

Management of Asthma in Children and Adults

2009



VA/DoD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF ASTHMA IN CHILDREN AND ADULTS

**Department of Veterans Affairs
Department of Defense**

GUIDELINE SUMMARY

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With support from:

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&

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QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and the Department of Defense (DoD) guidelines are based on the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

Variations in practice will inevitably, and appropriately, occur when providers take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

Version 2.0 – 2009

INTRODUCTION

The Clinical Practice Guideline for Management of Asthma in Children and Adults was developed under the auspices of the Veterans Health Administration (VHA) and the Department of Defense (DoD) pursuant to directives from the Department of Veterans Affairs (VA). VHA and DoD define clinical practice guidelines as:

“Recommendations for the performance or exclusion of specific procedures or services derived through a rigorous methodological approach that includes:

- Determination of appropriate criteria such as effectiveness, efficacy, population benefit, or patient satisfaction; and
- Literature review to determine the strength of the evidence in relation to these criteria.”

The intent of these guidelines is to:

- Reduce current practice variation and provide facilities with a structured framework to help improve patient outcomes
- Provide evidence-based recommendations to assist providers and their patients in the decision-making process concerning the diagnosis and management of patients with asthma
- Identify outcome measures to support the development of practice-based evidence that can ultimately be used to improve patient healthcare outcomes.

2009 UPDATED VERSION OF THE GUIDELINE

This clinical practice guideline updates the 1999 version of the DoD/VHA Guideline on Management of Asthma for Adults and Children Age 6 years and over. The current guideline incorporates the two sections of the 1999 guideline into one document. Where evidence suggests differences in the management between adults and children, age-specific recommendations are provided. The objective of the DoD/VHA Working Group in developing this guideline was to incorporate information from existing national recommendations into a format that would maximally facilitate clinical decision-making.

This effort drew heavily from the National Heart, Lung and Blood Institute's (NHLBI) National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, published in 2007, and the Global Initiative for Asthma (GINA), Global Strategy for Asthma Management and Prevention, published in 2007.

The DoD/VA Working Group reviewed these two guidelines and made the decision to adopt several of their recommendations. The Working Group developed a revised comprehensive clinical algorithm that incorporates the diagnosis and management of asthma in both children and adults. Additional recommendations were added addressing specific issues that the Working Group considered to be of importance to patients in the healthcare systems of the VA and DoD. Hence, this DoD/VA updated version of the Asthma guideline includes evidence-based recommendations for routine primary care and additional recommendations suggesting specific actions for diagnosis and treatment of exercise-induced asthma in active young adults. These specific recommendations may better serve providers caring for service persons with asthma among the active duty population.

The guideline/algorithms are designed to be adapted to an individual facility's needs and resources. They will also be updated periodically or when relevant research results become available. The guideline should be used as a starting point for innovative plans that improve collaborative efforts and focus on key aspects of care. Except in very unusual circumstances, the recommendations outlined in this guideline should also serve as a framework to the care that is provided or recommended in specialty care settings.

BACKGROUND

Asthma is a chronic inflammatory disease of the lungs characterized by episodic and reversible airway obstruction. During the 1990s, rates of asthma increased in all age and racial groups, from an average of 30.7 per thousand to 53.8 per thousand in 1994. In 1998, asthma affected an estimated 17.3 million people in the United States, including over 4.8 million children.¹ In 2005, asthma affected more than 22 million persons. In children, asthma is one of the most common chronic diseases, affecting more than 6 million children (current asthma estimates, 2006 National Health Interview Survey (NHIS), Centers for Disease Control and Prevention (CDC). [<http://www.cdc.gov/asthma/nhis/06/table3-1.htm>]

In 1995, asthma accounted for more than 5,000 deaths, 1.87 million emergency department visits, and over 100 million restricted activity days. There have been important gains since and the number of deaths due to asthma has declined, even in the face of an increasing prevalence of the disease (NHIS 2005). Fewer patients who have asthma report limitations to activities, and an increasing proportion of people who have asthma receive formal patient education (Department of Health and Human Services [DHHS], Healthy People 2010 midcourse review). Hospitalization rates have remained relatively stable over the last decade, with lower rates in some age groups but higher rates among young children 0–4 years of age. There is some indication that improved recognition of asthma among young children contributes to these rates. However, the burden of avoidable hospitalizations remains.

With the appropriate use of available therapies, asthma exacerbations and their consequences can be effectively controlled. The purpose of this clinical practice guideline is to help clinicians and patients make appropriate decisions about asthma care. This guideline can assist primary care providers or specialists in the diagnosis and initial management of symptoms, follow-up management, assessment of the ongoing clinical situation, emergency management of acute exacerbations, determination of appropriate treatment, and delivery of individualized interventions.

Goals of the Guideline

- Update the recommendations for the **diagnosis** of asthma in children and adults.
- Update the recommendations for the **management** of asthma in children and adults.
- Address the diagnosis and management of asthma in the **active duty population** (including deployed, non-deployed).
- Review the evidence regarding the assessment of severity definition of disease control (addressing risk and impairment) and the use of peak flow meters.
- Review the evidence regarding intervention for asthma (new treatment strategies, combination therapies, non-pharmacologic treatment, education, and written ongoing treatment plans involving the patient).
- Review the evidence and address the management of exercise-induced bronchospasm (EIB).
- Review the evidence regarding outpatient management of acute exacerbation of asthma.

¹ Centers for Disease Control. Forecasted state-specific estimates of self-reported asthma prevalence -- United States, 1998. *MMWR Morb Mortal Wkly Rep.* 1998;47:1022-1025.

Target population

The guideline will offer best practice advice on the following:

- Diagnosis and management of asthma in adults:
 - Special consideration for active duty members
 - Special consideration for diagnosis and management in the elderly (over age 65) or other co-morbidities
- Diagnosis and management of asthma in children.

Audiences

Primary care and allied health professionals who have direct contact with patients with asthma (in the outpatient setting), and make decisions concerning routine management their care.

Development Process

The development process of this guideline follows a systematic approach described in “Guideline-for-Guidelines,” an internal working document of VHA’s National Clinical Practice Guideline Counsel.

The literature was critically analyzed and evidence was graded using a standardized format. The evidence rating system for this document is based on the system used by the U.S. Preventative Services Task Force (USPSTF). (See [Appendix A to the full guideline – Development Process.](#))

Evidence Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients. <i>Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.</i>
B	A recommendation that clinicians provide (the service) to eligible patients. <i>At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.</i>
C	No recommendation for or against the routine provision of the intervention is made. <i>At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.</i>
D	Recommendation is made against routinely providing the intervention to patients. <i>At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.</i>
I	The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. <i>Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</i>

Lack of Evidence – Consensus of Experts

Where existing literature was ambiguous or conflicting, or where scientific data were lacking on an issue, recommendations were based on the clinical experience of the Working Group. These recommendations are indicated in the evidence tables as based on “Working Group Consensus.”

This Guideline is the product of many months of diligent effort and consensus building among knowledgeable individuals from the VA, DoD, and academia, and a guideline facilitator from the private sector. An experienced moderator facilitated the multidisciplinary Working Group. The draft document was discussed in two face-to-face group meetings. The content and validity of each section was thoroughly reviewed in a series of conference calls. The final document is the product of those discussions and has been approved by all members of the Working Group.

The list of participants is included in [Appendix H](#) to the full guideline.

Implementation

This guideline is not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns of care evolve.

The guideline and algorithm should serve as a guide that providers can use to determine best interventions and timing of care for their patients to optimize quality of care and clinical outcomes. This should not prevent providers from using their own clinical expertise in the care of an individual patient. Guideline recommendations are intended to support clinical decision-making but should never replace sound clinical judgment. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the provider, following discussion of the options with the patient or parent, in light of the diagnostic and treatment choices available.

Although this guideline represents the state of the art practice at the time of its publication, medical practice is evolving and this evolution will require continuous updating of published information. New technology and more research will affect and improve patient care in the future. The clinical practice guideline can assist in identifying priority areas for research and optimal allocation of resources. Future studies examining the results of clinical practice guidelines such as these may lead to the development of new practice-based evidence.

Outcomes

- Control Symptoms: Nighttime awakenings; need for Short-Acting Beta Agonists (SABA) for quick relief of symptoms; work/school days missed; ability to engage in normal daily activities/desired activities
- Optimize (normal) lung function: Forced Expiratory Volume in 1 Second (FEV1); FEV1/Forced Vital Capacity (FVC); peak flow
- Reduce risk of exacerbation
- Minimize adverse effects
- Utilization of healthcare
- Working knowledge of the asthma action plan
- Patient satisfaction

Content of the Guideline

The guideline consists of an algorithm that describes the step-by-step process of the clinical decision-making and intervention that should occur throughout the diagnosis, treatment, and follow-up of asthma patients. General and specific recommendations for each step are included in the annotation section. The links to these recommendations are embedded in the relevant specific steps in the algorithm.

Each annotation includes a brief background, discussion of the research supporting the recommendations and the rationale behind the grading of the evidence as well as the determination of the strength of the recommendations (SR). The SR is indicated in brackets for each of these recommendations. Readers should note that the grade relates to the strength of the evidence and not necessarily to the clinical importance of the recommendation.

Recommendations that were based on the clinical experience of the Working Group are not followed by an “SR” grade. A complete bibliography of the references used in this guideline can be found in [Appendix I to the full guideline](#).

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Additional contributor contact information is available in [Appendix H to the full guideline](#).

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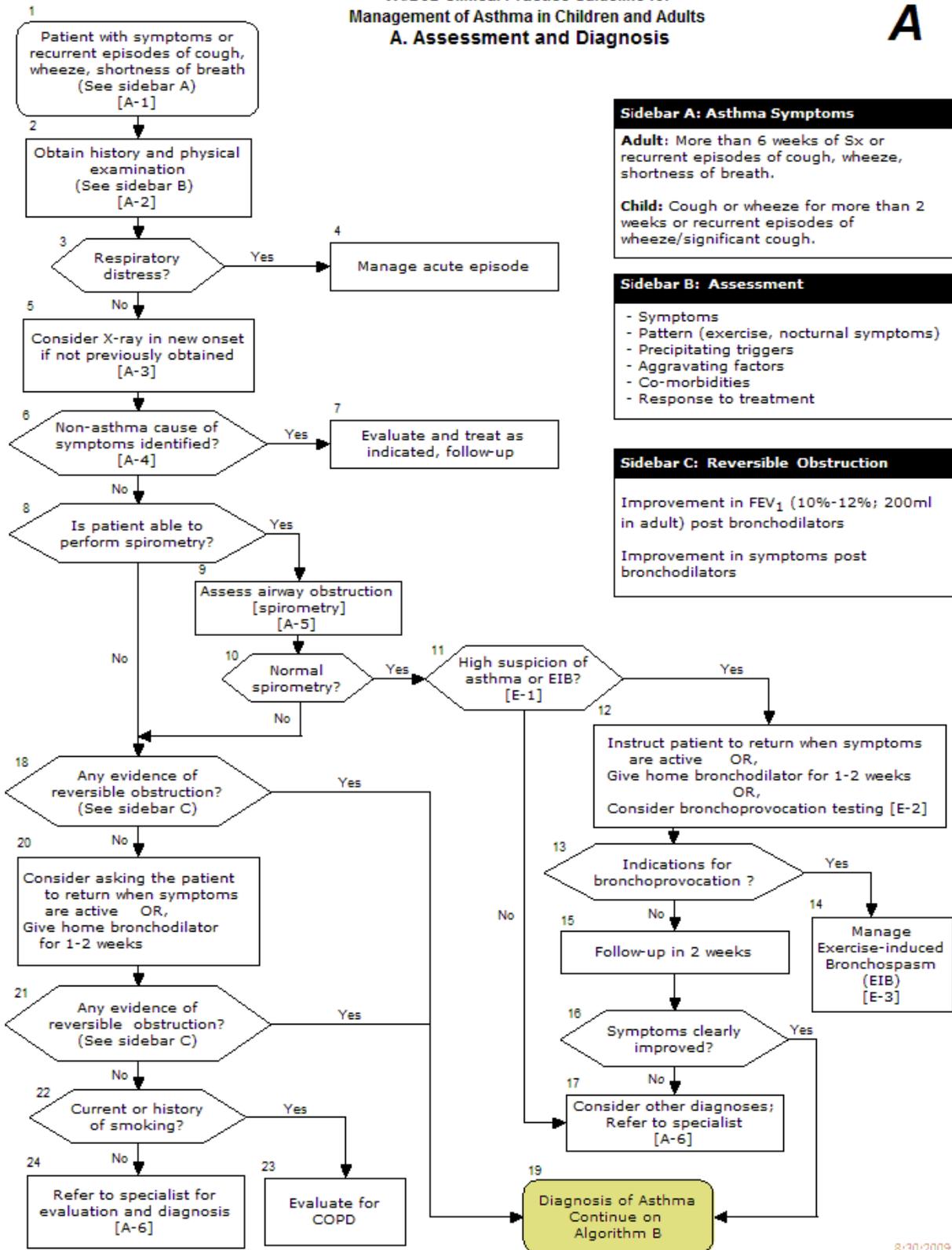
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Algorithms

VA/DoD Clinical Practice Guideline for Management of Asthma in Children and Adults A. Assessment and Diagnosis

A



Sidebar A: Asthma Symptoms

Adult: More than 6 weeks of Sx or recurrent episodes of cough, wheeze, shortness of breath.

Child: Cough or wheeze for more than 2 weeks or recurrent episodes of wheeze/significant cough.

Sidebar B: Assessment

- Symptoms
- Pattern (exercise, nocturnal symptoms)
- Precipitating triggers
- Aggravating factors
- Co-morbidities
- Response to treatment

Sidebar C: Reversible Obstruction

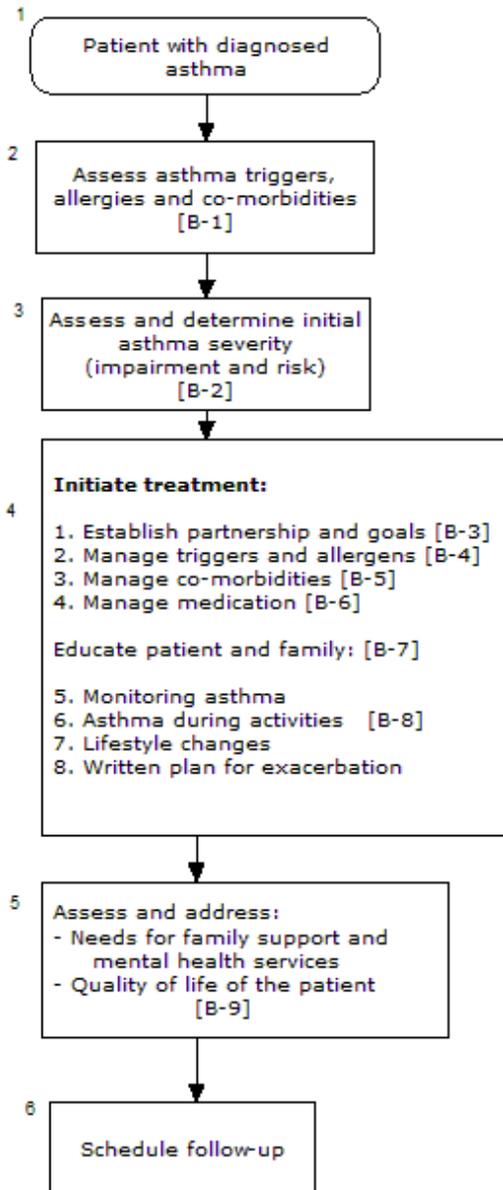
Improvement in FEV₁ (10%-12%; 200ml in adult) post bronchodilators

Improvement in symptoms post bronchodilators

8/30/2009

VA/DoD Clinical Practice Guideline for Management of Asthma in Children and Adults
B. Initiation of Therapy

