator MELCHER. You are saying that the common denominator is chorionic gonadotrophin?

Dr. ACEVEDO. Or a chorionic gonadotrophin-like material.

Senator MELCHER. Which is a glycoprotein?

Dr. ACEVEDO. It is a glycoprotein because it has biologic activity in people. The jump over the species is even greater because we have found that this material is also present in some bacteria. And these bacterial strains—every time we have found one that expresses the material at the level of the membrane, it is too coincidental that it has always been associated with cancer in human beings.

Senator MELCHER. Now we have discussed somewhat this morning the development of a vaccine for Marek's disease for poultry using a virus which has been successful. How does that use of a vaccine for a specific type of cancer where a virus is involved, as demonstrated in Marek's disease, how does that relate to chorionic gonadotrophin, or does it relate?

Dr. ACEVEDO. It does not relate at all, because with that vaccine you are eliminating the inducer, which is the virus.

Senator MELCHER. In other words, you think that chorionic gonadotrophin might be present and produced in the lymphoids, the malignant lymphoid cells in birds?

Dr. ACEVEDO. If we have the opportunity to study them, I am pretty sure we will find it. We have found it in Rauscher's leukemia, and they all show the same thing.

Senator MELCHER. There may be more questions, but I want to allow the other members of the panel to speak.

Dr. Naughton, I believe you are next.

STATEMENT OF DR. MICHAEL NAUGHTON, UNIVERSITY OF COLORADO HOSPITAL, DENVER, COLO.

Dr. NAUGHTON. I would just like to confirm Dr. Acevedo's observations. We originally came into this field asking the naive question: What is the placenta not rejected? We started to look at chorionic gonadotrophin, and found the placenta that was covered with it. And at that time there have been some observations that human chorionic gonadotrophin was high in some cancer patients, and we looked at a number of cancers and we found, sure enough, practically all the cells we looked at that were cancers did have the materials on the surface as defined by the antibodies technique.

Senator MELCHER. This probably is not even a question, but let me pursue that for a moment. You identified chorionic gonadotrophin on the placenta of what species?

Dr. NAUGHTON. Humans; this has always been humans.

Senator MELCHER. How did you identify chorionic gonadotrophin on the placenta?

Dr. NAUGHTON. By the immune proxidase system, which is a double antibody technique. You use an antibody directed against

the subunit, and you follow this with a sheep antibody that has the proxidase on it And then the stain shows where the antibodies are localized. And they were localized on the surface of the placenta.

Senator MELCHER. Is that the technique used to identify chorionic gonadotrophin on malignant cells?

Dr. NAUGHTON. That is exactly the same technique.

Senator MELCHER. What type of malignant cells, again?

Dr. NAUGHTON. All human. We looked at about some 30 tumors, and we only found 2 negatives. What we were calling negatives were cells we could not score.

One was a melanoma that had a brown color to it naturally and couldn't score it positive or negative. The others were negative. It was rather necrotic tissue, so we could not positively identify it.

Since that time, we have extended the investigation.

Senator MELCHER. Are all of these tumors malignant tumors?

Dr. NAUGHTON. Yes.

Senator MELCHER. Please proceed, then. I interrupted you.

Dr. NAUGHTON. It is just a confirmation of what Dr. Acevedo has found.

Senator MELCHER. The difference, perhaps, is that you were working with malignant tumors of animals.

Dr. ACEVEDO. Yes; we have also found the CG-like material in humans' cancers, practically 100 percent of the ones we have examined.

Senator MELCHER. Dr. Blume.

STATEMENT OF DR. MYRON BLUME, MOUNT ZION HOSPITAL, SAN FRANCISCO, CALIF.

Dr. BLUME. Let me first identify myself, and tell you what I can testify to and what I can't.

I am a physician and oncologist, specializing in cancer. All of my professional career I have been involved in cancer research, primarily human cancer, and particularly the immunologic aspect of human cancer, what the immune system has to do with cancer, and how it might be manipulated to treat cancer or prevent cancer.

So mainly I am here to answer any questions that the committee might have in regard to the biologic aspects of cancer in humans and experimental animals, and the relationship between animal cancer, animal models of cancer, and human cancer research.

I would like to emphasize at this time that I have not personally done, nor directed any research, concerning the question of human chorionic gonadotrophin, in animal or human cancer, but I am familiar with Dr. Acevedo's work, and I have scrutinized the literature relating to this question.

As far as anything I might say directly related to the legislation under consideration, I think that the veterinarian experts who have already testified are much more qualified than I. Simply from the point of view of a private citizen and a physician, I think that cancer research is not progressing as fast as anyone would like, and I think that additional moneys spent in doing cancer research, be it on animals, domestic animals, farm animals, or experimental animals, can only help the overall progress.

I am sure more money could be spent very effectively. I am sure in particular that more money could be spent more effectively at

the basic science level. I think earlier testimony pointed out that it is easy to justify such expenditures, if we spend a million we will save two.

This has been presented by the gentleman from the Department of Agriculture. And I am sure, when dealing with the human situation, one could make the same kind of economic analysis.

If we can prevent or treat more effectively a certain disease, in particular cancer, it would represent an economic saving.

It is much more difficult to justify basic research with that kind of economics. Nevertheless, basic research does need to be done, because the information gained by such research is the foundation of all practical advances in science.

One cannot rely on private industry to carry the burden of basic research because their commitment is more of a pragmatic or practical one. If the problem can be attacked by a trial-and-error method, that is usually what is tried first. There is nothing wrong with that, but sometimes it does not lead to the solutions. Sometimes you have to backtrack. I think that is where we are now in cancer research. I believe we have nearly exhausted the possibilities which can be investigated by trial-and-error. We need more emphasis on basic biological research.

I think also examining in more depth the tumors that occur in farm animals, in domestic animals, pets, and wildlife, is important. The animal models that are conventionally used in cancer research for the most part are very, very highly inbred mice, rats, and guinea pigs, which are susceptible to a variety of induced tumors, induced by chemicals or virus, or "spontaneous" tumors which seem to depend on the inbreeding of the animals for their expression.

I am aware that cattle and livestock are inbred, but not to the extent of the small animals used in laboratory research. In particular mongrel dogs, of which I am very fond, and cats, are much more outbred and the spontaneous tumors that occur in these animals may be a better model for human cancer than some of the models obtained more readily in laboratories.

I think I will stop there and answer any questions that I can.

Senator MELCHER. I am glad you made that point. Because while my background would not lead anyone to believe that my opinion was very weighty on that matter, I have always wondered why the most important medical research we are doing is so much tied up in hamsters, mice, rats and guinea pigs, which seems to me to be, on its face, very little relation to human beings in terms of what the environment is, and particularly the points you make on the inbreeding, very little relationship at all to the environment that man has on this planet, and therefore, probably significantly, the poor types of mammals to be tested to find out what is wrong with me, a different mammal.

Dr. BLUME. Without belittling the gains that have been made, it is very, very apparent that a mouse is not a man. On the other hand, these animals are very easily handled in a laboratory.

Senator MELCHER. They are cheap, too.

Dr. BLUME. They can be dealt with in large numbers and such experimentation is almost always productive of some kind of result which one can then publish, and thereby gain support for one's

research. The relevancy of such results to human cancer (or cancer occurring in domestic animals) then remains to be investigated. This method has been fruitful in the past and undoubtedly will be so in the future. I am only suggesting that other approaches and in particular, other animal models may provide additional information.

A human animal is a much more difficult creature to experiment upon. Human material, such as human tumor cells in culture, is much more difficult to use as an experimental model, more time consuming, and less productive of immediate results in terms of treating cancer patients. As a result it has been less successful in competing for the limited funds available.

Senator MELCHER. We mentioned, Dr. Sorensen and I, Jenner, and if he had only been working with mice, hamsters, or guinea pigs, I do not suppose we would have smallpox vaccine produced in that generation.

Maybe I am wrong. I am under the impression that laboratory work with mice and rats and guinea pigs is something that has developed in this century, has it not? I cannot recall that Pasteur did much with little rodents, did he?

Dr. BLUME. No; the small laboratory animal certainly has been used much more extensively in this century, and even in the last 50 years.

Senator MELCHER. What Pasteur used to produce his rabies vaccine, wasn't it the spinal column of a goat?

Dr. BLUME. A rabbit.

Senator MELCHER. Thank you very much, Dr. Blume.

Now it is Dr. Stevens.

STATEMENT OF DR. VERNON STEVENS, OHIO STATE UNIVERSITY HOSPITAL, COLUMBUS, OHIO

Dr. STEVENS. First of all, I will identify myself as well.

I am a Ph. D. in reproductive biology. I hold professorships in the obstetrics and gynecology, pathology and zoology departments, and also have major graduate study commitments in veterinarian and agriculture colleges.

I have been studying chorionic gonadotrophin for the last 17 years, and of course, my testimony here is related to that aspect of your bill; although I have certain opinions and thoughts about the other aspects as well.

I have reached the conclusion that chorionic gonadotrophin a long time ago was probably misnamed. As the gentleman from the Department of Agriculture indicated, it is used as a substitute for pituitary hormones in animals to induce ovulation. Therefore, it is a gonadotrophin.

But if one looks at the basic physiology and gets away from the standard textbook definition, you see it does a lot more. I was not at all surprised when Dr. Acevedo found an association with malignant diseases. In our work, which has been primarily aimed at developing a vaccine against chorionic gonadotrophin, it has been shown to be important to the normal acceptance of the placenta quite differently and separately from being a luteinizing hormone in early gestation.

The quantities produced in normal pregnancies cannot be explained by the need for continuing gonadotrophin support of pregnancies.

When we suggested some possible applications, we had the same kind of problems that some of these gentlemen are now having acquiring research funds.

In the sixties, when I was trying to obtain support for developing vaccines against human fertility, the governmental agencies responsible for that kind of research here in Washington practically threw me out of their offices for suggesting such an adventurous idea.

At any rate, I have persisted and have obtained considerable research funds from the World Health Organization, outside this country. We have now successfully developed a vaccine that will prevent fertility based on immunity to chorionic gonadotrophin.

Our research used baboons and chimpanzees. I have been working with, collaborating with, and supporting the efforts of the other gentlemen here interested in cancer research. I have been very sympathetic to their causes and have suggested someone examine the data that they have acquired, listen to the logic, and to consider the direct implications.

I have been very dismayed that they have not been able to acquire significant support for this research. I have talked to many of my colleagues in veterinarian schools about having a vaccine against chorionic gonadotrophin in animals? Their response is that this would probably be damaging to their image as a professional if I were to suggest something so unconventional.

I think the idea of being conservative in our research and to only do a little different than what is the common thing has been a great deterrent to creativity. At the risk of someone funding quacks, agencies have generally waited until a concept is already demonstrated, and then after you have shown it is feasible, they will give you money to dress up your laboratory.

I think the creativity expressed and the courage displayed by these workers to persist in this area of research should be applauded.

Senator MELCHER. Speaking of chorionic gonadotrophin, specifically, while it might be the desire in a species, I think one of the doctors from the Department of Agriculture mentioned sows, in order to bring them into a state of fertility, and therefore enhance the production process for that species, that domestic species of farm animals, is well and good, and he is coming at it from an entirely different point than what you would come at it if you were trying to inhibit fertility.

However, that is also necessary in terms of animals. We would like to inhibit the fertility in dogs and cats, although I have not practiced for 10 years, and I have not paid any attention to what is going on in that field specifically, we are very much interested in doing that.

Can you relate to me any work that has been done recently using chorionic gonadotrophin to inhibit, prevent pregnancy, for example, in dogs and cats?

Dr. STEVENS. Not chorionic gonadotrophin per se. As one of the gentlemen in the Department of Agriculture explained, biologically

chorionic gonadotrophin resembles a luteinizing hormone, and some work has been done at the Colorado State University for immunizing dogs with luteinizing hormones. The antibodies to it suppresses normal pituitary function, and thereby curtail the production of steroid hormones. Thus the heat period, as well as ovulation, is inhibited.

I think that some commercial firms have been interested in their work, and may be pursuing it as a practical product.

Also, there are other areas of work going on to develop vaccines for dogs other than against chorionic gonadotrophin. I think that in this whole area people are reluctant to pursue chorionic gonadotrophin, or as Dr. Acevedo has said, a chorionic gonadotrophin-like substance—a substance associated with a wide variety of malignant tumors—as a vaccine antigen. If you could use an antigen that was a common denominator, then a vaccine would be a very feasible approach.

The normal problem with tumor immunology is, each tumor is biochemically different. And if you had to develop antigens unique to each, it would be very impractical. But this common association of chorionic gonadotrophin with tumors makes it a very appealing approach. It is an across-the-board association, as far as species specificity, then it is applicable to humans as well.

Senator MELCHER. Have you been aware of the work that the Science and Education Administration has been doing on the physiology, what have you, of chorionic gonadotrophin?

Dr. STEVENS. No. I have not been aware of any work that they have done in this area. I do not claim to have followed the history of their funding throughout the years, but in knowing what work is being supported on chorionic gonadotrophin, since that is my field, I have never heard of any specific research grant being awarded to someone from that agency for the study of chorionic gonadotrophin.

Senator MELCHER. Ohio State University is a land-grant college?

Dr. STEVENS. Yes; it is. It has an experimental station associated with it as well in Wooster, Ohio.

Senator MELCHER. And therefore, I guess, that basic research and diagnosis, prevention and control of malignant tumors in animals and birds has not been adequately coordinated.

If chorionic gonadotrophin is involved, as has been demonstrated by Dr. Acevedo's work and others, then I guess this finding is adequate, that there has not been adequate coordination of information that is available.

Specifically, you come from a land-grant college. You have been cooperating with the veterinarians—school of veterinarian medicine there, and the research laboratory connected with the university.

I do not want to belabor the point. It is an obvious fact. There has not been enough coordination or enough money despite however satisfied the Office of Management and Budget is, and the administration, and for that matter, the Department of Agriculture, that \$6 million is adequate.