B



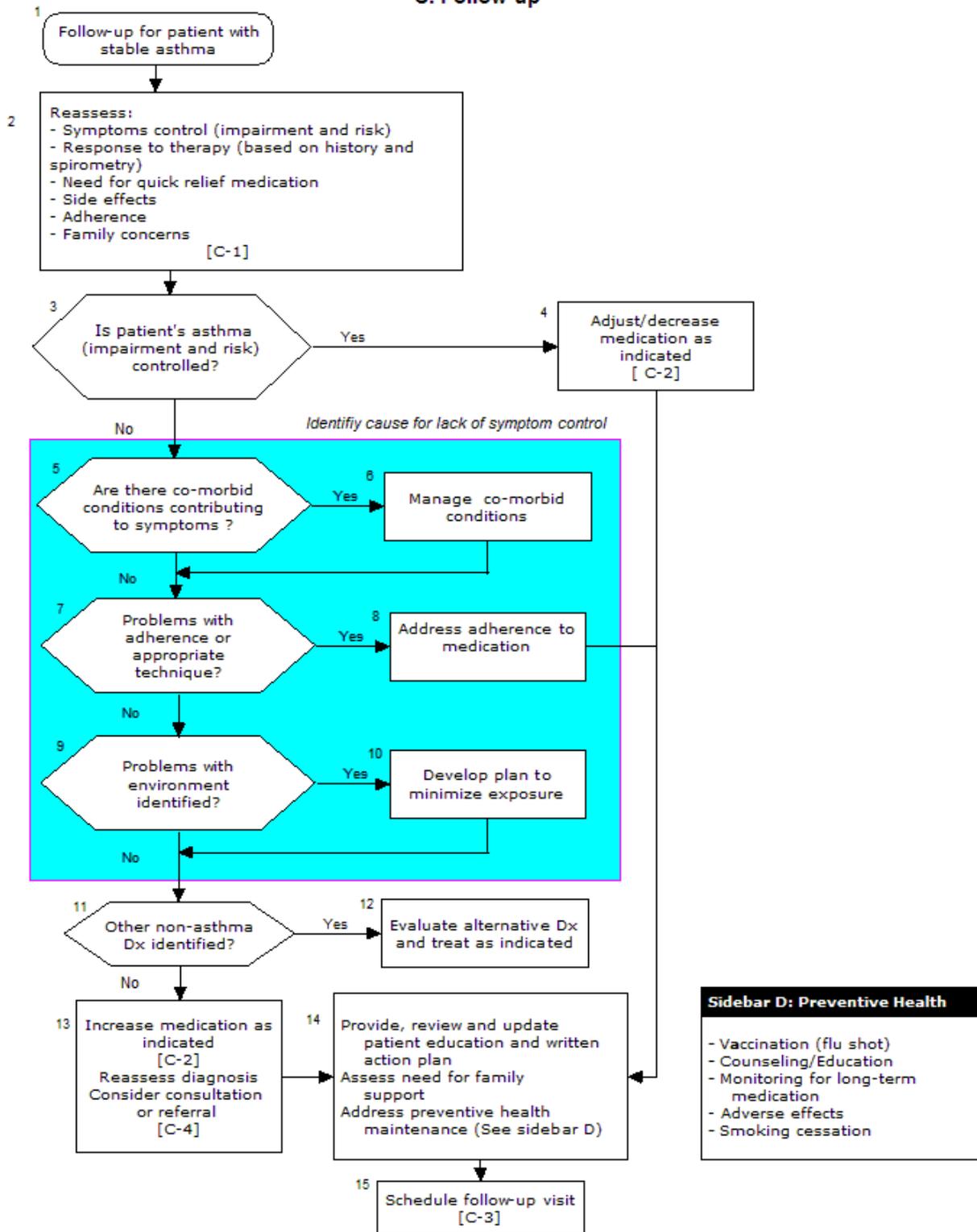
Initial Treatment	
1. Establish patient-provider partnership [B-3]	Describe goals of treatment Explain nature of asthma disease Utilize a variety of educational strategies
2. Manage the environment [B-4]	Describe environment controls Identify triggers and allergens Develop environment modification plan
3. Manage co-morbidities [B-5]	Co-morbidities contributing to symptoms Co-morbidities affecting adherence to treatment
4. Manage medication [B-6]	Describe the medication plan Explain use of drugs and side effects Teach use of devices

Patient and Family Education	
5. Monitoring asthma	Describe benefit of asthma control Teach use of peak flow meter Teach recognition of asthma symptoms Explain use of diary and zones if part of an Asthma Action Plan
6. Asthma at work /school/day care [B-8]	Explain exercise-induced asthma Plan for improving activity level Provide letter for school/day care
7. Lifestyle changes	Exercise Weight loss Smoking cessation
8. Plan for exacerbation	Describe warning signs of exacerbation Develop plan for episode Establish contact with clinic and provider

8/25/2009

C

VA/DoD Clinical Practice Guideline for Management of Asthma in Children and Adults
C. Follow-up



11/6/2009

Annotations

1. Definitions

Asthma is a chronic inflammatory disorder of the airways.

Chronically inflamed airways are hyperresponsive; they become obstructed and airflow is limited when airways are exposed to various risk factors. These episodes are usually associated with widespread but variable airflow obstruction, which is often reversible either spontaneously, or with treatment.

Control is the degree to which the manifestations of asthma (symptoms, functional impairments, and risks of untoward events) are minimized and the goals of therapy are met.

Exercise-induced asthma involves episodes of airway obstruction in individuals who have the underlying chronic condition that is triggered by exercise.

Exercise-induced bronchospasm or hyperreactivity is a disorder of the airways as a result of exercise in patients who have normal baseline spirometry, and are not considered to have chronic inflammation of the airways.

Impairment involves functional limitations the patient is currently experiencing or has recently experienced.

Severity refers to the intrinsic intensity of the disease process. Severity is most easily and directly measured in a patient who is not currently receiving long-term control treatment.

Risk is the likelihood of either asthma exacerbations, progressive decline in lung function (or, for children, reduced lung growth), or risk of adverse effects from medication.

ALGORITHM A: ASSESSMENT AND DIAGNOSIS

Annotation A-1 Patient with Symptoms or Recurrent Episodes of Cough, Wheeze, or Shortness of Breath
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2. ESTABLISHING THE DIAGNOSIS OF ASTHMA

Establishing the diagnosis of asthma primarily rests on obtaining a solid clinical history suggestive of airway hyperreactivity that includes symptoms such as shortness of breath (SOB), cough, wheezing, or chest tightness and objective evidence of reversible airway obstruction by either spirometry or bronchoprovocation testing. Since many disease processes share similar clinical symptoms, the clinician should not rely solely on symptoms for diagnosing asthma and should always consider alternative diagnoses that mimic asthma. Additional imaging studies, pulmonary function testing, or biomarkers of inflammation are often required to rule out other causes. Diseases such as chronic obstructive pulmonary disease (COPD), sarcoidosis, congestive heart failure, and vocal cord dysfunction require a much different approach for diagnosis and treatment. It is imperative that the clinician carefully examine the clinical history, spirometric findings, and response to treatment to reach the correct diagnosis and to provide the proper long-term care of patients with asthma. Some evidence suggests that many patients are incorrectly diagnosed and treated for asthma when they have an alternative diagnosis.

Annotation A-2 Obtain History and Physical Examination

2.1 Medical History and Physical Exam

(Episodic symptoms of airflow obstruction or airway hyper-responsiveness are present)

BACKGROUND

A complete history and physical exam is the first step in establishing the diagnosis of asthma. Characteristic symptoms of shortness of breath, wheezing, cough, chest tightness, or nocturnal awakenings may suggest the diagnosis. The history should emphasize recurrence of symptoms with associated factors such as exercise, viral infections, or environmental exposures. Physical exam may demonstrate wheezing or suggest other diagnoses. For pediatric patients, a thorough history and physical exam is particularly important. For children too young to perform spirometry, the diagnosis of asthma is often solely based on the history and physical exam without the benefit of objective evidence. Waiting to diagnose asthma until the child is old enough to perform spirometry or other objective measures is inappropriate and unnecessarily delays treatment.

ACTION STATEMENT

Complete and document a thorough history of asthma symptoms and physical examination in all patients suspected of having asthma.

RECOMMENDATIONS

1. During the diagnostic evaluation a thorough history should be performed to include focus on the following elements (see [Appendix B-1](#) for expanded details of the history):
 - a. Characterization of symptoms related to airway obstruction or airway hyper-responsiveness to include cough, wheezing, shortness of breath, chest tightness, and sputum production
 - b. In children, cough may be the only presenting symptom, while wheezing may not be present in some patients with asthma

- c. The pattern of symptoms should be characterized to include onset, duration, frequency, diurnal variation, and seasonality
 - d. Precipitating and aggravating factors (including occupational exposure)
 - e. Prior diagnosis, prior symptoms, prior exacerbations, and prior therapies
 - f. Review of all current medications including over-the-counter and supplements
 - g. Family and social history.
2. In children, a thorough birth history must also be obtained. Important factors in a birth history would include evidence of maternal smoking, prematurity, chronic lung disease, bronchopulmonary dysplasia, and postnatal smoke exposure.
 3. Careful review of systems for any condition which can mimic asthma, such as pulmonary emboli, congestive heart failure, congenital heart disease, viral syndromes, or hypersensitivity pneumonitis.
 4. During the diagnostic evaluation, a thorough physical examination should be performed emphasizing findings in the following areas (see [Appendix B-2](#) for expanded details of the physical exam):
 - a. Upper respiratory tract, including presence of increased nasal secretions, mucosal swelling, or nasal polyps
 - b. Chest, including wheezing during normal breathing or prolonged forced exhalation, hyperexpansion of the thorax, use of accessory muscles, or chest deformity
 - c. Skin, including the presence of atopic dermatitis or eczema
 - d. Absence of the above findings does not exclude the diagnosis of asthma and the examination should include findings that may support alternative diagnoses (see [Appendix B-2](#))
 - e. Consider cardiac evaluation of all murmurs or evidence of cardiovascular disease before initiating, or concurrent with initiating, asthma therapy.

Annotation A-3 Consider X-ray in New Onset if Not Previously Obtained

2.2 Chest Radiograph (Exclude alternative diagnoses)

BACKGROUND

The chest radiograph may be an invaluable tool for excluding other diagnoses that masquerade or complicate the diagnosis and/or treatment of asthma. A chest radiograph can provide key information regarding heart anatomy, lung parenchyma, and mediastinal structures not readily detected by physical exam. Every patient diagnosed with asthma should have at least one chest radiograph during their initial evaluation to help exclude other diagnoses. In children, chronic wheezing and cough may represent a vascular ring (suggested by a right-sided aorta), congestive heart failure, pneumonia, or a variety of other non-asthmatic diagnoses.

ACTION STATEMENT

Obtain a chest radiograph during the initial evaluation for asthma if not done recently.

RECOMMENDATIONS

1. In the pediatric and adolescent patients, a chest radiograph should be considered during the initial treatment period to rule out other diagnoses.
2. In the adult patient with new symptoms suggestive of asthma, a chest radiograph should always be obtained during the initial evaluation.

RATIONALE

The prevalence of other diseases in a pediatric patient with cough or wheezing makes a chest radiograph less useful during the evaluation and initial treatment of asthma in the pediatric patient.

There is a higher likelihood of other diseases found in the adult population being evaluated for asthma. In most cases, a chest radiograph during the initial evaluation will be normal but may exclude other diagnoses.

Annotation A-4 Non-Asthma Cause of Symptoms Identified**2.3 Exclude Alternative Diagnoses (Additional studies)****BACKGROUND**

A fundamental tenet of the diagnosis of asthma is a thorough evaluation and exclusion of alternative diagnoses that may masquerade as asthma or that may co-exist and complicate the evaluation and treatment of asthma. The accurate diagnosis of asthma requires the exclusion of alternative diagnoses that may present with shortness of breath (SOB), wheezing, cough, or other symptoms suggestive of asthma. Exclusion/inclusion of alternative diagnoses starts with a thorough history and physical exam from which a differential diagnosis and a rational approach to additional testing can be developed.

ACTION STATEMENT

Consider differential diagnoses when diagnosing asthma. Refer to a specialist when symptoms, examination, or testing suggests alternative diagnoses.

RECOMMENDATIONS

1. Alternative diagnoses should be considered in all patients, and in particular those over age 30 and under age two with new symptoms suggestive of asthma. (See [Table 2 and 3](#))
2. A significant history of smoking exceeding 20 pack years should make the diagnosis of COPD more likely than asthma.
3. Absence of airway obstruction on initial spirometry should prompt consideration for alternative diagnoses and additional testing.
4. Abnormalities found on Chest X-Ray (CXR) screening should prompt referral to a specialist for further evaluation.
5. When there is no clear response to initial therapy, other significant causes of airway obstruction must be considered.

Table 1. Clinical Features Differentiating COPD and Asthma

Clinical Features	COPD	Asthma
Smoker or ex-smoker	Nearly all	Possibly
Symptoms under age 35	Rare	Often
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent and progressive	Variable
Nighttime waking with breathlessness and/or wheeze	Uncommon	Common
Commonly associated with atopic symptoms and seasonal allergies	Uncommon	Common
Significant diurnal or day-to-day variability of symptoms	Uncommon	Common
Favorable response to inhaled glucocorticoids	Inconsistent	Consistent

Table 2. Identifying Alternative Diagnoses Based on Symptoms and Tests

Diagnosis	Symptoms	Test: Results	Radiographic Findings (CT, CXR)	Pulmonary Function Tests
Chronic Obstructive Pulmonary Disease (COPD)	<ul style="list-style-type: none"> • See VA/DoD CPG for COPD, Sec. 2.4 (see Table 1) 	<ul style="list-style-type: none"> • ABG: hypercapnia 	<ul style="list-style-type: none"> • Bullous disease • Hyperinflation 	<ul style="list-style-type: none"> • Lack of reversibility
Allergic Rhinitis	<ul style="list-style-type: none"> • Seasonal or chronic rhinorrhea/nasal obstruction • Daytime and/or morning cough 	<ul style="list-style-type: none"> • Trial of antihistamines • Allergy testing • Nasal steroids 	N/A	<ul style="list-style-type: none"> • Normal for allergies • Allergic rhinitis common co-morbid condition in asthma
Gastro-esophageal Reflux (GERD)	<ul style="list-style-type: none"> • Heartburn • Irritable after feeding [children] • Commonly asymptomatic 	<ul style="list-style-type: none"> • Trial of H2-blocker or proton pump inhibitors • Consider GI referral for pH probe: reflux 	N/A	N/A
Congestive Heart Failure / Coronary Artery Disease (CAD)	<ul style="list-style-type: none"> • Fatigue • Orthopnea • Paroxysmal nocturnal dyspnea • Dyspnea on exertion • Edema • Weight gain • Hypertension • Diabetes • Coronary Artery Disease 	<ul style="list-style-type: none"> • Echocardiogram: <ul style="list-style-type: none"> - low LVEF - diastolic dysfunction - BNP: Elevated 	<ul style="list-style-type: none"> • Cardiomegaly • Pulmonary congestion • Pleural effusion 	<ul style="list-style-type: none"> • Reversible obstruction uncommon
Vocal cord dysfunction (VCD)	<ul style="list-style-type: none"> • Poor response to asthma Rx • Inspiratory wheeze/stridor • Episodic dyspnea • Rapid onset/relief • Emotional trigger 	<ul style="list-style-type: none"> • Laryngoscopy: inspiratory vocal cord closure 	<ul style="list-style-type: none"> • Normal 	<ul style="list-style-type: none"> • Usually normal; 25% may have blunted inspiratory flow volume loop
Allergic bronchopulmonary aspergillosis (ABPA)	<ul style="list-style-type: none"> • Brownish sputum, wheezing, SOB, fever, malaise 	<ul style="list-style-type: none"> • Blood: eosinophilia • Serum precipitins to aspergillus • Very elevated IgE 	<ul style="list-style-type: none"> • Recurrent fleeting infiltrates, bronchiectasis 	<ul style="list-style-type: none"> • Obstruction
Sarcoidosis – Multisystem inflammatory disorder; granulomatous changes primarily found in lung	<ul style="list-style-type: none"> • Asymptomatic, SOB, wheezing, cough 	<ul style="list-style-type: none"> • ACE level: Elevated hypercalcemia • Non-caseating granulomas on biopsy 	<ul style="list-style-type: none"> • Stage 0 –None • Stage 1 –Hilar-adenopathy • Stage II–Adenopathy + infiltrates • Stage III-Infiltrates 	<ul style="list-style-type: none"> • Normal, restriction, 20% show obstruction
Bronchiectasis – Airway enlargement due to previous infections	<ul style="list-style-type: none"> • Chronic productive cough, wheezing, SOB 	None	<ul style="list-style-type: none"> • High Resolution CT: Localized infiltrates, airway enlargement 	<ul style="list-style-type: none"> • Normal or mild obstruction
Pulmonary embolus (PE)	<ul style="list-style-type: none"> • Unresponsive to bronchodilator • Hemodynamic compromise • Sudden chest pain • Presence of risk factors • Tachycardia 	<ul style="list-style-type: none"> • D-dimer: elevated • ABG: hypoxemia 	<ul style="list-style-type: none"> • CT: chest PE protocol • Ventilation/Perfusion (V/Q) mismatch • CXR normal 	N/A
Cystic Fibrosis	<ul style="list-style-type: none"> • Recurrent productive cough 	<ul style="list-style-type: none"> • Sweat chloride test: abnormal 	<ul style="list-style-type: none"> • Hyperinflation, cystic changes 	<ul style="list-style-type: none"> • Lack of reversibility

Key: ABG-Arterial Blood Gas; ACE-Angiotensin-converting Enzyme; BNP-b-type Natriuretic Peptide CT-Computed Tomography; CXR-Chest X-Ray; IgE-Immunoglobulin E LVEF-Left Ventricular Ejection Fraction.