I think it is, on its face, inadequate.

You say you are not surprised. You got some grants not through the National Institutes of Health—is that the agency you were bounced out of?

Dr. STEVENS. I have had several grants from NIH, but not for research in this field.

Senator MELCHER. Specifically, for chorionic gonadotrophin?

Dr. STEVENS. No; what you must do is know what is in vogue in a particular study section. You apply for money for that type of research, not necessarily your best ideas or ones you are most enthusiastic about. You must learn grantsmanship when you become an academic researcher.

I have never acquired 1 dime in 17 years from the Federal Government for research on chorionic gonadotrophin.

Senator MELCHER. But you have from the World Health Organization?

Dr. STEVENS. Yes; I spent over \$2 million of their money.

Senator MELCHER. Which is the most generous usually, NIH or the World Health Organization?

Dr. STEVENS. The particular program that supported me is a very small program, about \$20 million. The NIH has several billion dollars; of course the pocketbooks are no comparison in size but for chorionic gonadotrophin research, WHO has been far more generous.

Senator MELCHER. The grantsmanship you have talked about, what is in vogue—what is in vogue in getting grants through NIH?

Dr. STEVENS. In my particular field of reproductive biology, the subject in vogue currently is to study mechanisms of hormone action, hormone receptors, and other basic studies that happen to be the prime interest of certain scientifically politically powerful people in the country.

The kind of research that is supported is the kind that the chairman and the members of the review panel seem to think is important to be done.

There is nothing negative about such work in the sense it is not important. It is just that it is very resistant to new ideas.

I do not mean to be critical of these gentlemen representing the Federal Government, but I think the people involved in the bureaucracy of these funding agencies tend to select people for panels that take conservative approaches to research, and they don't get involved with some people that are reaching too far out for new ideas.

This is what I was referring to concerning a tendency to stifle creativity. It is easy to get money if you want to get on the bandwagon, but if you want to try something different, beyond the usual concepts, then I think you have an uphill struggle.

Senator MELCHER. I believe in May or June of 1978, we asked, here in this very room, we asked Dr. Upton to explain why the peer-review system seemed to be limiting basic research and some of the types we have been speaking about today.

With no reflection on Dr. Upton—after all, he did not create the peer-review system or the National Cancer Institute. I understand he will be leaving within the next few months to go back, I believe, to the University of New York. Without any reflection on his capabilities, it seems to me that his description of how the peer-

review system works in making awards of vast amounts of money was less than satisfactory.

We did ask him specifically at that hearing why he was turning down an application for a grant by Dr. Acevedo as well as some others, and asked him why, just for the sake of basic research, they did not say, go ahead and do it. It is not being done; why not do it?

The answer was that he could not get around the peer-review system.

I think you are right. I think it was obvious then, in this 1978 hearing, that they are so afraid of being criticized for allowing something that was not—I will use your term—that was not in vogue, that they were just afraid to do it.

What happened after that? Did you ever get a grant from NCI?

Dr. ACEVEDO. No. I have not applied again to the NCI because I know I will not get it. I know that a lot of my colleagues have exactly the same experience. In respect to NCI and the National Cancer Act, a tremendous system has been created that is self-perpetuating, and we just look at the amounts of money involved, from approximately \$1 billion, 55 percent in 1978, or 1977, 55 percent went only to 20 institutions in the United States; 55 percent.

Senator MELCHER. Of \$1 billion?

Dr. ACEVEDO. \$900 million or so.

Senator MELCHER. A half-billion dollars went to 20 institutions?

Dr. ACEVEDO. Yes, sir. The system is self-perpetuating. Things happen, for instance, around the National Cancer Act. There has been created some industry-type groups like the Fredricks Cancer Center, in which ex-scientists from the National Cancer Institute work there. According to the rules—I could be wrong, but I think no person from industry can take part in the peer-review system. That is we have persons from these institutions that are supported by grants or contracts from the National Cancer Institute that are part of the peer-review system.

From the American Cancer Society that gets money, \$125 to \$130 million per year, that is common knowledge, I have received a grant from an American Cancer Society new program. That program is called research development program. They have given me \$25,000 for 1 year.

Senator MELCHER. What year was that?

Dr. ACEVEDO. That started November of last year, and it would finish November 30 this year. And they extended it until July, without funds, of course, until my main research grant is re-reviewed again by the American Cancer Society peer review group.

So I have to wait to be funded, if I am funded, until July 1. It is a well-known fact, that one of the high officers of the American Cancer Society is retiring. From there he goes to one of our more-or-less well-known cancer centers, and at the same time that hospital is receiving, and that came out in the cancer letter, a fat amount of American Cancer Society money to continue investigation in that particular institution, medical school.

[The following information was subsequently submitted by Dr. Acevedo:]

[Excerpts from "The Cancer Letter"—Vol. 5, No. 46—pp. 1 and 2, Nov. 16, 1979]

ACS PLANS TO AWARD 10 NEW INSTITUTIONAL GRANTS FOR UP TO \$200,000 A YEAR IN CAUSE AND PREVENTION

The new special institutional grants announced last week by the American Cancer Society eventually may support long term programs at 10 institutions with up to \$200,000 a year each for research on cancer cause and prevention. Funds for the new grants will come from the ACS special donors program and will not be taken from the \$44 million traditional investigator initiated grants programs.

The first award under the new program will be to Mount Sinai School of Medicine of the City Univ. of New York, with Irving Selikoff as the principal investigator.

ACS in 1971 began its support of the Environmental Cancer Research Project, a three way collaborative intramural research venture involving E. Cuyler Hammond and his staff at ACS, Selikoff and staff at Mount Sinai and Oscar Auerbach and staff to the Veterans Administration Hospital in East Orange, N.J. This collaborative research effort will continue but will become incorporated administratively into the special institutional grant award at Mount Sinai.

Hammond, who recently retired as ACS vice president for epidemiology and statistics, will join the faculty of Mount Sinai as director of an epidemiology educational program and will continue as a consultant with ACS. Lawrence Garfinkel has assumed the position of vice president for epidemiology and statistics.

There are three major components to the Mount Sinai special institutional grant—the information unit, the Hammond faculty appointment, and the three way collaborative Environmental Cancer Research Project. The current annual budget will be about \$540,000, of which about \$190,000 will be from the special donors fund, contributed "generously and perceptively," ACS said, by the ACS Illinois Div. for the first two years of the project. Support of the Environmental Cancer Research Project already comes from regular ACS research funds.

[Excerpts from "The Cancer Letter"—Vol. 5, No. 46—p. 1, Nov. 16, 1979]

In Brief

GUSBERG HEADS ACS, WITH SCANLON AS PRESIDENT-ELECT; MDA HONORS HOLLAND, D'ANGIO, LANDING

Saul Gusberg, chairman of the department of obstetrics and gynecology at Mount Sinai School of Medicine, was installed as president of the American Cancer Society at the organization's annual meeting last week. He succeeds LaSalle Lefall. Edward Scanlon, director of surgical oncology at Northwestern Univ., was elected vice president and president-elect.

Dr. ACEVEDO. There is sort of a self-perpetuating system that unfortunately has been created, using the crash approach. We can take care of cancer the same way as we took care of going to the Moon. It is a natural thing when a system like that exists, and cancer centers are created. Besides, scientists, of course, are human beings, and there is perhaps a psychological sort of barrier, sometimes I ask myself—in reality I don't know if I have to say this or not—why kill the goose that lays the golden eggs?

Senator MELCHER Dr. Naughton?

Dr. NAUGHTON. I have been supported by a grant for perinatal medicine research—I am basically a protein chemist. I am a Ph. D. but I have a joint professorship in obstetrics-gynecology.

Senator MELCHER. Where does that grant come from?

Dr. NAUGHTON. From NIH. I have applied for three major grants since 1975 for research with HCG and have not been funded. I have applied for two minor ones in a block grant which, again, were not funded.

Senator MELCHER. NCI and they have not been granted?

Dr. NAUGHTON. Yes.

Senator MELCHER Dr. Blume, are you in on this?

Dr. BLUME. I have never applied to do work on HCG. I have had a number of grants turned down by the National Cancer Institute, some of which have been approved and not funded, some have simply not been approved.

It is a well-known fact that the National Cancer Institute itself has stated that they don't get enough money to fund all of the grants that they approve.

At the same time I very much agree with what Dr. Acevedo said, the grants that are funded generally go to a restricted group of investigators, most of whom sit on the review committees that are part of the peer review system.

So there are very few people that are part of the reviewing process who are not funded by the same process, and vice versa.

Senator MELCHER. I do not want to dwell any longer on the National Cancer Institute and its peer review system. I have made my thoughts known on it to Dr. Upton in the 1978 hearing, and I do not know whether it has improved any. I would hope it has.

What we are really attempting to do in this bill is just get somewhere else, very frankly, and see if by getting somewhere else, it is not constructive and conducive to progress.

I find myself really very—a very poor promoter of the economy when it comes to basic research, particularly in medicine. I encourage basic research; I encourage Federal funds for basic research in medicine.

I do not want to draw the purse strings; I want to open them up. All of us here in Congress, whether in the House or in the Senate, have to justify to our constituents how we can allow problems of the Federal deficit, problems of very worrisome inflation, damaging inflation, by our actions here, specifically, votes on specific appropriations.

We also all have our druthers on where we are going to try to save money and therefore cut the deficit. But I feel that in the case of basic research, whether it is in medicine, or for that matter, agronomy or soil or water pollution or hydrology, particularly in my State in the West, I do not want to draw the purse strings.

My druthers are to make the savings elsewhere. I firmly believe that when we use basic research, we are really attacking the very causes of our problems, including economic problems, inflation, Federal deficits.

We all benefit, and it will not necessarily take very long. It is not like it is somewhere in the next century. It is within the eighties or nineties. It will pay off, better than anything in Las Vegas.

That is my opinion and my judgment, and I am sure that you would echo that.

Dr. ACEVEDO. I would like to point out that from my point of view, and I think that also from several of my colleagues here, that research on cancer in animals, like cats and dogs, is of the utmost necessity, for the very simple reason, as you pointed out, that when we are working with the usual laboratory animals we are dealing with a very inbred, homogeneous type of animals, and the human being is not homogeneous at all.

In the cat and dog we have no such homogeneity like in the experimental animal. One of the big problems in the area of research in cancer is that everything we do at the level of human beings, we have to wait for 20, 30 years before we see the results.

Here, in place of the human being—we have an experimental animal, animals that we can use, like cats and dogs, in which their lifespan is much shorter, and we can have results of certain types of investigation, for example, effects of vaccines or things like that, that may be extrapolated more easily to the human beings because of their lifespans and heterogeneity.

We can have those observations in a relative short time, where in the human beings we would have to wait 40 years. So that part of the bill is of tremendous necessity. It is very interesting that I have not seen, not at NCI, not at any other level I have known, experiments of this type of basic experimentation in cancer utilizing these various types of domestic animals.

Senator MELCHER. You are echoing the exact point that Dr. Blume made, and the need to look at other species other than just laboratory species.

First of all, I take it that you all feel that there is a possibility of structuring a vaccine. I do not know if that is a good name, but some method of prevention of cancer by pursuing basic research on cancer.

Dr. STEVENS. Absolutely. Of course, as you said, it is premature to say exactly what kind of therapy would be involved, but I think the basic association of chorionic gonadotrophin with all these malignancies will provide some key to an effective therapy.

It should be investigated with high priority.

Dr. BLUME. I would like to modify that by taking a little more cautious stance, without losing any of my enthusiasm for pursuing the investigation of HCG and cancer. I think ever since people started to research cancer, to look at the malignant cell, one of the first questions that has always been asked is: "What makes this cell malignant, and what do malignant cells have in common that normal cells do not have in common?"

There have been a number of different ideas investigated, and none of them have been terribly productive. At the cellular or molecular level no common denominator has been found linking all, or even most malignant diseases. In this regard HCG may be a first.

Whether HCG synthesis is an accident resulting from malignant transformation, or something that caused the malignant transformation, is really not of great importance at this stage of the game.

So the finding so far that HCG or HCG-like material is almost universally present when it is sought for, is a very important observation. I think it cannot help but better our understanding of the malignant process, and the difference between malignant and nonmalignant growth.

The practical application of this information in the treatment or prevention of cancer is something that will take considerably more time to work out. Consequently I would refrain from trying to justify this area of investigation by postulating short-term gains in the treatment of cancer patients.

But I think it certainly needs to be pursued. It is as important, if not more important, than any other area of basic research that is currently being investigated with megabucks, and I think this is something that has been seriously neglected.

Dr. NAUGHTON. I am primarily interested in a reason for it. I think the vaccine is down the road, but I think if you have a reason, then you can logically start the thing.

Dr. ACEVEDO. As a scientist from the University of Colorado said, if I knew in the research I am going to do what the results are going to be 6 months from now, I will never do research.

Senator MELCHER. We have been talking about chorionic gonadotrophin and possibly identification as a possible agent. How does this fit into diagnosis? We have not talked about that.

Dr. NAUGHTON. I was at a meeting last week in Albuquerque, N. Mex., where they were using antibodies to HCG, and were able to visualize it. The amount of HCG in circulation in the serum, though, did not appear to bear any relationship to HCG presence on the surface of the cell.

There are two things people get mixed up in. The human placenta, for instance, at term, appears to have about the same amount on it as it does in the first trimester, even though the amount that is in circulation is enormous.

I think an explanation has to be sought for this.

Dr. ACEVEDO. We have been looking from two different points of view. One is the immunohistochemistry, that is being used more and more as an aid to the pathologist, because you can do the reactions in frozen sections; and we are working very hard in that aspect, and there are several places that it is being done, in England and Belgium.

There is another aspect that we have also run into. In the blood of patients having cancer that one of my collaborators was looking at, a possibility exists in those individuals where you don't find circulating serum chorionic gonadotrophin. This came up just by a hunch and some rationalization. We took a look at the lymphocytes. When HCG determinations are done in blood, it is done in serum, so the blood is separated.