Table 3. Identifying Alternative Diagnoses Based on Symptoms and Tests – Pediatric-Specific

Diagnosis	Symptoms	Test	Radiographic Finding (CT, CXR)
Foreign Body	<ul style="list-style-type: none"> • Unilateral wheeze • Sudden onset • Choking history • Age: 6 months-6 years 	<ul style="list-style-type: none"> • Bronchoscopy 	<ul style="list-style-type: none"> • CXR – Unilateral hyperinflation or atelectasis • Failure to deflate on expiratory or decubitus CXR
Bronchopulmonary dysplasia (BPD)	<ul style="list-style-type: none"> • Premature birth: • Hx prolonged mechanical ventilation/oxygen requirement in neonatal period. If responsive to bronchodilators and steroids, treat as asthma 	N/A	<ul style="list-style-type: none"> • CXR: May appear identical to asthma patients
Laryngomalacia	<ul style="list-style-type: none"> • Inspiratory wheeze • Onset prior to 6 weeks of age • Improves when prone • No bronchodilator response 	<ul style="list-style-type: none"> • Laryngoscopy 	N/A
Subglottic stenosis	<ul style="list-style-type: none"> • Hx of intubation • Biphasic wheeze, loudest in neck • No bronchodilator response 	<ul style="list-style-type: none"> • Bronchoscopy 	N/A
Tracheo/ bronchomalacia	<ul style="list-style-type: none"> • Inspiratory or expiratory monophonic wheeze • No bronchodilator response 	<ul style="list-style-type: none"> • Bronchoscopy 	N/A
Bronchiolitis (asthma exacerbation caused by viruses)	<ul style="list-style-type: none"> • Diffused wheeze and/or bronchi 	<ul style="list-style-type: none"> • No response to beta-2 agonist • Respiratory Syncytial Virus testing 	N/A
Recurrent upper respiratory infection	<ul style="list-style-type: none"> • Common cold symptoms 	<ul style="list-style-type: none"> • Reduction of respiratory symptoms after bulb suction or decongestion 	N/A

2.3.1 Full Pulmonary Function Testing (Exclude Alternative Diagnoses)

BACKGROUND

Full pulmonary function testing including flow volume loops, lung volumes, and diffusing capacity of the lung for carbon monoxide (DLCO) may be indicated in evaluating patients suspected of having asthma. Full pulmonary function testing can assist in clarifying the differential diagnosis when spirometry demonstrates a restrictive rather than obstructive process. Full pulmonary function testing can assist in the differentiating elements of COPD, interstitial lung disease, and restrictive lung disease due to chest wall mechanics.

ACTION STATEMENT

Consider full pulmonary function testing for patients with significant pulmonary symptoms and restrictive spirometry, and in many cases, those with normal spirometry.

RECOMMENDATIONS

1. The presence of restrictive indices on spirometry (reduction in both FEV1 and FVC) should prompt the clinician to perform full pulmonary function testing to include lung volumes and diffusing capacity.
2. In those patients with confirmed restriction on full pulmonary function testing, referral to specialty care is indicated.
3. In those patients with normal spirometry and significant pulmonary symptoms, consideration should also be given to full pulmonary function testing to exclude mild reductions in vital capacity or diffusing capacity.
4. Careful review of the flow volume loop should be performed on all spirometric exams to look for the presence of truncated or flattened loops suggestive of possible upper airway obstruction.

Annotation A-5 Assess Airway Obstruction (Spirometry)

2.3.2 Spirometry with Bronchodilators (Airflow is partially reversible)

BACKGROUND

While the diagnosis of asthma may be based on history and physical examination alone, the confidence in the diagnosis is substantially enhanced by objective techniques such as spirometry. Spirometry should be obtained on all patients older than five years of age. The classic spirometric finding in asthma is obstructive airflow changes that partially or completely normalize after bronchodilator treatment. For the purpose of diagnosis, spirometry is an essential technique that allows documentation of airflow reversibility and demonstrates baseline function prior to treatment.

ACTION STATEMENT

Perform spirometry (with bronchodilators if indicated) in all adult patients and older children suspected of having asthma, to establish the presence of airway obstruction as a diagnostic study, preferably prior to initiation of treatment.

RECOMMENDATIONS

1. Spirometry should be performed in accordance with published standards and documented in the medical record. In general, there is no minimum age for spirometry, but patients under age 5 may not be able to perform breathing maneuvers correctly. [A]
2. A diagnosis of expiratory airflow limitation can be made in accordance with validated reference values (such as National Health and Nutrition Examination Survey (NHANES) III as recommended by the ATS/ERS guidelines).
3. The presence of obstruction should be based on a forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) value less than the fifth percentile and not on the percent reduction of the FEV1. (Healthcare providers not trained in the interpretation of spirometry should have the results reviewed by a specialist.) [B]
4. If airway obstruction is present or there is suspicion of asthma, spirometry should be repeated post-bronchodilators to establish the presence and degree of reversibility of the FEV1. [B]
5. A 10-12 percent increase in the FEV1 (and > 200 ml in adults) may be considered significant airway reversibility. [C]

2.3.3 Bronchoprovocation Testing – Airway Hyperresponsiveness

BACKGROUND

Bronchoprovocation testing may be a useful tool when attempting to demonstrate airway hyperresponsiveness in a patient with symptoms suggestive of asthma and normal baseline spirometry. A common diagnosis in adolescents and young adults who exercise regularly is exercise-induced bronchospasm (EIB). Common methods of assessing airway hyperresponsiveness include methacholine challenge testing, exercise spirometry, or eucapnic voluntary hyperventilation. These tests in particular should be conducted on patients who exhibit symptoms consistent with asthma, but the diagnosis is not established by baseline spirometry and bronchodilator studies. Bronchoprovocation testing is usually performed by a specialist familiar with the procedure and knowledgeable on indications and pitfalls with each type of testing procedure.

ACTION STATEMENT

Consider referral for bronchoprovocation testing for those patients with symptoms suggestive of asthma with 1) normal baseline spirometry (no evidence of obstruction) and/or minimal clinical response to initial treatment; or 2) symptoms primarily associated with exertion.

For further discussion of EIB see [Annotations E-1, E-2, E-3](#).

RECOMMENDATIONS

1. Refer patients to a pulmonary function laboratory capable of performing bronchoprovocation testing in accordance with American Thoracic Society (ATS) standards.
2. The preferred method for bronchoprovocation testing is histamine or methacholine challenge testing. Other established methods are less commonly available such as cold air or eucapnic hyperventilation.
3. Exercise challenge testing is a less sensitive test for detecting the presence of airway hyperreactivity and may be considered for symptoms primarily associated with exertion.

2.3.4 Other Diagnostic Tests

BACKGROUND

Multiple biomarkers such as exhaled nitric oxide, sputum eosinophils, and serum arginase levels are available measurements of airway inflammation. However, no specific biomarkers have been validated prospectively in regards to impacting either diagnosis or response to therapy. Furthermore, the equipment required for such measurements is prohibitively expensive and performed in specialized clinical settings.

RECOMMENDATIONS

1. Biomarkers such as nitric oxide are not currently validated clinical indicators of asthma severity or control and should not be used in the primary care setting as a means of diagnosis or evaluating response to therapy.
2. Biomarker evaluation is best performed in specialty clinics where such testing is frequently conducted and interpreted.

2.3.5 Allergy Testing

BACKGROUND

Allergy testing is an important tool in the evaluation and management of patients with asthma. Assessing for specific IgE can assist in demonstrating the presence or absence of atopy as well as identifying specific

antigens that may trigger or contribute to symptoms. The presence of atopy is common and an important risk factor for the development of asthma. The absence of atopy, especially in children with other atypical features, may lead to a more aggressive pursuit of alternative diagnosis. Identification of atopy, specific allergic sensitization, and co-morbid allergic rhinitis can help focus strategies for education and avoidance techniques. They may also assist to identify or strengthen indications for selection of medication and immunotherapy, and may play a role in identifying patients at risk of severe or fatal episodes.

ACTION STATEMENT

Consider allergy testing to assist in the diagnosis of asthma.

RECOMMENDATIONS

1. Consider allergy testing in patients with asthma with symptoms suggesting significant co-morbid allergic rhinoconjunctivitis or if recommended by specialty referral.
2. Allergy testing may be useful in the diagnostic evaluation of asthma to: [B]
 - a. Identify atopy and co-morbid allergic rhinoconjunctivitis as risk factors for the development of asthma
 - b. Identify precipitating factors and/or triggers related to asthma symptoms and worsening co-morbid allergic rhinoconjunctivitis
 - c. Allergy testing in children is less sensitive.

Annotation A-6 Refer to Specialist for Evaluation and Diagnosis

2.4 Indication for Specialty Consultation

BACKGROUND

While the majority of patients with asthma should be diagnosed and treated at the primary care level, some patients with more severe asthma or those whose symptoms present a diagnostic dilemma may benefit from an evaluation by a pulmonologist, allergist or other asthma specialist.

ACTION STATEMENT

Refer patients with atypical presentation for evaluation and diagnosis to a specialist.

RECOMMENDATIONS

1. Patients who are under consideration for an asthma diagnosis by their primary care provider should be referred to a subspecialist (Allergist / Immunologist, Pulmonologist, Gastroenterologist, Otolaryngologist) if any of the following are present: [C]
 - a. Findings NOT consistent with typical asthma diagnosis that should prompt referral to specialty:
 - Poor growth / failure-to-thrive (especially in infants and children)
 - Cyanosis at feeding (infants and children)
 - Vomiting at feeding (infants and children)
 - Clubbing
 - Stridor / upper airway wheeze
 - Hemoptysis
 - Any significant chest radiograph abnormality

- Lymphadenopathy
 - Persistent oxygen requirement
 - Chest pain
 - Pneumothorax
 - Recurrent bacterial pneumonia
 - Monophonic or unilateral wheeze
 - Recurrent bronchitis (only for adults)
 - History of anaphylaxis
 - Chronic productive cough or irreversible airway obstruction on spirometry in the absence of a diagnosis of COPD
- b. Signs and symptoms are atypical, or there are problems in differential diagnosis such that the primary care provider is uncertain of making an asthma diagnosis
 - c. Patient requires confirmation of a history that suggests that an occupational or environmental inhalant or ingested substance is provoking or contributing to asthma.
2. Patients who have significant psychiatric, substance abuse, psychosocial, or family problems that interfere with their asthma therapy may need referral to an appropriate mental health professional for counseling or treatment. [B]
 3. Patient/parent requests for consultation with subspecialist.

ALGORITHM B: INITIATION OF THERAPY

Annotation B-1 Assess Asthma Triggers, Allergies and Co-morbidities

3. CO-MORBIDITIES FOR ASTHMA

BACKGROUND

Patients diagnosed with asthma should be investigated for co-morbidities regardless of age. Patients with asthma commonly have other diagnoses that exacerbate their respiratory complaints or act to trigger asthma symptoms. Failure to identify these co-morbidities may lead to difficulty fully controlling respiratory symptoms resulting in increased asthma symptoms and exacerbations. Evidence suggests that appropriate treatment of these co-morbidities can improve asthma control. A thorough history, physical exam, and focused review of systems should be obtained to determine if these co-morbidities are present and contribute significantly in an individual patient (see Table 4).

Table 4. Co-morbidities of Asthma in Adults and Children

Children	Adults
Allergic rhinitis and sinusitis	Gastroesophageal Reflux Disease (GERD)
Gastroesophageal Reflux Disease (GERD)	Allergic rhinitis and sinusitis
Allergic bronchopulmonary aspergillosis (ABPA)	Allergic bronchopulmonary aspergillosis (ABPA)
	Obstructive Sleep Apnea (OSA)

3.1 Gastroesophageal Reflux Disease (GERD)

BACKGROUND

Gastroesophageal reflux disease (GERD) is the retrograde regurgitation of stomach contents into the esophagus and, in some individuals, the upper airway. Acid stimulation of the esophagus has been demonstrated to cause bronchospasm and involvement of the upper airway may cause laryngospasm or even aspiration events. Investigation for GERD should be a routine part of an initial asthma evaluation in all patients, regardless of age, and should be particularly addressed in those patients with frequent heartburn or nocturnal asthma symptoms.

ACTION STATEMENT

Obtain a detailed history of the frequency of heartburn symptoms and treat for GERD if symptoms or nocturnal asthma is significant.

RECOMMENDATIONS

1. Patients with asthma should be questioned about the frequency of heartburn symptoms, effectiveness of previous treatments, and the presence of symptoms such as nocturnal cough or wheezing, morning hoarseness, or sore throat even in the absence of heartburn. [B]
2. Parents of children under age 5 should be questioned about irritability after feeds, regurgitation while supine, or complaints of chest pain that may be a manifestation of GERD. [B]
3. Treatment should include specific food avoidance (especially caffeine and alcohol), avoidance of food and drink 3 hours before bedtime, elevation of head of bed, and appropriate pharmacologic therapy. [C]

3.2 Allergic Rhinitis/Sinusitis

BACKGROUND

There is a strong association between allergic rhinitis and asthma. The majority of school-age children with asthma have co-morbid allergic rhinitis; the association remains strong in adults and wanes in the elderly. Consistent with the concept of the airway as a continuum, treatment of allergic rhinitis can improve asthma outcomes. Accumulation of fluid in the sinuses with resultant chronic nasal drainage and post-nasal drip is a common complication in asthma patients, even in young children. A common misperception among physicians is that children do not get sinusitis. In fact, the maxillary and ethmoid sinuses are present at birth and sinusitis as a co-morbidity must be considered in all patients regardless of age.

ACTION STATEMENT

Evaluate patients with asthma who have chronic nasal drainage, nasal congestion, or postnasal drip for the presence of allergic rhinitis or chronic sinusitis as a co-morbidity affecting asthma control.

RECOMMENDATIONS

1. Patients with asthma should undergo an assessment for allergic rhinitis or sinusitis that is either seasonal or year-round in variation. This assessment should include a history of seasonal variations, specific triggers, diurnal variation, and changes in the workplace. [B]
2. Physical examination of all patients with asthma should include evaluation for the presence of conjunctival inflammation, nasal mucosal inflammation, nasal discharge, polyps, and post nasal drip. [B]
3. Consideration for allergy testing should be given to patients with asthma who have allergic rhinitis and who experience year-round symptoms or difficulty controlling asthma. [B]
4. Adequate treatment of allergic rhinitis or sinusitis should be undertaken in an effort to improve asthma outcomes. Treatment may include allergen avoidance, medications, immunotherapy, or surgical therapy. [B]

3.3 Obesity

BACKGROUND

Obesity is an increasing problem in industrialized nations and has a significant effect on the development of asthma and asthma control. There is a higher prevalence of asthma in the overweight pediatric population. Weight loss is associated with improved asthma control and should be highly encouraged in patients with asthma.

ACTION STATEMENT

Clinicians advising patients with asthma who are overweight or obese should recommend weight loss to improve overall health and possibly asthma control.

RECOMMENDATIONS

1. Weight loss should be highly encouraged in patients with asthma who are overweight or obese to improve pulmonary mechanics, decrease exacerbations, and reduce the use of steroids especially in children who are more likely to have asthma persistence. [C]

3.4 Obstructive Sleep Apnea

BACKGROUND

Obesity is associated with persistent asthma and severity in both children and adults. Sleep disturbances in patients with asthma are common. In the patients with uncontrolled asthma, recurrent cough and wheeze may interrupt sleep. Obstructive sleep apnea (OSA) as a cause for sleep disordered breathing is also relatively common. In children, OSA is often a manifestation of tonsillar and adenoidal hypertrophy and surgery may be curative. Addressing OSA effectively can dramatically improve the quality of sleep and a patient's daytime academic / work performance.

ACTION STATEMENT

Clinicians evaluating patients who are overweight or obese and have unstable or poorly controlled asthma (particularly those with nocturnal asthma or awakenings) should assess for the presence of obstructive sleep apnea.

RECOMMENDATIONS

1. Overweight patients with asthma should be questioned about their sleep habits and hygiene and in particular a history of loud snoring, excessive daytime somnolence, and witnessed apneas.
2. Patients with excessive daytime somnolence or witnessed apneas should be referred for sleep testing (polysomnography). [B]
3. Patients with unstable uncontrolled asthma and sleep apnea should be treated with continuous positive airway pressure (CPAP). Weight loss, dental appliances, and evaluation for surgery may be considered in selected patients. [C]

Annotation B-2 Assess and Determine Initial Asthma Severity (Impairment and Risk)

4. SEVERITY CLASSIFICATION

BACKGROUND

Asthma is a heterogeneous disorder with a wide range of severity. An assessment of severity is essential for determining appropriate initial therapy and need for specialty referral. The system for assessing severity has been refined from previous guidelines. It now includes the domain of risk as well as current impairment from asthma. Asthma severity is classified using standardized, widely accepted terminology. This allows for clear communication among medical providers and gives a uniform framework for the assessment of asthma.

NHLBI and GINA classifications of asthma severity are based on expert consensus. In order to provide a clear and practical initial assessment of severity, elements of both guidelines were adopted in constructing the VA-DoD severity classification table (Table 5).

ACTION STATEMENT

Assess current impairment and risk of exacerbation as part of initial evaluation, to determine and classify the severity of the asthma.

RECOMMENDATIONS

1. Current impairment and risk of exacerbations should be assessed in the initial evaluation of asthma to classify severity (see [Table 5](#)).
2. A history of asthma symptoms, nighttime awakenings, need for SABA for relief of symptoms and interference with activities should be used to assess current impairment.

3. The frequency and severity of asthma exacerbations should be used in assessing the domain of risk. Lung function and psychosocial factors may also help predict risk.
4. Spirometry should be used in the initial assessment of all patients who are capable of performing an adequate expiratory maneuver. Lung function is a measure of impairment but may also predict risk.
5. Classification of severity of the disease should be based on initial assessment of the patient who is not on long-term control therapy.

Table 5. Initial Assessment of Asthma Severity

SEVERITY (Assess over a period of at least 4-6 weeks)		Classifying Asthma Severity and Initiating Therapy			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤ 2 days/week	> 2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤ 2 x/month	> 2x/month	> 1x/week but not nightly	Nightly
	Use of quick-relief for symptom control	≤ 2 days/week	> 2 days/week but not daily, and not more than once on any day	Daily	Several times/day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Lung Function: Normal FEV1/FVC: ≤ 19 yr - 85% 20-39 yr - 80% 40-59 yr - 75%	FEV1	> 80% predicted Normal between exacerbations	> 80% predicted Normal between exacerbations	60-80% predicted	<60% predicted
	FEV1/FVC	Normal	Normal	Abnormal	Abnormal
Risk	Exacerbations requiring systemic corticosteroids (consider severity and interval since last episode)	0-1 x/year	Age 0-4 years: ≥ 2 exacerbations in 6 months requiring oral or intravenous corticosteroids, OR > 4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma		
			Age ≥5 years and adult: ≥ 2 exacerbations per year requiring oral or intravenous corticosteroids		

Modified from NHLBI 2007 and GINA 2007 guidelines.

5. INITIAL TREATMENT

Annotation B-3 Establish Partnership and Goals

5.1 Establishing Patient-Provider Partnership

BACKGROUND

A proactive partnership between the patient and provider that identifies the patient's perception of their asthma control and quality of life will enable the development of a treatment plan that emphasizes long-term control through medications, avoidance mechanisms, and asthma self-management.

ACTION STATEMENT

Establish an interactive partnership with patient and caregiver to optimize the patient self-management of asthma.

RECOMMENDATIONS

1. Patient and parent education on asthma self-management should begin at diagnosis and be reviewed regularly.
2. Patients and parents should be familiar with, and receive education from, the entire healthcare team: physicians, nurses, pharmacists, respiratory therapists, etc.
3. Communication with the patient/parents should focus on patient-centered goals of treatment; at every visit, reinforce self-management of asthma.
4. Written asthma action plans, developed jointly between patient and provider, should focus on daily management and techniques to manage exacerbations for all patients with asthma.

Annotation B-4 Manage Triggers and Allergens

5.2 Reduction of Exposure to Risk

BACKGROUND

Asthma symptoms may be triggered by a wide variety of occupational and aeroallergen exposures or exacerbated by certain medications. Education that addresses recognition and avoidance of these triggers will help improve long-term asthma control and decrease the frequency and severity of exacerbations. Patients with chronic asthma are at increased risk for complications from influenza and pneumococcal pneumonia.

RECOMMENDATIONS

1. Patients with persistent asthma should be evaluated for possible allergen and environmental triggers that can be avoided (see Section 9 - Environmental Control), including outdoor activity if levels of air pollution are high.
2. Patients should be advised to avoid non-selective beta-blocker therapy. [B]
3. Encourage avoidance of sulfite-containing foods or other foods determined by history to trigger exacerbations. [B]

4. NSAID and aspirin use in patients with nasal polyps, severe persistent asthma, or known NSAID/ASA sensitivity should be strictly avoided. [B]
5. All patients with asthma who are older than 6 months of age should receive inactivated flu vaccine to decrease the risk of complications from infection with influenza. Patient or parents should be counseled that the vaccination will not decrease the frequency or severity of exacerbations during the flu season. [A]
6. Pneumococcal polysaccharide vaccine should be administered to adults with chronic persistent asthma. [B]

Annotation B-5 Manage Co-morbidities

5.3 Co-morbid Conditions

BACKGROUND

Multiple conditions exist that can provoke or exacerbate asthma symptoms if left untreated. Inadequate treatment of co-morbid conditions may result in false assessments of asthma severity and control, thus complicating the long-term management and increasing the risk of treatment failure (see [Annotation B-1](#)).

RECOMMENDATIONS

1. Patients who do not respond to typical asthma therapy should be reevaluated for the presence of unmanaged co-morbid conditions.
2. Identify and treat conditions such as allergic rhinitis, sinusitis, gastro-esophageal reflux, obstructive sleep apnea, obesity, substance abuse, depression, or other mental health disorders to ensure optimal control of asthma.

Annotation B-6 Manage Medications

5.4 Medication

BACKGROUND

The goals of therapy are to prevent or reduce the frequency and intensity of symptoms, prevent recurrent exacerbations, prevent decline in lung function, and improve quality of life. Medications to treat asthma are categorized into long-term control medications and quick relief medications. Long-term control medications are taken daily to achieve and maintain control of persistent asthma. Quick relief medications are used to treat acute symptoms and exacerbations. The initial medication regimen is based on asthma severity, optimal delivery devices, and safety.

RECOMMENDATIONS

1. Patients diagnosed with persistent asthma require treatment with an inhaled corticosteroid to reduce inflammation. Additional long-term control medications such as long-acting beta agonists (LABAs) or leukotriene inhibitors may be added based on initial asthma severity and subsequent assessment of control to relieve bronchospasm. **Patients must never be treated solely with long-acting beta2-agonists.**
2. Short-Acting Beta Agonists (SABAs) should be used for relief of acute asthma symptoms. An asthma action plan is needed to guide home use of SABAs. Two to six puffs of SABA may be used in

accordance with the asthma action plan. Patients who do not experience relief after 3 doses in a one hour period OR who need a dose more frequently than every 4 hours, should seek medical care.

3. To ensure adequate medication delivery, an appropriate inhaler device should be used. Device selection must include consideration of the patient's developmental age and ability to perform proper technique (see [Table 8 Comparison of Inhaler Devices](#)).
4. A large volume spacer such as the Aerochamber should be used in patients who have difficulty using metered-dose inhalers.

(For detailed recommendations, see [Section 8: Intervention – Pharmacotherapy](#).)

Annotation B-7 Educate Patient and Family

5.5 Patient Education

BACKGROUND

Asthma self-management education is imperative and effective in attaining validated patient outcomes and improved asthma control. Targeted asthma education provided to patients and their caregivers affords asthma knowledge, skill sets for home management, action steps for changes in asthma control, and empowerment. Integration of self-management educational components by patients and their providers reduces urgent care clinic visits and hospitalizations, improves health status, reduces symptoms, lessens limitation of activity, improves quality of life and perceived control of asthma, and improves medication adherence. Reinforcement of asthma self-management education is essential at all points of contact with the patient and their caregivers.

See [Section 10: Intervention: Smoking Cessation, Nutrition, Weight loss, and Complementary Alternative Medicine](#).

See [Section 11: Self-Management/Patient Education](#).

ACTION STATEMENT

Provide formal asthma education to all patients diagnosed with asthma and reinforce self-management skills of patients and caregivers as part of each follow-up visit.

RECOMMENDATIONS

1. Patients and their caregivers should be educated regarding the essential and basic facts about asthma that includes: [B]
 - a. What defines well-controlled asthma
 - b. Roles of medications
 - c. Appropriate technique in using inhaler devices
 - d. Self-monitoring (either symptom or peak flow-based)
 - e. Identification of triggers and environmental exposure control measures
 - f. When and how to handle signs and symptoms of worsening asthma
 - g. When and where to seek care.
2. Asthma self-management education should be incorporated into all points of contact with the patient and his/her caregivers. [B]

Annotation B-8 Educate About Asthma During Activities**5.6 Plan for Improving Activity Level (Asthma at Work/School/Daycare)***BACKGROUND*

A major goal of asthma therapy should be maintenance of normal, age-appropriate activity levels (this includes routine exercise as well as desired extracurricular activities). Patients should exhibit minimal, if any, symptoms during exercise and should experience regular attendance at work or school.

RECOMMENDATIONS

1. Patients should be encouraged to continue regular exercise and activities of daily living. [A]
2. Ensure family members, teachers, coaches, and school nurses are aware of the basic principles of asthma symptom recognition and management for acute exacerbation.
3. All patients should have a written asthma action plan that includes instructions for recognition of worsening conditions along with actions to take at home/work/school/daycare. [A]
4. Patient should be educated about the instructions included in the action plan.
 - a. Education regarding exercise-induced asthma: [A]
 - Explain that pharmacologic therapies and other strategies may improve exercise tolerance and decrease the occurrence of exercise-related symptoms
 - Use SABA 20 minutes prior to planned exertion; if symptoms appear during activity, a repeated dose of SABA may be offered as addressed in the written asthma action plan
 - Extend warm-up periods prior to exercise.
 - b. Education regarding occupational asthma: [B]
 - Obtaining serial peak flow values both at work and away from work may suggest a relationship between work and asthma
 - Patients with occupation-related asthma may require referral to an occupational health specialist.
5. Managing asthma during school/day care activities:
 - a. The asthma action plan for children should be provided to the school and/or daycare. [C]
 - b. Establish a partnership with schools and/or daycare centers to provide education programs for staff and/or peers. [B]
 - c. Use of medication:
 - Controller medication:
 - If possible, schedule controller medications to be given at home and not at school or daycare
 - If patient adherence is questionable, medication may need to be given at school to ensure compliance during the school year
 - When daily controller medication is required at school/daycare, the ability of school/daycare personnel to administer should be determined.
 - Rescue medication:
 - Rescue medications should be available at school/daycare
 - For school-age children, determine availability of rescue medication; some school systems do not allow children to personally carry any medication
 - For daycare or young school-age children, the ability of the staff to administer medication should be determined.

Annotation B-9 Assess Needs for Family Support and Mental Health Services; Assess Quality of Life of the Patient

5.7 Psychosocial Assessment

BACKGROUND

Psychosocial factors such as socioeconomic status, educational level of caregivers, and the presence of emotional or psychiatric disorders among family members may adversely affect asthma care. Cultural and ethnic beliefs or perceptions about asthma or other chronic illnesses may also impact compliance with an asthma care plan. Patients with depression or other psychiatric disorders often report impairments that are more significant. Social or mental health services may improve not only symptom treatment, but also patient perception of symptom control.

ACTION STATEMENT

Develop and tailor the comprehensive asthma treatment plan to the individual needs of the patient with specific sensitivity to cultural, ethnic, educational, or other social or psychological barriers to care.

RECOMMENDATIONS

1. Asthma care should be provided in an environment that is culturally and ethnically sensitive and at an educational level appropriate to the patient and caregivers. [A]
2. Socio-economic barriers to patient adherence to asthma care should be identified with the patient and caregivers, and addressed by education or appropriate referrals. [B]
3. Psychiatric disorders, to include chronic stress or depression, should be identified and patients referred as appropriate. [B]

ALGORITHM C: FOLLOW-UP

6. MONITORING FOR CONTROL AND FOLLOW-UP

BACKGROUND

A stepwise approach to therapy is recommended, in which the dose and number of medications and frequency of administration are increased as necessary and decreased when possible, to achieve and maintain control of asthma. Assessing both the domains of impairment and risk emphasizes the need to separately consider asthma's effects on quality of life and functional capacity on an ongoing basis (impairment), as well as the risks asthma presents for adverse events in the future. These include exacerbations or progressive reduction in lung growth in children. The two domains may respond differently to treatment. For example, a large study of children with asthma revealed that 30 percent of the low-dose ICS treatment group, whose levels of impairment (symptoms, SABA use, and lung function) improved, remained at risk for exacerbations requiring oral systemic corticosteroids.

The goal for therapy is to control asthma by: (NHLBI, 2007)

Reducing Impairment

- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness during the day, at night, or after exertion)
- Require infrequent use (< 2 days /week) of SABA for quick relief of symptoms, not including prevention of exercise-induced bronchospasm (EIB)
- Maintain (near) normal pulmonary function
- Maintain normal activity levels (including exercise and other physical activity and attendance at work or school)
- Meet patient and family expectations of and satisfaction with asthma care.

Reducing Risk

- Prevent recurrent exacerbations of asthma and minimize the need for emergency department (ED) visits or hospitalizations
- Prevent progressive loss of lung function; for children, prevent reduced lung growth
- Provide optimal pharmacotherapy with minimal or no adverse effects.

Annotation C-1 Reassess Symptom Control
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6.1 Assessment of Control

BACKGROUND

Since asthma is a dynamic condition, ongoing monitoring is essential to maintain control and establish the lowest step and dose of treatment. Through proper monitoring, the control of asthma can be reassessed and the responsiveness to therapy noted. The severity and control of asthma can be further broken down into the domains of asthma impairment and risk. Specific assessment measures can be utilized in the monitoring process including the monitoring of signs/symptoms of asthma, pulmonary function, missing days of school/work/duty, quality of life, history of asthma exacerbations, adherence to and adverse effects from prescribed medical regimens, and patient satisfaction with current asthma treatment.

ACTION STATEMENT

Continue monitoring asthma symptoms to maintain control and establish the lowest step and dose of treatment.

RECOMMENDATIONS

1. Patients with a new diagnosis of asthma, regardless of initial severity, should be seen frequently until they are on an effective regimen and demonstrate sufficient understanding of their disease management. Thereafter, patients with intermittent and mild persistent asthma should be seen at least every 6 months. Those asthma patients with more labile or persistent symptoms should have more frequent follow up. [B]
2. Every patient with asthma should be taught to recognize their asthma symptoms and a written asthma action plan, developed in partnership with the patient, should detail the daily management (medications and environmental control strategies), and how to recognize and handle worsening asthma. The action plan is particularly recommended for patients who have moderate or severe asthma, a history of severe exacerbations, or poorly controlled asthma. The written plan can be either symptom or peak flow-based; evidence shows similar benefits for each. [B]
3. Periodic pulmonary function tests or spirometry to assess asthma control should be performed: [A]
 - a. At the initial evaluation
 - b. After treatment and stabilization
 - c. If symptoms worsen
 - d. If change of medication is considered.
4. Periodic spirometry should be considered in patients with controlled symptoms to assess changes in airways function.
5. Providers should consider giving patients a peak flow device and including peak flow values in written action plans for adults. Peak flow devices would be especially useful in patients with moderate-severe asthma, poor perceivers of symptoms, and those with frequent asthma exacerbations. Peak flow devices may help the patient and provider assess changes in therapy and detect changes in disease state.
6. Self-assessment tools should be considered in monitoring patients with asthma. Examples would include: [B]
 - a. Asthma Control Test (ACT) scores used for assessment of symptoms over the past 4 weeks
 - b. Quality of life monitors to determine a patient's satisfaction with asthma control and care.
7. Patient adherence and inhaler technique should be evaluated at every asthma visit.
8. Adherent patients with poorly controlled asthma or intolerance of medications should be referred to a specialist.

Table 6. Asthma Control (All Ages)

Components of Control		Assessing Asthma Control and Adjusting Therapy All Ages	
		Controlled	Not Controlled
Impairment Normal FEV1/FVC: ≤19 yr – 85% 20-39 yr – 80% 40-59 yr – 75%	Daytime Symptoms	≤ 2 brief symptomatic episodes per week	> 2 symptomatic episodes per week
	Nighttime awakening	≤ 2 nights/month	> 2 nights/month
	Interference with normal activities	None	Some Limitation
	SABA use for symptom control (not for prevention of EIB)	≤ 2 treatments/week	> 2 treatments/week
	Spirometry (if obtained) * predicted/personal best	FEV1 ≥ 80% AND FEV1/FVC normal	FEV1 ≤ 80% OR abnormal FEV1/FVC
	Asthma Control Test (ACT) Score ages ≥4 years	≥ 20	≤ 19
Risk	Exacerbation requiring oral systemic steroids	0-1 x/year	≥ 2/year
	Progressive loss of lung function	Evaluation requires long-term follow-up and is best assessed by spirometry conducted at regular intervals (at least every 1-2 years)	
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk	
Action for Treatment		Maintain current therapy step Follow up every 1-6 months Consider step down	Step up therapy; Reevaluate in 2-6 weeks - Consider a 5 to 10-day course of oral steroids if acute exacerbation and reevaluate in 1-2 weeks - If persistently uncontrolled or worsening, consider referral to specialist

Modified from the NHLBI (2007) and GINA (2007) guidelines

Annotation C-2 Adjust/Decrease Medication as Indicated

6.2 Adjustment of Treatment

BACKGROUND

With routine monitoring, proper adjustments can be made to a patient's asthma treatment plan. The goal is to 'step up' or 'step down' therapy based on the interim symptoms and current control of asthma. When it appears that the patient has optimal control of his/her asthma through routine monitoring, he/she may be able to 'step down' the medical management. Conversely, if it appears the patient is more symptomatic during reassessment, he/she may need to 'step up' asthma therapy in order to help control the asthma. Whenever there is any change made to a patient's asthma therapy, closer follow-up should be implemented to assure the asthma remains under control.