What we did was the contrary to that. We found in our preliminary studies there was high a percentage of the lymphocytes of cancer patients that attach the material that we are calling chorionic gonadotrophin to their cell membrane. This was done by separating the lymphocytes from the rest of the blood cells, and they're doing the chemistry, and we found that there was a relationship.

It looks like there is a relationship with the stage of the disease, something that did not happen when the correlations were done with the circulating hormones and the amount of tumoral mass. Now there is one, due to that special activity of the membrane, a certain percentage of attachment to the antibody.

In our quantification, by counting the lymphocytes, it comes out that in all the cancer patients we have studied, they show an attachment that was from 10 up to 90 percent over the baseline.

We do not know exactly that what we are looking at is HCG, but we are sure that they are lymphocytes. We think there is a popula-

tion that concentrates or that attaches the material. You cannot find this when you are looking only at serum.

So, a blind study is being done, without any help from Government agencies, using our own scarce funds, and we will see. We think that there is a big possibility with respect to diagnosis.

The other type of diagnostic use that Dr. Naughton talked about, is the work using tagged antibodies, especially technetium that has a much shorter half-life, therefore is much better for use in human beings. And this looks also, in the hands of the investigators, very, very promising, and I personally think we have there a very useful diagnostic method to be applied practically.

Senator MELCHER. Thank you.

I would like to make as part of the record chapters 4 and 5 of the publication, "The Road Not Taken: Toward a Cancer Vaccine," by Dr. Robert Netterberg and Robert Taylor.¹

I believe they provide some background information.

I want to thank you all very much for being present today to help us with the hearing. Your testimony has been most helpful in demonstrating the lack of pursuing, with any type of figure at all, this opportunity in basic research.

We would hope to improve on the bill after the hearings today and make some changes in it. One of the changes we probably will make is to make sure that qualified research facilities could be considered by the Science and Education Administration.

Furthermore, I am very much in agreement with the point that Dr. Sorensen made, and I do not think I need to ask any of you about that since the amount of funding is very minimal and it should be increased. I suspect that you would all agree with that.

Thank you all very much. This concludes the hearing today.

The hearing record will be held open for 10 days for any further testimony.

[Whereupon, at 12:20 p.m., the subcommittee adjourned, subject to call of the Chair.]

¹See p. 34.

APPENDIX

[S. 2043, 96th Cong., 1st Sess.]

A BILL To provide for research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That this Act may be cited as the "Animal Cancer Research Act".

SEC. 2. Congress finds—

(a) that basic research on malignant tumors or cancers is essential to protect the health of domestic animals, poultry, and wildlife, including birds;

(b) that carcinogenic agents have not been adequately identified in domestic animals, poultry, and wildlife management;

(c) that basic research in diagnosis, prevention, and control of malignant tumors in animals and birds has not been adequately coordinated;

(d) that significant theories of a common factor in malignant tumors, such as chorionic gonadotrophin, have not been pursued in depth; and

(e) that research on diagnosis, prevention, and control of cancer in animals and birds will be beneficial to identify any such common factors in both human and animal malignant tumors, if such exist.

SEC. 3. There is hereby authorized to be appropriated to the Science and Education Administration of the Department of Agriculture \$1,500,000 for fiscal year 1980, \$3,000,000 for fiscal year 1981, and \$5,000,000 annually thereafter for the conduct of basic research on cancer in animals and birds at appropriate facilities within the Department of Agriculture or by grants to other qualified veterinary research facilities.

SENATE COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY STAFF EXPLANATION OF S. 2043

S. 2043 would authorize the appropriation of funds to the Science and Education Administration of the Department of Agriculture for the conduct of basic research on cancer in animals and birds. The research would be conducted at appropriate facilities of the Department of Agriculture or by grants to other qualified veterinary research facilities.

Under the bill, the level of funding would be \$1.5 million for fiscal year 1980, \$3 million for fiscal year 1981, and \$5 million for each fiscal year after 1981.

The bill contains Congressional findings that—

(1) basic research on malignant tumors or cancers is essential to protect the health of domestic animals, poultry, and wildlife, including birds;

(2) all carcinogenic agents have not been adequately identified in domestic animals, poultry, and wildlife;

(3) basic research in the diagnosis, prevention, and control of malignant tumors in animals and birds has not been adequately coordinated; and

(4) research on the diagnosis, prevention, and control of cancer in animals and birds will be beneficial in determining whether there are common factors that cause malignancies in both humans and animals.

[The following material was submitted by Senator Melcher and referred to on p. 3:]

THE ROAD NOT TAKEN: TOWARD A CANCER VACCINE
(By Robert E. Netterberg, D.D.S., and Robert T. Taylor)

CHAPTER FOUR*

THE FATAL EMBRYONIC HORMONE

If the persistent scientists we have discussed in previous chapters had not sacrificed time, money, recognition, and even reputation to work on the problem of cancer-connected bacteria, we doubt that the promising discoveries we are about to describe would have been made in our lifetime, or, if made, understood. If, as we believe, the discoveries are among the most important in the history of biological science as well as in cancer research, then the work of these scientists will not have been in vain. Their faith in their work will ultimately be vindicated.

To understand these discoveries, we must again enter the world of normal cells and normal growth.

When the egg and the sperm unite in mammals, the original cell begins to divide, and the new creature, which is to become a human being or an animal, attaches itself to the wall of the uterus by layers of cells known technically as the trophoblast (literally "nourishing growth").

These cells synthesize and secrete a substance with the jaw-breaking name *chorionic gonadotropin* or *choriogonadotropin*, which we will henceforth abbreviate CG. According to evidence now available,^{14 23 26 28 29} one of the functions of CG is to protect the embryo, which, because it has chromosomes from the father would be subject to attack as foreign protein. In 1976, this substance was also located in human spermatozoa.^{1 6}

From about 1970, different investigators have also found the presence of a CG-like substance in the serum of a great number of patients with cancer,^{9 10 22} suggesting that the cancer cells, like the trophoblasts and sperm, are also producers of CG or a CG-like substance. Further studies by investigators at Denver and Pittsburgh^{2 30} demonstrated that cancer cells, irrespective of origin, type of cancer and even *species*, do indeed synthesize the CG-like compound. These discoveries vindicate, in a sense, the pioneer scientist Beard,⁸ who in 1902 theorized that cancer cells were much like trophoblastic cells.

The mechanism by which CG on the surface of fetal cells, spermatozoa, and cancer cells defends such cells, appears to be physical-chemical in nature. CG, because of the presence in its molecules of a substance called sialic acid, has a high density negative electric charge.^{15 24 32 34} Agents of the immune system also carry a negative electric charge, but of lesser magnitude. A very basic principle of electricity states that objects with similar electric charges repel each other, an effect easily demonstrated by the action of small charge foam balls or the leaves of a potentiometer. Indeed, such agents of the immune system such as the white blood cell macrophages cannot get close enough to attack the cancer cell, although the lymphocytes have signaled that the tissue is foreign. Further, some of the immune system white blood cells become coated with CG themselves and this renders them ineffective against the cells, even if they actually touch them.⁷ The presence of CG in the cell membrane in quantities large enough to repel the agents of the immune system is a practical definition of malignant transformation or *cancer*.