ACTION STATEMENT

Adjust treatment using a step-wise approach to maximize asthma control.

RECOMMENDATIONS

1. Ongoing monitoring is essential to maintain control of asthma. Patients should be monitored at 2-6 week intervals after initial evaluation and treatment to re-evaluate their response and current symptoms.
2. Regular follow-up contacts at 1 to 6-month intervals, depending on level of control, are recommended to ensure that control is maintained. A closer follow-up and objective measurement of airway obstruction should be obtained whenever the patient's asthma medication regimen is changed.
3. When adjusting medications: (see [Table 7](#))
 - a. If asthma is not controlled on current regimen, a 'step up' in therapy is indicated, after assuring that the patient has good adherence and technique with the medication
 - b. If asthma is partially controlled, the provider should consider 'stepping up' the patient's medication until control is achieved
 - c. If the patient is able to maintain control of asthma symptoms for at least 3-6 months on their medicine regimen, a 'step down' or decrease in their asthma control medication may be considered.

Table 7. Step Care for Medications Required to Maintain Long-Term Control

Initial Severity	Use of Quick relief ^[b]	Activity limits	Symptoms		FEV1	Daily Medications ^[a]	
			Day	Night		Preferred	Alternative
Step 1 Intermittent	< 2 days/week	NONE	< 2 days/week	≤ 2x/month	> 80%	SABA PRN	--
Step 2 Mild	> 2 days/week not daily	Minor limitation	> 2 days/week not daily ^[c]	> 2x/month	> 80%	Low-dose ICS	--
Step 3 Moderate	Not more than once a day	Minor limitation	> 2 days/week not daily ^[c]	> 1x/week not nightly	60-80%	Age 0-4: Medium-dose ICS or Low-dose ICS +LTRA	--
						Age ≥ 5 to Adult: Low-dose ICS + LABA or Medium-dose ICS	Low-dose ICS + LTRA
Step 4 Severe	Daily	Some limitations	Daily ^[c]	Nightly	< 60%	Age 0-4: Medium-dose ICS + LTRA	Consider referral to specialist
						Age ≥ 5 to Adult: Medium-dose ICS + LABA	Medium-dose ICS + LTRA
Step 5 Severe	Several times a day	Extremely limited	Throughout the day ^[c]	Nightly	< 60%	Age 0-4: Medium-dose ICS + LABA + LTRA	Refer to specialist
						Age ≥ 5 to Adult: High-dose ICS + LABA Consider oral corticosteroids	Medium-dose ICS + LABA + LTRA Consider referral to specialist
Step 6 Severe	Several times a day	Extremely limited	Several times a day ^[c]	Nightly	< 60%	Age 0-4: High-dose ICS + LABA + LTRA (Consider 5-10 day course of oral corticosteroids)	Refer to specialist
						Age ≥ 5 to Adult: High-dose ICS + LABA + oral corticosteroids	High-dose ICS + LABA + LTRA Refer to specialist

[a] Every step: Patient education, environmental control, and management of co-morbidities.
 Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma.
 Steps 4-6: Consider referral to specialist for evaluation and/or management.
 Steps 5-6: Consider Omalizumab for patients with allergies and elevated IgE.

[b] Quick-relief medications for all patients:
 SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20 minute-intervals, as needed. Short course of oral systemic corticosteroids may be needed.

[c] More than 2 exacerbations per year (requiring oral systemic steroids) should prompt step up in therapy

The stepwise approach is meant to assist, not replace, the clinical decision-making required to meet individual patient needs.

Annotation C-3 Schedule Follow-up Visit**7. FOLLOW-UP OF PATIENT WITH STABLE ASTHMA***BACKGROUND*

Appropriate follow-up visits and management for stable asthma patients should be arranged. Care should be focused on preventive visits rather than waiting for symptoms to arise or asthma getting out of control. The follow-up visits should include assessment of control, adherence to treatment and reinforcement of self-management skills. Patient education and written Action Plans should be reviewed and updated. Close follow-up may minimize need for emergency department visits and/or admissions, preventing progressive loss of lung function, and providing optimal pharmacotherapy with minimal adverse effects.

ACTION STATEMENT

Schedule routine follow-up visits for evaluating asthma control and monitoring disease progression and response to treatment.

RECOMMENDATIONS

1. Stable asthma patients with persistent mild, moderate, or severe asthma should be seen for a visit every 6 months unless symptoms warrant sooner follow-up.
2. Stable asthma patients with persistent mild, moderate, or severe asthma should receive spirometry at initial evaluation, after treatment and stabilization, if they experience worsening of symptoms, and at least every 1-2 years.
3. Aspects of the follow-up visit should include:
 - a. An interim focused history, review of signs and symptoms, and physical exam
 - b. Obtaining history of acute exacerbations
 - c. Assessing the impact of co-morbid conditions affecting asthma control
 - d. Identifying new environmental triggers
 - e. Reviewing previous spirometry and peak flow monitoring
 - f. Assessing adherence to treatment, spacer use or MDI technique
 - g. Assessing indications for step-down or step-up therapy
 - h. Reviewing and updating patient education and written Action Plans
 - i. Preventive health maintenance, including smoking status of patients and family members
 - j. Scheduling the next follow-up visit.

Annotation C-4 Reassess Diagnosis, Consider Consultation or Referral**7.1 Indications for Consultation/Referral to Specialist***RECOMMENDATIONS*

1. Patients may benefit from referral for assistance in asthma management in the following circumstances:
 - a. Patient has had a life-threatening asthma exacerbation

- b. Patient is not meeting the goals of asthma therapy after 3–6 months of treatment. An earlier referral or consultation is appropriate if the primary care provider concludes that the patient is unresponsive to therapy
- c. Patient requires step 4 care or higher (step 3 for children 0–4 years of age). Consider referral if patient requires step 3 care (step 2 for children 0–4 years of age)
- d. Patient required more than two bursts of oral corticosteroids in 1 year or had an exacerbation requiring hospitalization
- e. Other conditions complicate asthma or its diagnosis (e.g., recurrent sinusitis, nasal polyps, aspergillosis, severe rhinitis, VCD, GERD, COPD) that do not respond to appropriate management
- f. Additional diagnostic testing is indicated (e.g., allergy skin testing, rhinoscopy, complete pulmonary function studies, bronchoscopy)
- g. Patient is being considered for immunotherapy or specialized medication such as omalizumab
- h. Patient requires additional education and guidance on complications of therapy, problems with adherence, or allergen avoidance (Asthma Educator)
- i. Patient / parent requests consultation with a subspecialist.

INTERVENTIONS

8. PHARMACOTHERAPY

8.1 Step Care Approach

BACKGROUND

While there are differences in the implementation of step care in children and adults, the basic principles are similar. The goal of asthma therapy is to maintain long-term control of asthma with the least amount of medication and minimal risk for adverse effects (NHLBI, 2007).

To achieve and maintain control of asthma, a stepwise approach to therapy is recommended, in which the dose and number of medications and frequency of administration are increased as necessary and decreased when possible. Assessing both domains (impairment and risk) emphasizes the need to separately consider asthma's effects on quality of life and functional capacity on an ongoing basis (i.e., at present) and the risks asthma presents for adverse events in the future, such as exacerbations or progressive reduction in lung growth. These domains may respond differentially to treatment. For example, a large study of children with asthma revealed that 30 percent of the low-dose ICS treatment group, whose levels of impairment (symptoms, SABA use, lung function) improved, remained at risk for exacerbations requiring oral systemic corticosteroids (CAMP, 2000).

Deciding which step of care is appropriate for a patient depends on whether long-term control therapy is being initiated for the first time or whether therapy is being adjusted. The classification of asthma severity, which considers the severity of both impairment and risk domains, provides a guide for initiating therapy for patients who are not currently taking long-term control medications. Once therapy is initiated, or if the patient is already taking long-term control medication, the patient's response to therapy will guide decisions about adjusting therapy based on the level of control achieved in both the impairment and risk domains. Therapy may be stepped up to regain control, or stepped down for patients who have maintained control for a sufficient length of time, to determine the minimal amount of medication required to maintain control and/or reduce the risk of side effects.

As indicated, a key to implementing step care involves assessing asthma control. Implementation involves assessing severity and monitoring response to therapy with appropriate follow-up. Determining the severity in response to treatment can be accomplished by assessment of the number of recent exacerbations, frequency of use of rescue medication, impairment of daily activities, nighttime symptoms, and pulmonary function levels. In children, this may mean questioning the child's parents. Another monitoring activity involves determining the patient's acceptance and adherence to the medication regimen and the avoidance of asthma triggers such as exposure to plants, pets, or cigarette smoke.

ACTION STATEMENT

Use the step-up and step-down approaches to initiate and adjust pharmacotherapy for the treatment of intermittent and persistent asthma (see [Table 7: Step Care for Medications Required to Maintain Long-Term Control](#)).

RECOMMENDATIONS

1. Always prescribe an inhaled short-acting bronchodilator for use as needed for intermittent symptoms.
2. Always prescribe an anti-inflammatory controller medication for use in persistent asthma.
3. Inhaled corticosteroids are the preferred anti-inflammatory controller.

4. Alternative anti-inflammatory controllers include anti-leukotriene, and cromolyn sodium medications.
5. Consider prescribing a long-acting bronchodilator controller medication for use in persistent asthma in addition to an anti-inflammatory controller.
6. The preferred long-acting bronchodilator controller is an inhaled long-acting beta2-agonist.
7. Alternative controller medications include oral theophylline, oral beta2-agonists, and anti-IgE antibody injections.
8. The dosage of inhaled corticosteroids and added use of combination controller therapy is determined by the degree of initial and ongoing impairment and risk.
9. Step-care includes both stepping up and stepping down the dosage and use of combination controller therapy. Stepping down therapy may be considered after a minimum period of stability (3-6 months).

8.2. Medication

8.2.1 Quick Relief

Short Acting β 2-adrenergic Agonists (SABAs) are bronchodilators that relax smooth muscle and are the treatment of choice for relief of acute symptoms, exacerbations of asthma, and prevention of EIB. SABAs should only be used on an as-needed basis at the lowest dose and frequency required. Increasing use of SABA treatment or the use of SABA >2 days a week for symptom relief (not prevention of EIB) indicates inadequate asthma control and the need for initiating or intensifying anti-inflammatory therapy. Equally, failure to achieve a quick and sustained response during an exacerbation mandates medical attention. Regularly scheduled, daily, chronic use of SABA is not recommended.

RECOMMENDATIONS

1. All patients should have a SABA as needed for acute relief of symptoms. [A]
2. SABAs should not be used on a scheduled basis for maintenance therapy.
3. Providers should evaluate frequency of SABA use. Use of SABA more than 2 days/week for symptom control, increasing use, or lack of expected response may indicate inadequate asthma control and the need to intensify maintenance drug therapy.
4. Clinical efficacy and safety are comparable between racemic and non-racemic agents; therefore, the least costly agent may be selected.

8.2.2 Long-term Controllers

Inhaled Corticosteroids

Inhaled Corticosteroids (ICS) reduce airway hyperresponsiveness, inhibit inflammatory cell migration and activation, and block late-phase reaction to an allergen. ICS do not appear to alter progression or underlying severity of asthma but do reduce impairment and risk of exacerbations. Currently, ICS are the most effective anti-inflammatory medications for long-term control of persistent asthma across all age groups and in all the therapy care steps.

RECOMMENDATIONS

1. ICS should be used as first-line therapy to control persistent asthma. [A]
2. ICS initial dosing should be based on the asthma severity.

3. ICS should be integrated into a step care approach. [A]
4. ICS treatment should be monitored for adverse effects and the patient/parent should be counseled regarding management adverse effects.
5. ICS delivery via nebulization should be administered using specific nebulizer equipment.

Long Acting β 2-adrenergic

Long Acting β 2-adrenergics (LABAs) do not have anti-inflammatory activity. LABAs are bronchodilators that act by increasing cyclic adenosine monophosphate in airway smooth muscle, thereby causing bronchodilation. A LABA is always used in combination with an anti-inflammatory agent, preferably an inhaled corticosteroid, in maintenance treatment of asthma.

RECOMMENDATIONS (ADULTS)

1. LABAs are not recommended for treatment of acute symptoms or exacerbations. [I]
2. LABAs must NOT to be used as monotherapy for maintenance treatment of asthma. [D]
3. LABAs are the preferred agents for add-on therapy to ICS. [A]
4. LABAs should be integrated into a step care approach: [A]
 - a. For patients who are not adequately controlled on low-dose ICS, consider increasing the dose of ICS or adding a LABA. Strong preference should be given to increasing the dose of inhaled corticosteroid due to safety concerns, while recognizing that efficacy is greater with the addition of a LABA.
 - b. For patients who are not adequately controlled on moderate/high-dose ICS, the addition of a LABA is preferred to further increasing the ICS dose.
 - c. Combining a LABA + ICS is preferred to combining a LABA + leukotriene receptor antagonist (LTRA) for greater efficacy.
5. Patient/parent counseling and monitoring for LABA adverse effects should be performed.

Leukotriene Modifiers

Leukotriene Modifiers interferes with the pathway of leukotriene mediators released from mast cells, eosinophils, and basophils. Leukotriene modifiers have a small and variable bronchodilator effect and reduce airway inflammation. These drugs can be further classified as leukotriene receptor antagonists (LTRA) (montelukast, zafirlukast) and 5-lipoxygenase inhibitors (zileuton). In children with allergies, there may be some benefit for the use of Leukotriene.

RECOMMENDATIONS

1. Monotherapy with leukotriene modifiers may be considered as an alternative (not preferred) to ICS for mild persistent asthma. [A]
2. Leukotriene modifiers may be used as an alternative (not preferred) to LABA for add-on therapy to ICS. [A]
3. Zileuton is NOT recommended for use in children < 12 years of age, and is discouraged from use in adults due to safety concerns (liver toxicity). [D]
4. Leukotriene modifiers should be integrated into a step care approach. [B]

Cromolyn sodium

Cromolyn sodium stabilizes mast cells and interferes with chloride channel function. Its anti-inflammatory effect is weak and considered less effective than low-dose ICS. Mast cell stabilizers for the long-term

treatment of asthma are considered as an alternative medication (not preferred) for mild persistent asthma (step 2). It can be used before unavoidable exposure to known allergens or as preventative treatment before exercise. Cromolyn is no longer available in a metered-dose inhaler; however, it remains available as a solution for nebulizer use.

RECOMMENDATIONS

1. Cromolyn may be considered as an alternative for mild persistent asthma when other preferred options have not been successful. [A]
2. Consult a specialist if the use of cromolyn is being considered. [I]

Xanthine

Xanthine derivatives are mild to moderate bronchodilators and may have mild anti-inflammatory effects. Patient-specific variables should be reviewed due to potential toxicity and significant interactions with other drugs. When reference is made to theophylline, it is to the long-acting/slow-release formulations, unless otherwise stated.

RECOMMENDATIONS

1. Theophylline may be considered as an alternative for maintenance of mild persistent asthma when other preferred options have not been successful. Consult a specialist if maintenance therapy with theophylline is being considered.
2. Theophylline may be considered as an adjunctive therapy with ICS for maintenance of moderate or persistent asthma.
3. Patients on theophylline should be maintained at a serum level of 5-15 mcg/ml with routine monitoring of serum level.

Immunomodulators anti-IgE (Omalizumab)

Immunomodulators anti-IgE (Omalizumab) is a monoclonal antibody that prevents binding of IgE to high-affinity receptors on basophils and mast cells. Omalizumab may be used as adjunctive therapy for severe persistent asthma (step 5 or 6) in patients with sensitivity to a relevant allergen (e.g., dust mite, cockroach, cat, or dog). Anaphylaxis may occur, therefore clinicians administering omalizumab (prescribed by a specialist) should be prepared and equipped to identify and treat anaphylaxis (prescribed by a specialist).

RECOMMENDATIONS

1. Omalizumab may be considered, in consultation with a specialist, as adjunctive therapy for severe persistent asthma (step 5 or 6) in patients with sensitivity to relevant allergens. [I]

Oral Systemic Corticosteroids

Oral Systemic Corticosteroids reduce airway hyperresponsiveness, inhibit inflammatory cell migration and activation, and block late-phase reaction to allergen.

RECOMMENDATIONS

1. Consult a specialist if maintenance therapy with an oral corticosteroid is being considered.

8.2.3 Combination

BACKGROUND

Combination therapy is used to take advantage of the different mechanisms of action of each drug class. When single-agents do not provide adequate control, combining agents from different therapeutic classes may result in added efficacy.

RECOMMENDATIONS

1. Combination ICS with LABA is preferred over ICS and LTRA, or zileuton or theophylline for the treatment of moderate persistent asthma. [A]
2. Combination of low-dose ICS with LABA may be considered equivalent to medium dose ICS for the treatment of moderate persistent asthma. [C]
3. Combination of high-dose ICS with LABA is the preferred therapy for severe persistent asthma. [A]
4. Addition of LABA is preferred to further increasing the ICS dose for patients who are not adequately controlled on medium-dose ICS. [A]

8.3 Use of Devices (MDI without Chambers), Training Technique

BACKGROUND

Inhaled medications for the treatment of asthma are typically delivered through metered dose inhalers (MDIs), or air powered nebulizer units. The MDIs are used with or without valved holding chambers (VHC). The most effective delivery of inhaled medication via MDI is with a VHC. Use of a VHC should be the primary method of MDI delivery, especially for inhaled corticosteroids, in all patients. Optimal medication delivery is dependent upon the patient's ability at the time of treatment to physically coordinate and manipulate the delivery device, the ability to reproduce optimal delivery technique, and the availability of any additional required resources (i.e., electrical power). Additional considerations include the patient's attitude and compliance with the need to properly clean and maintain the selected device.

Regardless of the delivery device selected, detailed education on the use, care and maintenance of the delivery device is essential. The patient should demonstrate proper technique initially and with each follow-up visit to ensure proper (optimal) medication delivery.

The use of a VHC eliminates most physical coordination and manipulation issues associated with MDI-only therapy and can be carried easily by the patient. MDIs with VHC do not require filters, batteries, or access to electrical power. This delivery combination requires little cleaning and maintenance and is easily replaced. Studies show that when compared to nebulized medication delivery, the use of MDIs in conjunction with VHC demonstrated a reduced admission rate in pediatrics (over age 5) and no negative impact on adults (Castro et al., 2004, Cates et al., 2006). These same studies suggest that severity scores by patients improved when using the MDIs with VHC in both adults and pediatrics (Castro et al., 2004). MDIs with VHC are recommended as the primary delivery system for inhaled medications in the treatment of asthma (see Table 8: Comparison of Inhaler Devices).

ACTION STATEMENT

Metered Dose Inhalers (MDIs) in conjunction with Valved Holding Chambers (VHC) are recommended as the primary delivery system for inhaled medications in both pediatric and adult patients.

RECOMMENDATIONS

1. Metered Dose Inhalers with Valved Holding Chambers are as effective as nebulizer therapy for delivery of aerosolized medications (quick relief) in the adult and pediatric patient. [B]

Table 8. Comparison of Inhaler Devices

Device	Advantages	Disadvantages
Metered Dose Inhaler (MDI) Beta2–Agonists Corticosteroids Cromolyn Sodium Anticholinergics	<ul style="list-style-type: none"> • Portable – compact • Little or no preparation time • Short treatment time • High dose-to-dose reproducibility • No content contamination 	<ul style="list-style-type: none"> • Requires significant breath and actuation coordination • Physical dexterity for actuation required • Not all inhaled medications available in this form • Few with dose counters
Metered Dose Inhaler (MDI) with Valved Holding Chamber (VHC) See above	<ul style="list-style-type: none"> • Portable • Little or no preparation time • Short treatment time • High dose-to-dose reproducibility • Less pharyngeal deposition vs. MDI • Reduced coordination vs. MDI • No content contamination 	<ul style="list-style-type: none"> • Less compact vs. MDI only • Physical dexterity for actuation required • Not all inhaled medications available in this form • Few with dose counters
Dry Powder Inhaler (DPI) Beta2–Agonists Corticosteroids Anticholinergics	<ul style="list-style-type: none"> • Portable – compact • Little or no preparation time • Short treatment time • Breath actuated • Less patient coordination • Propellant not required • Most have dose counters 	<ul style="list-style-type: none"> • Requires 30-60 lpm inspiratory flow for optimal delivery • Some units require loading with each dose • Not all medications available in this form
Small Volume Jet Nebulizer Beta2–Agonists Corticosteroids Cromolyn Sodium Anticholinergics	<ul style="list-style-type: none"> • Patient coordination minimal • Effective with tidal breathing • Can be used with supplemental oxygen 	<ul style="list-style-type: none"> • Lengthy treatment time • Contamination possible • Device cleaning required • Pressurized gas source required • Limited portability • Not all medications available in this form • Device preparation required • Performance variability

Adapted from Dolovich et al., 2005

9. ENVIRONMENTAL CONTROL

9.1 Inhaled Allergens

BACKGROUND

There is an important association between inhaled allergens and asthma. The presence of IgE-mediated sensitization to inhaled allergens is a risk factor for the development of asthma. Furthermore, allergic sensitization and exposure to elevated levels of inhaled allergens have been linked to airway hyperreactivity and a variety of adverse asthma outcomes including fatal asthma. These links have been shown for indoor environmental allergens such as dust mites, animal dander, cockroaches and molds as well as outdoor allergens including grass, ragweed, and molds. As a result, the approach to every patient with asthma should include a thorough history to assess for associations between inhaled allergens and their asthma symptoms.

A thorough history and knowledge of specific sensitizations can be used to determine the relevant inhaled allergen exposures and serve as the foundation for patient education on triggers, avoidance, and possibly immunotherapy when indicated. The role of specific strategies for avoidance of indoor inhaled allergens is controversial.

Understanding potential triggers and associations of symptoms with inhaled allergen exposure can also serve an important role in patient selection for consideration of immunotherapy.

RECOMMENDATIONS

1. For all patients with asthma at any level of severity [B]:
 - a. Use the patient's medical history to identify allergen exposures that may trigger the patient's asthma
 - b. Use the patient's history to assess sensitivity to seasonal allergens
 - c. Educate the patient and consider measures to reduce exposure to the identified inhaled allergen(s).
2. For patients with persistent asthma and indoor-related symptoms, the investigation of the potential role of allergens should be considered [C]:
 - a. Allergy testing should be performed to reliably determine sensitivity to common inhaled allergens to which the patient is exposed (skin testing or serum-specific IgE [i.e., RAST] testing)
 - b. The patient's history should be used to assess the significance of positive allergen-specific IgE tests
 - c. Educate the patient and consider measures to reduce exposure to the identified allergens.
3. A comprehensive approach to inhaled allergen avoidance in sensitized patients should be employed rather than implementing a single specific environmental avoidance strategy or regimen. [C]
4. Consider allergen immunotherapy when there is clear evidence of a relationship between symptoms and exposure to an allergen to which the patient is sensitive. [B]

9.2 Inhaled Irritants

BACKGROUND

There are convincing links and concerning associations between a variety of environmental irritants and asthma. Understanding possible associations between asthma and the environmental tobacco smoke, particulate air pollution, nitrogen dioxide (NO₂), sulfur dioxide (SO₂), diesel exhaust, volatile organic compounds, formaldehyde, fumes from wood burning stoves and fireplaces, and gas appliances can be important in developing plans for avoidance and treatment of patients with asthma.

RECOMMENDATIONS

1. Patients who have asthma at any level of severity should: [C]
 - a. Avoid exposure to environmental tobacco smoke and other respiratory irritants, including smoke from wood-burning stoves and fireplaces and, if possible, substances with strong odors
 - b. Avoid exertion outdoors when levels of air pollution are high.
2. There is insufficient evidence to recommend any specific environmental strategies to prevent the development of asthma.

9.3 Occupational Exposure

BACKGROUND

Certain occupations may expose patients to inhaled allergens, inhaled irritants, or other unique substances that may contribute to or even be the proximate cause of their asthma. Early diagnosis and intervention can be important to reduce the risk of worsening or inducing a more persistent/permanent element to the patient's asthma. History to include exposures to allergens, irritants, chemicals, dusts and the links of the workplace with symptoms and/or objective measures of lung function can be crucial.

RECOMMENDATIONS

1. Patients who have asthma and are employed, particularly those who have new-onset disease, should be queried about possible occupational exposures that may include allergens, irritants, or other exposures. [C]
2. Specialist care management over a period of time, or to co-management with the primary care provider, should be considered when history suggests that an occupational or environmental inhalant or ingested substance is provoking or contributing to asthma. Treatment or intervention may be required in the work environment.

10. OTHER INTERVENTIONS

10.1 Smoking Cessation

BACKGROUND

Personal use of tobacco products and exposure to environmental tobacco smoke (ETS) is common in the United States and directly affects asthma management. Second-hand smoke exposure in all asthma patients is associated with increased asthma severity and poorer outcomes, including a decreased responsiveness to some asthma medications. Exposure to maternal smoking has been shown to be a risk factor for the development of asthma in infancy and childhood.

RECOMMENDATIONS

1. All patients should be asked about tobacco use and should have their tobacco use status documented on a regular basis. [A]
2. All providers should strongly advise every patient who smokes to quit. [A] (See the VA/DoD Clinical Practice Guideline for Tobacco Use.)
3. Asthma patients and their families and/or caregivers should be instructed to avoid ETS. [A]
4. All pregnant patients should be instructed not to smoke and to avoid exposure to ETS. [A]

10.2 Nutrition

BACKGROUND

A well-balanced diet that includes a variety of foods promotes general good health. In brief, most Americans need to consume diets with more fruits, vegetables, and whole grains, and eat less solid fats (saturated fat, transfat), salt, and added sugars. While food allergies are rarely an aggravating factor, some asthma patients are sensitive to sulfites in foods and are at higher risk for severe reactions to foods to which they are sensitized.

RECOMMENDATIONS

1. Advise patients who have asthma symptoms associated with consuming foods to which they are sensitized and/or foods high in sulfites (e.g., processed potatoes, shrimp, dried fruit, beer or wine) to avoid these products. [C]

10.3 Weight loss

BACKGROUND

Obesity has been associated with asthma persistence and severity in both children and adults, with a correlation between excess weight and selected inflammatory mediators that may negatively impact asthma control. Weight loss in adults can result in improved FEV1, reductions in exacerbations, and improved quality of life.

RECOMMENDATIONS

1. Advise patients with asthma who are overweight or obese that excess body weight may have negative effects on asthma control and that weight loss may be associated with improvement of symptoms. [B]
2. Encourage all patients with asthma to attain and maintain healthy body weight (see the VA/DoD Guidelines for Overweight and Obesity). [B]

10.4 Complementary and Alternative Medicine (Meditation, Acupuncture)

BACKGROUND

Increasing numbers of the U.S. population are exploring options in complementary and alternative medicine (CAM), which includes chiropractic therapy, acupuncture, meditation, breathing or relaxation techniques, hypnosis, homeopathy, herbal products and nutritional supplements. While some cultural beliefs and practices may be incorporated into evidence-based asthma management, patients and caregivers must be educated on the potential dangers associated with utilizing unproven therapies.

RECOMMENDATIONS

1. In the process of interviewing the patient and reconciling medications, query every patient for the use of complementary and alternative medicine (CAM). [I]
2. Discourage patients and caregivers from substituting alternative therapies for evidence-based conventional asthma management by providing evidence-based information. [D]
3. No quality evidence was found for supporting the use of CAM to improve asthma control or management.

11. SELF-MANAGEMENT/PATIENT EDUCATION

Providing limited asthma education to patients and families does not improve clinical outcomes. There is strong evidence that practice models incorporating comprehensive education on asthma self-management, including self-adjustment of medications in response to worsening symptoms, regular medical review and provision of a written action plan, significantly improve asthma control and quality of life.

11.1 Patient and Family Education (Self-Management)

BACKGROUND

Asthma self-management education is essential to provide patients and their caregivers with the skills necessary to control asthma, improve outcomes, and maintain a healthy lifestyle. Patient and family involvement is central to optimal asthma control and self-management education must be tailored to literacy levels and sensitive to diverse cultural beliefs and backgrounds. Asthma education is most effective when initiated at the time of diagnosis and reinforced at every encounter, and when it includes information on daily and acute management with self-adjustment of medications. By establishing joint treatment goals and demonstrating responsiveness to patient concerns, the primary care manager builds the foundation of a strong partnership in asthma management.

RECOMMENDATIONS

1. Assess patient and/or family for educational needs as well as for preferences and/or barriers to learning, which may include limited medical and/or English literacy, physical, developmental, emotional or psychological challenges as well as specific cultural and/or spiritual beliefs. [A]
2. Provide asthma self-management education at all points of care where health professionals interact with patients and their families. [A] Education may be effective at other points of care such as pharmacies, hospitals, schools, and emergency departments. [B]
3. Teach and review core asthma education and self-management concepts at every visit with return demonstration when appropriate. [B]
4. Encourage a varied diet that is consistent with the Dietary Guidelines for Americans. [B]
5. Encourage asthma patients to participate in regular exercise to maintain general health and improve pulmonary conditioning. [B]

Table 9. Core Education and Self-Management Concepts

Core Education and Self-Management Concepts
<ul style="list-style-type: none"> ○ Basic information about asthma (inflammation vs. bronchoconstriction, chronicity of disease, definition of good control) ○ Components and utility of a written asthma action plan, including recognition of worsening conditions along with actions to take at home (monitoring and medication adjustment) ○ Triggers, allergen avoidance, and environmental controls ○ School/daycare-specific instructions ○ Medications' mechanisms of action, roles in management, and possible side effects ○ Specific instructions for emergency situations ○ Delivery devices and their appropriate use emphasizing that MDI/HFA with spacer device is equally effective for administration of nebulized medication ○ Contact names and telephone numbers for professional support to answer questions about home management ○ Method of routine monitoring (symptoms and/or peak flow) ○ Appointment information for the next visit

11.2 Strategies to Deliver Patient and Family Education

BACKGROUND

Effective patient and/or caregiver education can be accomplished using a variety of instructional methods. Comprehensive disease management programs may rely on interdisciplinary teams for patient education and include physicians, physician assistants, nurse practitioners, nurses, respiratory therapists, pharmacists, and asthma educators. Many patients and families may benefit from the myriad of easily accessible emerging technologies that include audiovisual materials and internet-based programs.

RECOMMENDATIONS

1. Utilize a variety of educational strategies to include frequent appointments with asthma educators, individualized case management, and/or patient age-appropriate standard curriculums. [B]
2. Consider utilizing interactive, multi-media resources in providing asthma education. [B]
3. Consider providing information on web-based comprehensive education sites that may include journaling, bulletin boards, support systems, electronic symptom questionnaires, and/or quality of life surveys to track and reinforce patient self-monitoring and management skills. [B]

11.3 Optimal Self-Management Tools (Use of Symptom or Peak Flow and/or Symptom-Based Action Plans)

BACKGROUND

Programs providing limited asthma education (transfer of information only without self-management techniques/written action plans) have not had positive effects on clinical outcomes with the exception of some possible benefit in the emergency department. Since all individuals diagnosed with asthma are susceptible to asthma exacerbations, patients with asthma should know how to prevent and manage these episodes. Optimal self-management includes self-monitoring (symptoms or symptoms and peak flow), regular medical review, and the provision of a written action plan. Previous guidelines emphasized the use of peak flow meters, but the most recent evidence shows that symptom-based plans are also effective. In patients with asthma, training programs that enable patients and/or caregivers to adjust medication using a written plan leads to improved health outcomes.

RECOMMENDATIONS

1. Ensure optimal self-management by providing education on self-monitoring, use of a written asthma action plan and regular medical review. [A]
2. Develop asthma action plans that include instructions for daily management and recognition of worsening conditions along with actions to take at home (monitoring and medication adjustment) based on symptoms or peak expiratory flow (PEF) measurements as appropriate. [A]

Table 10. Information Included in Written Asthma Action Plans

Personal Information and Daily Management	Worsening Symptoms and Actions to Take at Home
Patient name Provider/clinic name and contact number Personal best peak flow (when applicable) Monitoring method and frequency (symptoms or symptoms and peak flow) Description of optimal control (e.g., no coughing, wheezing, shortness of breath, chest tightness, interference with activities or sleep, peak flow > 80% of personal best) Trigger recognition, mitigation and/or avoidance (consider pollen count, air quality, etc.) Medications (quick relief, long-term controller, adjunctive therapies) Guidance on prophylactic medication prior to trigger exposure (exercise, environmental allergens or irritants)	Patient-specific asthma symptoms/peak flow values requiring action: <ul style="list-style-type: none"> - Acute asthma symptoms (e.g., cough, wheeze, shortness of breath, chest tightness, etc.) - Daytime symptoms > 2 times/week - Nighttime awakenings > 2 times/month - Increased limitation of normal activity - Increased use of bronchodilator (> 2 times/week) - Peak flow value < 80% of personal best Initial response to increased symptoms <ul style="list-style-type: none"> - Stop the provoking activity/move away from trigger(s) - Evaluate symptom severity/peak flow value Appropriate use of quick-relief medication When to reassess effectiveness of treatment through symptoms/peak flow When and how to modify medication regimen (add and/or increase) How to continue self-monitoring How to identify a failure of home treatment if increased use of rescue medication is required until symptoms and peak flow stabilize When to call the healthcare provider for evaluation
What symptoms/peak flow values require emergency medical treatment: <ul style="list-style-type: none"> - Lack of response to quick-relief medication - Inability to talk in complete sentences - Extreme shortness of breath - Retractions, lips/fingernails are blue - Increased respiration rate - Peak flow < 50% of personal best 	
Directions for accessing emergency care (e.g., 911)	

12. ACUTE EXACERBATION

BACKGROUND

Exacerbations are characterized by decreases in expiratory airflow that should be documented and quantified by simple measurement of lung function (either spirometry, if readily available, or peak expiratory flow). Objective measures are a more reliable indicator of the severity of an exacerbation than reported symptoms. In general, milder exacerbations may be managed at home without requiring an office visit, whereas exacerbations that are more serious may require an office visit, referral to the emergency department, or a hospital admission. The most severe exacerbations require admission to the intensive care unit (ICU) for optimal monitoring and treatment. Although assessment and treatment of young children, especially infants, pose unique challenges, the management of asthma exacerbations in older children and adults is fairly similar.