We have already discussed the long work of Dr. Virginia Livingston-Wheeler in classifying and studying a microbe she has named *Progenitor cryptocides*. In a 1974 issue of the Transactions of the New York Academy of Sciences,³³ Dr. Livingston-Wheeler announced the confirmation of a hunch that the microbe also synthesizes a CG-like material much like the material synthesized by cancer cells. Her observation was confirmed by two other scientists, Drs. Herman Cohen and Alice Strampp of Princeton Laboratories, Inc. in a paper published in 1976.

An extraordinary discovery! Did the scientific world applaud and shout "Eureka!?" Hardly. The announcement fell upon the scientific community with all the clamor of soft snow.

Yet this was the first time that any bacterium had been shown to produce a substance virtually identical to a human hormone, one so similar that only very sophisticated tests could measure any difference. Further, this compound was the same compound synthesized by cancer cells, spermatozoa, and the trophoblast. Obviously, some direct link exists between the bacterial microbes and cancer cells!

Not all scientists ignored this extraordinary discovery. Two alert scientists who did not ignore it were Hernan F. Acevedo and Malcolm Slifkin. Both of them are

*See footnotes at end of chapter.

well known and recognized scientists, members of several of the most prestigious scientific societies, national and international. Dr. Acevedo is the Senior Scientist in the Division of Experimental Pathology of the Department of Laboratory Medicine, William H. Singer Memorial Research Institute of the Allegheny General Hospital, in Pittsburgh, Pennsylvania, which he joined in 1966. Since 1968, he has also held the position of Adjunct Assistant Professor of Microbiology and Cell Biology, Pennsylvania State University. He has been principal author or co-author of more than 100 scientific papers, abstracts, and chapters of books on such diverse topics as hormones in cancer and mesenchymal diseases, pituitary and adrenal dysfunction, biochemistry of reproduction, and hormone metabolism in normal and abnormal tissues.

Dr. Malcolm Slifkin has been the Head of the Section of Microbiology and Immunology, Department of Laboratory Medicine, Allegheny General Hospital since 1964, and Adjunct Professor of Microbiology, Pennsylvania State University since 1965. Since 1975, he is also Clinical Assistant Professor of Pathology, University of Pittsburgh School of Medicine.

Dr. Slifkin is also main author or co-author of many papers in the fields of bacteriology, virology, immunology and cancer research.

Acevedo and Slifkin wrote the first account of the identification of choriogonadotropin in human spermatozoa.¹ In 1976, they also reported for the first time the synthesis of the CG-like material by cancer cells in tissue culture and from animal models at the Third International Symposium on Detection and Prevention of Cancer, that was held in New York City.^{2,30}

One of their most significant publications appeared in the April, 1978 issue of *Cancer*, the official research journal of the American Cancer Society. This was an article entitled "Immunohistochemical Localization of a Choriogonadotropin-like Protein in Bacteria Isolated from Cancer Patients."³

This paper contains three important and interesting findings: (a) that fifteen strains of bacteria isolated from tissues of cancer patients show the property of synthesizing a CG-like substance; (b) that the CG-like substance was absent in non-cancerous human cells and in bacteria not isolated from cancer tissues; and (c) that the CG-like protein was found on the surface of bacteria and cancerous cells.

In a later scientific paper, published in the June 1979 issue of *Infection and Immunity*, one of the official journals of the American Society of Microbiology, Acevedo, Slifkin, and associates also described the presence of the CG-like substance in a strain of bacterium called *Eubacterium lentum*.⁴ This was the first time that an anaerobic bacterium (one that lives without air) has been shown to synthesize the hormone-like substance. Of further interest is the fact that this bacterium was originally isolated in 1938 from a rectal tumor in France! The bacterial strain was obtained from American Type Culture Collection which keeps microbial strains in culture and on file for scientists to utilize in research. This discovery shows that the property of CG-like hormone synthesis is transmitted by the bacterium from generation to generation. This publication further supported the original observation of these scientists that all bacteria exhibiting the CG phenomenon were isolates from a cancer patient, although *not all* bacteria isolated from cancer patients exhibit this ability.

In other writings, these researchers have described that in a manner almost identical to that of cancer cells, the CG-like material is localized in the membranes of the cell wall of bacteria.³¹ A further publication by researchers from the Rockefeller University²⁰ demonstrated that the material isolated from cultures of above-mentioned bacteria possessed the most important characteristic of the hormone, that is, to stimulate the uterus of a rat when injected into a live animal, in other words what scientists call *in vivo* (in life) biological activity.

Acevedo and Slifkin are applying at present for grants (a) to systematically screen bacteria of known origin for the presence of the CG-like hormone, (b) to determine the clinical frequency of the CG-like protein in bacteria isolated from patients with different types and stages of cancer as well as from non-cancerous patients, (c) to study further if any structural differences exist between bacteria that synthesize the CG-like protein and those that do not, and (d) to determine the intracellular location of the CG-like protein.

If it turns out that only bacterial strains that are growing in or have grown in the presence of cancer cells synthesize the CG-like protein, several possible results can follow:

(a) The question of the possibility of a CG-producing bacterium being the *cause* of cancer needs to be reconsidered. As Acevedo writes: "An old area of research will have to be reopened and started with a fresh approach."

(b) The presence of the CG hormone might be an excellent diagnostic tool to detect cancer in early stages.

(c) If CG or the CG-like protein are found *only* in cancer cells, spermatozoa, trophoblasts, and cancer-related bacteria, this would offer a real possibility for developing a cancer vaccine!

The National Cancer Institute has refused grants to Dr. Acevedo and his group to proceed with these studies.

A paper by Canadian researchers Malkin, Kellen, Cameron, and Farber, recently published in the *Scandinavian Journal of Immunology*,¹⁹ reports that CG is present in pre-malignant liver cells in rats, suggesting that the production of CG is part of a "programed phenomenon."

To sum up, these basic discoveries that cancer-related bacteria and cancer cells share this remarkable ability to synthesize CG or a CG-like protein suggests to us some new facts about cancer.

First of all, if it is true that every cancer, whether in the bloodstream, the lymphatic system, or in organs, is producing CG or a CG-like material, then from this standpoint all cancer is *one* disease, not many, as traditional teaching suggests. Of course, it may attack different parts of the body.

Second, the presence of this CG protein in every cancer cell suggests that the mechanism of the cancer cell is *one* mechanism, regardless of the different triggering causes such as carcinogens or radiation.