12.1 Indication for Immediate Triage

BACKGROUND

Patients at high risk for asthma-related death should be managed with special attention. These patients should be advised to seek medical attention early during acute exacerbations. In general, primary care providers without expertise in asthma management should not attempt to manage these patients at home or in the office; they should instead be referred for treatment that is more intensive and monitoring in an emergency department. In the pediatric setting, infants seen by a primary care provider should also be referred immediately for acute management.

ACTION STATEMENT

Patients at high risk for hospitalization or complications related to an asthma exacerbation should be referred to the nearest emergency department for management.

RECOMMENDATIONS

1. Patients are considered high risk for complications from an acute exacerbation in the following situations: [C]
 - a. Previous severe exacerbation (e.g., intubation or ICU admission for asthma)
 - b. Two or more hospitalizations or greater than three Emergency Department visits in the past year
 - c. Use of greater than two canisters of short-acting beta-agonist per month
 - d. Difficulty perceiving airway obstruction or the severity of worsening asthma
 - e. Recent use of oral glucocorticoids for exacerbation
 - f. Major psychosocial problems or psychiatric disease (including illicit drug use)
 - g. Co-morbidities such as cardiovascular disease or other chronic lung disease
 - h. History of non-compliance with asthma medication plan.
2. Patients in respiratory failure or at imminent risk of respiratory failure should be treated very aggressively and transported immediately to the emergency department. Treatment using nebulized bronchodilators (albuterol or levalbuterol) and/or systemic bronchodilators (subcutaneous epinephrine or terbutaline) should be initiated in the office setting pending transport.

12.2 Assessing Severity of Exacerbation

BACKGROUND

One of the essential steps in managing an acute exacerbation of asthma is to determine the severity of the exacerbation. There are several indicators based on history, physical examination, and objective measurements of lung function that may guide whether a patient can be effectively managed in a primary care setting or should be referred to a higher level of care. Likewise, severity may indicate how quickly a patient should be transferred for acute management.

ACTION STATEMENT

An overall assessment of the severity of an asthma exacerbation should guide the location (home, office, or hospital) and rapidity of treatment.

RECOMMENDATIONS

1. The severity of acute exacerbation should be determined by assessing specific characteristics of the symptoms, signs, and by objective measurement of SAO₂ and PaCO₂ (see [Table 11](#)).

Table 11. Classification of Acute Exacerbation: Severity and Treatment

Severity of Asthma Exacerbation				
	Mild	Moderate	Severe	Respiratory Arrest Imminent
SIGNS / SYMPTOMS				
<i>Activity Level:</i>	Walks briskly	Walks slowly	Walks with assistance	Unable to walk
<i>Feeding (infant):</i>	Normal	Difficulty feeding	Unable to feed	Unable to suck
<i>Talks in:</i>	Sentences	Phrases	Words	Too dyspneic to speak; perspiring
<i>Sounds (infant):</i>	Normal cry, cooing	Short, clipped cry	Faint cry, grunting	
<i>Alertness:</i>	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
<i>Respiratory rate:</i>	Increased	Increased	Often > 30/min	
	Normal rates of breathing in awake children: Age Normal rate < 2 months < 60/min 2-12 months < 50/min 1-5 years < 40/min 6-8 years < 30/min			
<i>Retractions & accessory muscle use:</i>	Usually not	Usually	Usually	Paradoxical thoraco-abdominal movement (see-saw breathing)
<i>Wheeze:</i>	Moderate, often only end expiratory	Loud expiratory	Usually loud, may be biphasic (inspiratory and expiratory)	Absence of wheeze
<i>Pulse/min. > 8 yrs:</i>	< 100	100-120	>120	Bradycardia
<i>Pulse/min. < 8 yrs:</i>	Guideline limits of normal pulse rate in children: Infants (2-12 months): < 160/min Preschool (1-2 years): < 120/min School age (2-8 years): < 110/min			
<i>Pulsus paradoxus:</i>	Absent < 10 mm Hg	May be present. 10-25 mm Hg	Often present > 25 mm Hg (adult) 20-40 mm Hg (child)	Absence suggests respiratory muscle fatigue
TESTS				
<i>SaO₂% (on room air)</i>	> 95%	91-95%	< 90%	
<i>PEF after initial bronchodilator treatment</i>	Over 80%	Approx. 60-80%	< 60% predicted	
<i>PaO₂ (on room air)</i>	Normal Test not usually necessary	> 60 mm Hg	< 60 mm Hg Possible cyanosis	Cyanosis
<i>PaCO₂</i>	< 45 mm Hg	< 45 mm Hg	> 45 mm Hg	>50 mm Hg
	Note: Hypercapnea (hypoventilation) develops more readily in young children than in adolescents and adults.			
INTERVENTION				
<i>Response to inhaled Short-Acting Bronchodilator (SABA)</i>	Prompt relief	Complete relief after multiple treatments	Partial relief after multiple treatments. Requires continuous inhaled SABA	Minimal or no relief from inhaled SABA. Requires systemic bronchodilator (subcutaneous epinephrine, terbutaline)
<i>Location of care</i>	Home Management	Office or emergency department	Emergency department; possible hospitalization	Hospitalization following stabilization in emergency department
*Note: The presence of several parameters, but not necessarily all, indicates the general classification of the exacerbation.				

12.3 Non-Urgent Management of Acute Exacerbations (Home or Office)

BACKGROUND

The general principles and goals for managing asthma exacerbations (AE) defined by the 2007 NHLBI asthma guidelines include early treatment of exacerbations, and identification of patients who are at high risk for asthma-related deaths, with special attention to infants. In those patients who are not at high-risk for hospitalization or death, beginning treatment at home avoids treatment delays, prevents exacerbations from becoming severe, and adds to patients' sense of control over their asthma. The degree of care provided in the home depends on the patient's (or parents') abilities and experience, and on the availability of emergency care.

ACTION STATEMENT

Patients with mild to moderate asthma and without significant risk factors may be able to manage their asthma exacerbation at home or during a routine office visit without requiring management in an urgent care or emergency department setting.

RECOMMENDATIONS

1. Early treatment of exacerbations is best; patients (or parents) should be able to recognize early indicators of an exacerbation to include cough and/or worsening peak expiratory flow.
2. All patients should be provided with – and instructed on how to use – a written asthma action plan that includes an individualized daily management plan and instructions on recognizing and handling worsening asthma. It should also include self-adjustment of medications in response to acute symptoms or changes in peak flow measures in the event of an exacerbation.
3. Initial adjustments in medication should include an increase in frequency of SABA. [B] [For mild - moderate AE up to 3 treatments within an hour (i.e., to 2-6 puffs per treatment); for severe AE 4-8 puffs and seek medical care.]
4. Addition of a short course of oral systemic corticosteroids may be considered for 4-7 days following frequent use of SABA. [A]
5. The dose of inhaled corticosteroids should NOT be doubled [D] and patients should contact their healthcare provider before instituting a course of oral systemic corticosteroids.
6. Patients should be advised to withdraw from any environmental allergens or irritants that may contribute to the exacerbation.
7. Response to treatment should be monitored and communicated to the provider to determine if an office visit or referral to the emergency department is warranted.

12.4. Management of Exacerbation in the Emergency Department

BACKGROUND

The emergency department is the best place for managing moderate to severe asthma exacerbations and for patients with a high-risk past medical history. Primary care physicians should notify the closest emergency department and arrange for patient ACLS transport. Once in the emergency department, patients will be cared for according to their asthma severity. Emergency department interventions for moderate exacerbations may include continuous or separate albuterol nebulized treatments, nebulized anticholinergics, and systemic steroids. Severe exacerbations may need magnesium, subcutaneous adrenergic agents or possibly full airway support. The majority of patients will be sent home on a 5-day course of oral steroids and

SABA. Following all emergency department visits, patients should be seen by their primary care physician within 1-2 days for outpatient evaluation and review of long-term asthma control medications.

RECOMMENDATIONS

1. A brief history and physical examination pertinent to the exacerbation should be conducted concurrently with the prompt initiation of therapy.
2. The history should include:
 - a. Severity and duration of symptoms, including exercise limitation and sleep disturbance
 - b. All current medications, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy
 - c. Time of onset and cause of the present exacerbation
 - d. Risk factors for asthma-related death.
3. The physical examination should assess exacerbation severity by evaluating pulse rate, respiratory rate, use of accessory muscles, the patient's ability to complete a sentence, and other signs.
4. Any complicating factors should be identified (e.g., pneumonia, atelectasis, pneumothorax, or pneumomediastinum).
5. Without unduly delaying treatment, a baseline PEF or FEV1 measurement should be made before treatment is initiated.
6. Subsequent measurements should be made at intervals until a clear response to treatment has occurred.
7. Oxygen saturation should be closely monitored, preferably by pulse oximetry. This is especially useful in children because objective measurements of lung function may be difficult. Oxygen saturation in children should normally be greater than 95%, and oxygen saturation less than 92% is a good predictor of the need for hospitalization [C].
8. A chest X-ray (CXR) is not routinely required unless there are signs of infection such as fever or cough productive of purulent sputum. A patient presenting for the first time with signs and symptoms of asthma may require a CXR to rule out other causes of airway hyperreactivity. Additionally, if the clinician suspects secondary complications such as pneumothorax based on history and physical examination, a CXR should be obtained.

12.5 Follow-up in Primary Care after Discharge from Emergency Department

BACKGROUND

Most patients who fail outpatient therapy after discharge from the emergency department will return to the emergency department or make an unscheduled clinic visit within 72 hours. Therefore, patients should be evaluated by the primary care provider or asthma specialist within 72 hours after emergency department treatment to assess for clinical and subjective improvement or deterioration.

RECOMMENDATIONS

1. Patients discharged from the emergency department should contact the primary care provider within 1-2 days and schedule a follow-up visit as considered appropriate by the provider.
2. An acute exacerbation episode may indicate a lack of control of the patient's chronic asthma. A step-up adjustment of the patient's routine care and/or a consultation with a specialist may be considered.

13. EXERCISE-INDUCED BRONCHOSPASM

BACKGROUND

Exercise-induced bronchospasm (EIB), commonly referred in the medical literature as exercise-induced asthma or exercise-induced bronchoconstriction, can be diagnosed in two distinct groups of patients. The first group consists of those patients with established asthma who, during exercise, have a component of bronchospasm that limits their activities. It is reported to occur in up to 80% of patients with asthma and is usually a self-limited process that resolves with cessation of exercise (see Section 13.1: [EIB in the Patient with Asthma](#)).

There is a separate group of patients who do not have underlying asthma but may develop symptomatic bronchospasm with prolonged exercise. These patients are generally competitive athletes or active duty military who exercise on a regular basis. The evaluation of these patients always demonstrates normal resting spirometry but airway hyperreactivity with bronchoprovocation testing (see Section 13.2: [EIB in the Athlete](#)).

Annotation E-1 High Suspicion of Asthma or EIB?

13.1 EIB in the Patient with Asthma

BACKGROUND

Exercise-induced bronchospasm (EIB) should be anticipated in all asthma patients. It is frequently referred to as exercise-induced asthma in the medical literature. A history of cough, shortness of breath, chest pain or tightness, wheezing, or endurance problems during exercise suggests EIB in the patient with asthma. An exercise challenge (in which there is a 15 percent decrease in PEF or FEV₁) can help establish the diagnosis. An important dimension of adequate asthma control is a patient's ability to participate in any activity he or she chooses without experiencing asthma symptoms. EIB should not limit either participation or success in vigorous activities.

ACTION STATEMENT

Consider the diagnosis of exercise-induced bronchospasm (EIB) in the patient with asthma who has significant symptoms associated with exercise. Optimal treatment for such a patient may consist of an increase in long-term controller medications or prophylactic beta-agonist use prior to exercise.

RECOMMENDATIONS

1. All patients with asthma should have a regular exercise program and be asked about any limitations to exercise.
2. Bronchoprovocation testing (exercise spirometry) should be considered if the patient notes increased symptoms suggestive of EIB during or immediately following exercise. [C]
3. Primary treatment is a warm-up period prior to exercise and pretreatment with short-acting beta-agonists is recommended. [A]
4. Alternative treatments include LTRAs, which can attenuate EIB in up to 50 percent of patients. [C]
5. Cromolyn sodium or nedocromil taken shortly before exercise is an alternative treatment, but it is not as effective as SABAs. [C]
6. Consideration for increasing controller medications may be indicated to control or alleviate increased asthma symptoms during exercise.

Annotation E-2 Consider Bronchoprovocation Testing

13.2 EIB in the Athlete

BACKGROUND

Exercise-induced bronchospasm (EIB) in the athlete is a common pulmonary disease diagnosed primarily in competitive athletes at all levels. EIB may also be common in the active duty military population given the nature of their duties and requirements for aerobic conditioning. These patients are defined in the following manner: 1) symptoms (dyspnea, cough, wheezing, or chest tightness) only associated with exercise with no other resting or nocturnal symptoms; 2) normal resting baseline spirometry and examination; 3) nonspecific airway hyperreactivity with bronchoprovocation testing; and 4) response to treatment. Optimal treatment for these patients has not been well delineated. Treatment usually consists of prophylactic beta-agonist use prior to exercise. There is little indication for controller medications as the pathophysiology is strikingly different from asthma and resolves spontaneously after cessation of exercise.

ACTION STATEMENT

In competitive athletes and active duty military with symptoms of exertional dyspnea and a normal baseline spirometry, the diagnosis of exercise-induced bronchospasm (EIB) should be actively pursued.

RECOMMENDATIONS

1. The patient's history should focus on the correlation of symptoms (dyspnea, wheezing, cough, or chest tightness) with exertion during or immediately after prolonged exercise such as running.
2. Normal baseline resting spirometry (no evidence of obstruction or restriction with a normal flow volume loop) should prompt referral for bronchoprovocation testing.
3. The preferred method for bronchoprovocation testing is histamine and methacholine challenge testing or eucapnic hyperventilation as other methods are less sensitive for detecting airway hyperreactivity.

13.3 Bronchoprovocation Testing

BACKGROUND

Bronchoprovocation testing is a useful adjunct in establishing the presence or absence of airway hyperreactivity in patients being evaluated for asthma or exercise-induced bronchospasm (EIB). Indications for testing include patients with asthma symptoms with normal spirometry who are suspected of having mild asthma or EIB. There are numerous methods established to include methacholine, histamine, cold air, eucapnic hyperventilation, and exercise challenge. The indications for using each specific type of bronchoprovocation test depend on the availability of equipment and clinical indication.

ACTION STATEMENT

Bronchoprovocation testing should be considered for patients with symptoms suggestive of asthma with normal spirometry, or for establishing the diagnosis of exercise-induced bronchospasm in patients with asthma who exhibit exertional symptoms.

RECOMMENDATIONS

1. Methacholine or histamine challenge testing is indicated to establish the presence of airway hyperreactivity in patients with exertional symptoms (cough, wheezing, dyspnea, chest tightness) and normal resting spirometry. [C]

2. Exercise challenge testing is indicated to establish the diagnosis of exercise-induced bronchospasm (or exercise-induced asthma) in known patients with asthma who exhibit exertional symptoms. [B]
3. Eucapnic hyperventilation or cold air testing are equivalent to methacholine or histamine challenge testing but should be used in laboratories experienced in these techniques. [B]

Annotation E-3 Manage Exercise-Induced Bronchospasm (EIB)

13.4. EIB Treatment

BACKGROUND

Optimal treatment for EIB patients has not been well delineated. Treatment usually consists of prophylactic beta-agonist use prior to exercise. There is little indication for controller medications as the pathophysiology is strikingly different from asthma and resolves spontaneously after cessation of exercise.

ACTION STATEMENT

EIB in the athlete should be treated prior to exercise to improve exercise tolerance and decrease post-exercise symptoms related to airway hyperreactivity.