Third, the presence of the CG protein on the surface of every cancer cell and also on bacteria found in the cancerous tissue (including urine) of cancer patients suggests that *something* connects the two phenomena, although just what the relationship is not entirely clear. Dr. Livingston-Wheeler hypothesizes that the bacterium (she still insists that it is one and the same bacterium and that its "filterable phase" may contaminate other bacteria in the cancerous patient) invades the cell and perhaps lies dormant within it. Then some internal or external outside disturbance—chemical or radiation—produces a crisis in the cell and the genetic coding of the invader either begins the synthesis of CG or somehow sets off the latent gene for CG in the cell itself. Another hypothesis suggests that the bacteria takes on the property of synthesizing the CG protein somehow from the cancer cell as *it* becomes a cancer cell.

Fourth, if cancer is one disease, then perhaps by attacking the CG protein, with its heavy negative charge, particularly as this seems to be the mechanism by which cancer avoids the immune system, cancer may be stopped by chemicals that neutralize CG.

This immensely promising line of research, with future possibilities to be discussed more fully in the next chapter, is the direct result of over eighty years of research into cancer-related bacteria, research that has been swept under the rug, denied, and mocked, while thousands of victims have died unnecessarily in the terrible pain of cancer. The implications that lie ahead are incomprehensible when this nation finally does come to the realization of what has happened since 1924.

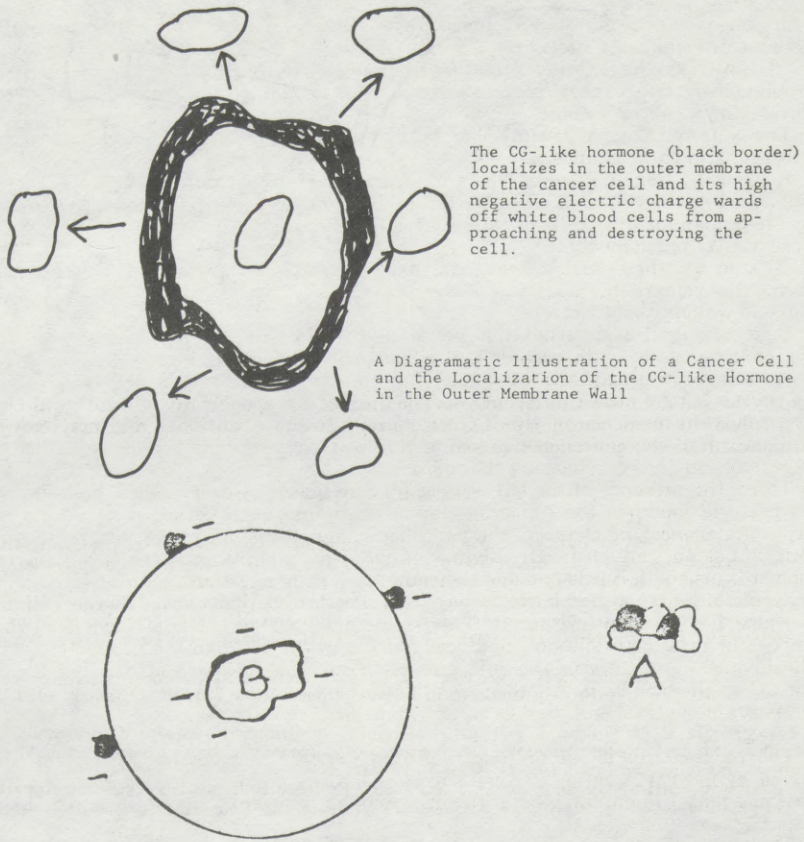
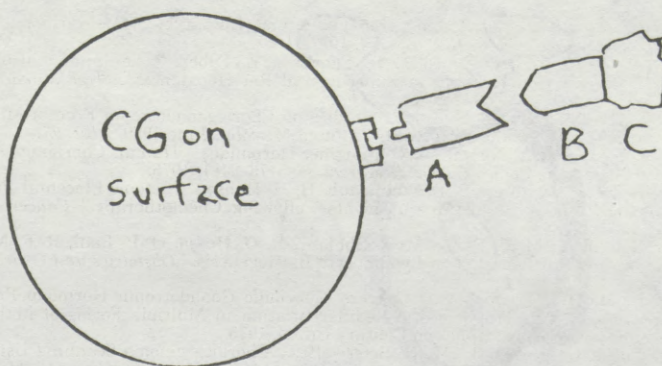


FIGURE A. This represents a classic experiment. Foreign liver cells (A) were immediately attacked and devoured by agents of the immune system (black bodies). The cancer cell (B) is not attacked because the negative charges repel the agents of the immune system at a distance too far for destructive effects to reach the cell.



Antibody and double antibody action. The antibody A specifically will lock unto CG. Antibody B (from another animal) is specific to the A antibody and may carry a marker (C) such as radioactive iodine.

CHAPTER FOUR FOOTNOTES

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CHAPTER FIVE*

WHY WE CAN HAVE A UNIVERSAL CANCER VACCINE

As we have said, cancer experts have long held to the belief that there are many forms of cancer. Some believe that these forms may number as many as 300. They also believe that each of these forms of cancer is a completely different disease rather than one disease. The malignant cells of one form, they say, have nothing in common with cells of another form. For example, leukemia is cancer of the blood forming tissues, but leukemia itself is subdivided into several different types. Carcinomas are cancers of the epithelial cells such as the skin, breast, or the cells that line the stomach. Sarcomas are cancers of connective tissue cells like muscle, fat tissue, or lymph glands.

"Scientific authorities," therefore, have consistently reported to the news media and the public that there can be no "magic bullet" to cure or prevent cancer because we are dealing with many diseases under the heading of the word *cancer*. According to this line of thinking, cancer is not a specific disease like tuberculosis or leprosy.

With the discovery that CG is found on the surface of all cancer cells thus far tested, both animal and human, this long-expounded theory of the cancer establishment—that cancer has various forms or that it is many diseases—literally goes out the window. In reality, the discovery and demonstration of the CG hormone provides for the first time in history a common biochemical denominator for all cancer cells.

So cancer can now be looked upon not as many diseases, but one disease with 300 clinical manifestations, which exhibit themselves as "forms". We can explain further by an example. Tuberculosis is caused by one bacterial microbe, *Mycobacterium tuberculosis*. However, the disease can be located on the skin, lung, or other organs of the body, like cancer. Tuberculosis of the adrenal glands, for example, the

*See footnotes at end of chapter.

classical form of a disease, is called Addison's Disease. These are clinical manifestations or different forms of the same bacterial disease—tuberculosis.

CG is technically what we call an *antigen*. An *antigen*, by definition, is any substance that stimulates the production of antibodies or reacts with them. Antibodies are biological protein substances that "lock on" to that particular antigen associated with bacteria responsible for the disease and stop them from producing their harmful disease effects. They also attack any foreign protein—a reason for rejection of skin grafts or organ transplants. The antigen-antibody reaction is the basis for all vaccines from polio and measles to tetanus. The Salk polio vaccine, a typical example, is made by what is known as attenuation of the polio virus. The polio virus cultures are killed by chemical solutions like carbolic acid or formalin. The Sabin polio vaccine is prepared in a different manner by using for the vaccine live virus which has been weakened by other methods of preparation.

Because CG seems to be a universal antigen, then the possibility of a universal vaccine automatically exists.

The whole purpose of any vaccine is to stimulate specific antibody formation by the immune mechanism of the individual against a particular agent—an antigen. The same antibody development sometimes results when the person acquires the disease. Vaccination is a shortcut to the antibody-development process. The immune system produces specific antibodies against a disease without causing the disease. Antibodies of one disease do not protect against another disease because these are highly specific reactions.

In cancer, an additional promising fact about the CG hormone being synthesized by the cancer cell is its localization in the outer wall membranes of the cell (see diagrams), since this increases its vulnerability to be attacked.

Myron Blume, M.D., Ph.D., Director of the Immunology Center at Mount Zion Hospital in San Francisco, California, and an expert in the field of oncology (tumors) and immunology has this comment:

"The presence of a universal marker, one that is confirmed, will allow us to take a big step in the right direction. If that turns out to be true, it will be the first time, in my vocabulary, what could be called a breakthrough has happened in cancer in the last forty years. If you can prove that every single human cancer cell synthesizes CG, I think that would be very significant."

This statement is in reference to the already existent cancer cell, which the white blood cells cannot attack, not because they are not alerted to do so, but because they cannot approach to attack. The cancer cell must be disarmed by removing the CG hormone shield from the outer border of the cell, because the CG functions somewhat like an electric fence warding off the killer white blood cells.

We should make it clear at this point that if the outer membrane of the cancer cell can be destroyed, the cell cannot survive. This principle applies to any type of cell, normal or cancer.

Further, if the CG synthesis is a normal function in the development of the cancer cells, then obviously its formation can be prevented from happening in the first place. As we have pointed out, once the CG synthesis begins to take place in a cell, and becomes concentrated on the cell membrane, the malignant process is underway. The cells have returned to a primordial or underdeveloped stage and divide completely unchallenged by the body's immune system if they accumulate or utilize the hormone in their membranes. The killer capacity of the immune mechanism of white blood cell response has been neutralized by this hormone.

How would the proposed cancer vaccine work? Thus far, Dr. Virginia Livingston-Wheeler and Dr. Hernan F. Acevedo, working independently in different parts of the nation, have shown that bacteria isolated from cancer patients are also synthesizing CG. Because the microbes share what is known in immunology as common antigenic determinants with the cancer cells, namely the CG-like substance, selected strains of these bacterial microbes can be used as the basis for the preventive vaccine. Hopefully, specific antibody formation will therefore prevent a normal cell from undergoing malignant transformation.

To some degree, antibodies are constantly being formed by the body against normal CG, even though it is a natural body substance, but these are antibodies with very low affinity, meaning the amount of reaction is negligible.* Now, because of CG-producing bacteria, the potency can be raised to produce antibodies that will really do the job necessary and with the power required for immunity protection.

Dr. Acevedo has said that we can never stop the cell from its attempt at CG production because cancer is a part of life. But with the production of specific antibodies by vaccine inoculation against these microbes, the malignant transformation process by the cells will be stopped in its tracks from becoming a clinical manifestation, that is, the formation of deadly tumors and lesions which spread and

kill. We will, in essence, be attacking and preventing cancer at its very roots. We will be preventing the survival of malignant cells after the cellular transformation has occurred, therefore eliminating the presentation of the clinical disease we call cancer.

No more blind shotgun approach of chemotherapy or deadly radiation in the futile attempt to try and kill cancer cells resulting in torturous and toxic effects to the already cancer-weakened patient. No more attacking an enemy cell which is not understood, because we now know how it functions in its sinister way, being closely and ironically linked to life itself. Cause and effect arguments are no longer important. Because of the universal CG hormone antigen, it does not matter how the cancer was produced, or as the NBC Nightly News reported on December 1, 1977, the antigen can be demonstrated by cancer cells regardless of how the malignant transformation was caused. It does not matter whether it was caused by chemical or viruses. It is always present!

Dr. Acevedo has also had much experience in the field of human reproductive biochemistry. He feels that we may have not only a universal vaccine against cancer but also a vaccine against pregnancy. CG hormone is normally present, as we have shown, in the embryonic trophoblast and male sperm cells. If the vaccine works in preventing a cancer cell from developing, we must entertain the possibility that the CG hormone protection of the trophoblast and of the sperm cells will be destroyed upon administration of the bacterial cancer vaccine. Antibodies against a developing cancer cell would have the effect of destroying the trophoblast or preventing fertilization by destroying the sperm cell's potential.³ As a matter of fact, in a series of reports of studies in India and reported in the February, 1976, issue of *Contraception*,¹ it was shown that a vaccine that neutralized the biological activity of CG significantly lowered the fertility of female rhesus monkeys. The immunization against human CG was obtained with a conjugate of beta subunit of CG and tetanus toxin. A preliminary report of this work was published in the January, 1976 issue of the *Proceedings of the National Academy of Sciences*.⁴

To many, a pregnancy vaccine may be a Godsend in itself. But if everyone took the cancer vaccine early, then the human race could possibly become extinct. How would this problem be solved? Neither Dr. Acevedo nor Dr. Livingston-Wheeler or other investigators see this as a serious problem. 90% of all human cancers occur after the age of 40. For those who wish to have children, the obvious solution would be to take the vaccine after age 40, because generally that is past the age people usually have children. The question arises, however, as to how many people would want to take that risk. Have children in the hope of not developing cancer or take the vaccine before the age of 40 and not have children? Before anyone becomes too concerned, we must look at some other possibilities for the future.

Various vaccines, such as the tetanus vaccine, proven effective in preventing diseases, do not provide a lifetime protection. If the cancer vaccine is a type requiring periodic shots to maintain immunity against the cellular process, then the matter of pregnancy can be regulated. Dr. Acevedo believes that we will probably need a booster type of vaccine for cancer with periodic renewal of immunity.

A study by Florence B. Seibert and Robert L. Davis of the Veterans Administration of Bay Pines, Florida, further supports the idea that the vaccine will need boosters. In a report in the *Journal of the Reticuloendothelial Society*, April 1977,² they discuss the use of a heat-killed vaccine made from a filterable bacterial strain isolated from a mouse breast tumor. This vaccine depressed the incidence of spontaneous breast cancer about 20% from 39 to 58 weeks. However, about the 60th week, the effect weakened rapidly, so that by the 72nd week, incidence of cancer in vaccinated and control mice was about the same.

On the basis of some studies, critics of the CG proposal have felt that the substance might also be present in normal tissues. Should this be the case, then a vaccine against the CG synthesis could cause harm or destroy normal and vital tissues. However, most recent studies suggest that the substance which reacted in their experiments was not genuine CG or a CG-like substance but rather a common body protease that can mimic CG in certain concentrations and certain diagnostic methods.⁵ Therefore, the opposition has lost their final argument when it comes right down to the demonstration of scientific facts.

In light of the CG-like substance produced by the microbes and cancer cells, the possibility of cancer being a low grade contagious disease must be considered (also dismissed as nonsense by the cancer establishment in the past) as evidenced by the leukemia outbreaks in high schools in New Jersey and the epidemic levels of cancer in China and elsewhere in the world.

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