RECOMMENDATIONS

1. The initial treatment regimen should consist of a warm-up period (gradual increase in exercise) and short-acting beta-agonist use 15-20 minutes prior to exercise. [C]

The use of LTRA or inhaled cromolyn prior to exercise may be considered. [C]

Lack of symptomatic improvement to inhaled beta-agonists or continued poor exercise tolerance should prompt referral for further evaluation by a specialist.

14. MILITARY (ACTIVE DUTY)-SPECIFIC ISSUES

RECOMMENDATIONS

Evaluation for possible asthma

1. Active duty service members should be diagnosed with asthma or exercise-induced bronchospasm on the basis of the following criteria:
 - a. Chronic symptoms of cough, dyspnea, or wheezing
 - b. Associated decrease in tolerance of exercise and/or running
 - c. Normal chest radiograph (should be obtained in all active duty patients)
 - d. Demonstration of persistent airway hyperreactivity
 - Baseline spirometry with reversible airflow obstruction post-bronchodilator
OR
 - Reactive bronchoprovocation testing or lower dose of methacholine (preferred method of bronchoprovocation testing).

See [Appendix C](#)- DoD Service-Specific Regulation Concerning Asthma.

Deployment issues

2. Guidelines for deploying or redeploying service members with asthma to/from a theater of operations:
 - a. In general, service members should be able to perform all required duties, wear protective gear, and have stable disease not requiring frequent treatments or oral corticosteroids
 - b. Failure to meet these criteria should prompt consideration for redeployment
 - c. See [Appendix C](#) – DoD Service-Specific Regulation Concerning Asthma
 - d. Army; AR 40-501, Section 5–14. Medical fitness standards for deployment and certain geographical areas:

“Asthma. See paragraph 3–27a for profile guidance and for MEB/PEB processing criteria. If it is determined that the Soldier can be returned to duty, the Soldier should not deploy if he/she cannot wear protective gear, has experienced recent emergency room visits, or requires repetitive use of oral corticosteroids.”
 - e. Navy, Air Force, Coast Guard – No specific regulatory guidance.

Appendix B-1

Details of a Comprehensive History

1. The history should focus on the characterization of symptoms related to airway obstruction or airway hyperresponsiveness:
 - Cough
 - Wheezing
 - Shortness of breath
 - Chest tightness
 - Sputum production.

2. The pattern of symptoms should be characterized:
 - Onset
 - Duration
 - Frequency
 - Diurnal variation
 - Seasonality.

3. Precipitating and aggravating factors should be explored:
 - Viral infections
 - Exercise
 - Environmental indoor allergens:
 - Mold
 - House dust mites
 - Cockroaches
 - Pets
 - Rodents
 - Environmental outdoor allergens:
 - Pollens
 - Molds
 - Secondary tobacco exposure
 - Occupational chemicals, irritants, or allergens
 - Irritants:
 - Strong odors
 - Air pollution
 - Chemicals
 - Dusts/particulates
 - Vapors, gases, and aerosols
 - Emotions and/or stress
 - Drugs (i.e., aspirin, NSAIDs)
 - Sulfites in food
 - Cold air
 - Characteristics of the home and/or office:
 - Carpeting
 - Wood burning stoves
 - Chemicals
 - Co-morbid conditions (sinusitis, rhinitis, GERD).

4. The development of disease and prior symptoms, diagnosis and treatment should be explored:
 - Age of onset and/or diagnosis
 - Early life airway injury such as BPD or pneumonia
 - Present or recent management
 - Frequency of SABA use and response
 - Requirement for oral steroids, frequency, and response.
5. Family history:
 - Asthma
 - Allergy
 - Rhinitis
 - Sinusitis
 - Nasal polyps
 - Eczema.
6. Social history:
 - Daycare, workplace, school characteristics
 - Social factors interfering with adherence such as substance abuse
 - Social support networks
 - Level of education
 - Employment.
7. History of prior exacerbations:
 - Prodrome
 - Rapidity of onset
 - Duration
 - Frequency
 - Severity (hospitalizations, ICU admissions, intubations)
 - Life-threatening exacerbations (intubation, ICU)
 - Number and severity of exacerbations in last 12 months
 - Usual pattern and management.
8. Impact of the disease on the patient and family:
 - Unscheduled care (Emergency Department, urgent care, hospitalization)
 - Missed school days
 - Limitations in activity including work, sports, and play
 - Nocturnal awakenings
 - Effect on growth, development, behavior
 - Economic impact.
9. The history should include an assessment of the patient's and family's perceptions of disease:
 - Patient's, parent's, spouse's, partner's knowledge of and belief in disease and treatment
 - Ability of patient and family/support system to cope with disease
 - Level of support
 - Economic resources
 - Sociocultural beliefs.

Appendix B-2

Details of a Comprehensive Physical Exam

Physical examination of the upper respiratory tract, neck, chest, heart and skin may support the diagnosis of asthma. However, the absence of supportive findings does not exclude the diagnosis of asthma.

() May suggest an alternative diagnosis or co-morbid condition.*

1. Vital signs	Hypertension* Increased Body Mass Index*
2. Eyes	Erythema of the conjunctive
3. Nasopharynx	Increased nasal secretions Mucosal swelling Nasal polyps
4. Oropharynx	Enlarged tonsils* Cobblestoning of the posterior pharynx Evidence of upper airway obstruction*
5. Ears	Evidence of otitis media in children
6. Neck	Adenopathy or mass* Increased intravenous pyelogram (IVP)* Stridor*
7. Chest	Wheezing at rest Prolonged phase of forced exhalation Hyperexpansion of the thorax Use of accessory muscles Chest deformity Crackles* Dullness to percussion*
8. Heart	Rate Rhythm Presence of murmurs Presence of gallops
9. Abdomen	Organomegaly*
10. Skin	Presence of atopic dermatitis
11. Extremities	Edema* Clubbing* Pulses*

Physical Findings in Review of Systems

Physical Findings	Asthma	Co-morbid Conditions	Alternative diagnosis
Eyes		Conjunctivitis	
Ears		Otitis media	
Oropharynx	Normal	Cobblestoning	Evidence of upper airway obstruction
Neck	Normal		Mass, stridor increased JVP
Chest	Wheeze, prolonged expiration		Crackles, dullness to percussion
Heart	Normal		Murmurs or gallops
Abdomen			Organomegaly mass or bruit
Skin	Atopic dermatitis		
Extremities			Edema, clubbing

Appendix C

DoD Service-Specific Regulation Concerning Asthma

PPG-TAB A: AMPLIFICATION OF THE MINIMAL STANDARDS OF FITNESS FOR DEPLOYMENT TO THE CENTCOM AOR; TO ACCOMPANY MOD 7 TO USCINCCENT INDIVIDUAL PROTECTION AND INDIVIDUAL/UNIT DEPLOYMENT POLICY

1. General. This tab accompanies MOD 7 Para 15.g., and provides amplification of the minimal standards of fitness for deployment to the CENTCOM AOR, including a list of medical conditions that should usually be sufficient basis to deny medical clearance for or to disapprove deployment of a civilian employee, volunteer, or contractor's employee. The list of conditions is not comprehensive; there are many more conditions that could be cause to deny medical clearance for deployment. Possession of one or more of the conditions listed in this chapter does not automatically mean that the individual may not deploy. Rather, it imposes the requirement to obtain a knowledgeable physician's opinion as to the deployable status of the individual. "Medical conditions" as used here also includes those health conditions usually referred to as dental, oral, psychological and/or emotional conditions. (Uniformed service members will be evaluated for fitness according to service regulations and policies, in addition to the guidance in the parent PPG Modification (MOD). The services' parent regulations are as follows.

- **Army: AR 40-501, Standards of Medical Fitness, February 2004;**
- **Air Force: AFI 48-123, 22 MAY 2001, Medical Examinations And Standards;**
- **Navy: NAVMED P-117, The Manual of the Medical Department;**
- **Marine Corps: NAVMED P-117, article 15-5;**
- **Coast Guard: Medical Manual, COMDTINST M6000.1B.)**

Deployment Issues

Documented medical conditions usually precluding medical clearance. While a list of all possible diagnoses and their severity that should not be approved would be too expansive to list here, the following conditions, in general, should usually not be approved. *The medical evaluator must carefully consider whether there is any question whether the climate, the altitude, the nature of available food and housing, the availability of medical, behavioral health, dental, and surgical services, or whether other environmental and operational factors may be hazardous to the deploying person's health because of a known physical condition.*

Usually, medical clearance to deploy for persons with any of the following documented medical conditions should be granted only after consultation with theater medical authority. The theater medical authority can determine if adequate treatment facilities and specialist support is available at the duty station.

A. Conditions resulting in inability to wear personal protective equipment, including protective mask, ballistic helmet, body armor, and chemical/biological protective garments, regardless of the nature of the condition that causes the inability.

Service-specific regulations regarding medical standards of fitness for asthma or other deployment issues are available on the asthma CPG homepage under resource material at:

<https://www.qmo.amedd.army.mil/asthma/Asthfr.htm>

Appendix D Medication Tables

Table D1: Drugs Used in Treatment of Asthma

Drug Class§	Uses	Cautions and Monitoring‡
<p><u>Inhaled Corticosteroids (ICS)</u></p> <p>Beclomethasone Budesonide Ciclesonide Flunisolide* Fluticasone Mometasone Triamcinolone*</p> <p>(See Table D2 for Dosage)</p> <p>*CFC MDIs are being phased out and will no longer be available in the near future</p>	<p>Considered first line agents for maintenance treatment of asthma</p>	<ul style="list-style-type: none"> • Local adverse effects include oral candidiasis, dysphonia, and reflex cough/bronchospasm <ul style="list-style-type: none"> ○ Use of a spacer or holding chamber (for non-breath activated inhalers) and rinsing mouth after inhalation can reduce the incidence of oral candidiasis ○ Use of a spacer or holding chamber (for non-breath activated inhalers) is used as a measure to prevent dysphonia. To treat dysphonia, temporarily reducing the dose of ICS, or rest for vocal stress has been used ○ Use of a spacer or holding chamber (for non-breath activated inhalers), slower inspiration, or pretreatment with a SABA may be tried for reflex cough/bronchospasm • Higher doses have been associated with adrenal suppression, glaucoma, cataracts, skin thinning, and bruising • High dose may increase the risk of developing osteoporosis • Smoking may decrease the effectiveness of ICS; regardless, patients with asthma should be encouraged to stop smoking
<p><u>Short-acting Beta-agonists (SABA)</u></p> <p>Albuterol Levalbuterol Pirbuterol</p> <p><u>Long-acting Beta-agonists (LABA)</u></p> <p>Formoterol Salmeterol</p> <p>Note: Formoterol and arformoterol are available in a nebulizer solution approved for maintenance therapy for COPD; at present, they are not approved for use in asthma.</p>	<p>Short-acting agents are used for acute relief of bronchospasm and prevention of exercise-induced bronchospasm</p> <p>Long-acting agents are used as the preferred add-on agents to inhaled corticosteroid</p>	<ul style="list-style-type: none"> • May cause palpitations, chest pain, rapid heart rate, increased blood pressure, tremor, nervousness • Decreases in potassium levels or hyperglycemia have occurred • Frequent use of SABA (>2 days/week) may indicate uncontrolled asthma and the need to intensify maintenance drug therapy • 2 to 6 puffs of SABA may be used in accordance with the asthma action plan. Patients who do not experience relief after 3 doses in a one hour period OR who need a dose more frequently than every 4 hours should seek medical care • Long-acting beta-agonists are CONTRAINDICATED AS MONOTHERAPY for maintenance treatment of asthma. If a long-acting beta-agonist is used, an inhaled steroid must also be prescribed and used by the patient on a daily basis • Long-acting beta-2 agonist are not to be used for the acute treatment of bronchospasm • Formoterol: Capsules are for oral inhalation only (capsules should not be swallowed). Administer using supplied inhalation device (Aerolizer) only

Drug Class§	Uses	Cautions and Monitoring†
<p><u>Combination ICS/LABA</u> Budesonide/formoterol Fluticasone/salmeterol</p>		<ul style="list-style-type: none"> • See comments for inhaled corticosteroids and beta-agonists
<p><u>Leukotriene Modifiers</u> Montelukast Zafirlukast Zileuton extended-release</p>	<p>Monotherapy may be considered as an alternative (not preferred) to ICS for mild persistent asthma</p> <p>May be used as an alternative (not preferred) to a LABA for add on therapy to ICS</p> <p>Montelukast may be used for prevention of exercise-induced bronchospasm (zafirlukast and zileuton are not FDA approved)</p>	<ul style="list-style-type: none"> • Rare cases of Churg-Strauss have occurred with montelukast and zafirlukast; however, the association is unclear • Zafirlukast should be taken at least 1 hour before or 2 hours after meals due to decreased bioavailability when taken with meals. • Zafirlukast and zileuton can inhibit the metabolism of warfarin. INRs should be monitored during co-administration • Zileuton can inhibit the metabolism of theophylline; therefore, monitoring of theophylline levels is recommended • Zileuton is contraindicated in patients with active liver disease or persistent hepatic function enzyme elevation (> 3x ULN) • Assess hepatic function enzymes prior to initiation of zileuton, monthly for the first 3 months, every 2-3 months for the remainder of the first year, and periodically thereafter • Postmarketing surveillance of zafirlukast has reported cases of reversible hepatitis and, rarely, irreversible hepatic failure resulting in death and liver transplantation. Consider periodic hepatic enzymes (ALT) monitoring • Patients and providers should be aware of the potential for neuropsychiatric events (e.g., suicidal ideation, depression, agitation, aggression, anxiousness, irritability, restlessness, dream abnormalities, hallucinations, and insomnia) with these medications. Patients should be told to contact their healthcare provider if these events occur. Consider discontinuing these medications if patients develop neuropsychiatric symptoms
<p><u>Mast cell stabilizer</u> Cromolyn Nebulizer solution</p> <p>Note: Cromolyn is no longer available as a MDI</p>	<p>Monotherapy may be considered as an alternative (not preferred) to ICS for mild persistent asthma.</p> <p>May be used for prevention of exercise-induced bronchospasm; however, generally not as effective as SABA</p>	<ul style="list-style-type: none"> • Generally well tolerated although may cause coughing and wheezing • Improvement can occur in 1-2 weeks; however, maximal benefit may not be seen for 4-6 weeks • Needs to be dosed four times daily (may be reduced to three times daily once symptoms have stabilized) • Cromolyn is no longer available as a MDI; therefore, limiting the usefulness of this agent

Drug Class§	Uses	Cautions and Monitoring‡
<p><u>Methylxanthines</u></p> <p>Theophylline</p> <p>Aminophylline</p>	<p>May be considered as an alternative for maintenance of mild persistent asthma when other preferred options have not been successful</p> <p>May be considered as an adjunctive therapy with ICS for maintenance of moderate or persistent asthma.</p>	<ul style="list-style-type: none"> • Monitor theophylline levels. The usual therapeutic range is 5-15mcg/mL but some toxicity may be noted at the upper end of this range. • Adverse reactions include stomach upset, nausea, insomnia, tremors, palpitations, and irritability which may be lessened by initiating the dose low and increasing gradually • Serious adverse events including cardiac arrhythmias and seizures can occur at higher concentrations • Instruct patient not to take extra doses of theophylline for acute asthma attack. • Sustained-release products should not be crushed or chewed. • Scored tablets may be split without affecting absorption characteristics • Several drugs or other factors can influence theophylline concentration (list not intended to be inclusive of all interactions) <ul style="list-style-type: none"> ○ Drugs or factors decreasing theophylline clearance: cimetidine, ciprofloxacin, clarithromycin, disulfiram, enoxacin, erythromycin, mexiletine, pentoxifylline, propranolol, ticlopidine, troleandomycin, zileuton, allopurinol (≥ 600 mg/day), fluvoxamine, interferon, propafenone, tacrine, verapamil, congestive heart failure, cor pulmonale, elderly (> 60 yrs.), hepatic insufficiency (cirrhosis, acute hepatitis, cholestasis), fever (> 24 hrs.) ○ Drugs or factors increasing theophylline clearance: charcoal-broiled food; low carbohydrate, high protein diet; smoking (tobacco or marijuana); phenobarbital; phenytoin; rifampin, carbamazepine; isoniazid; moricizine
<p><u>Immunomodulators anti-IgE</u></p> <p>Omalizumab</p>	<p>Used as adjunctive therapy for severe persistent asthma (Step 5 or 6) who have a positive skin test or <i>in vitro</i> reactivity to a perennial aeroallergen</p>	<ul style="list-style-type: none"> • Not to be used in patients who have had a prior allergic reaction to omalizumab • Patient should have pre-treatment serum IgE 30-700IU/ml and positive skin test or <i>in vitro</i> reactivity to common aeroallergen (e.g., dust mites, pet dander, cockroach) • Give patient the omalizumab Medication Guide and instruct them to read it before each dose of omalizumab • Educate patient on signs and symptoms of severe hypersensitivity and anaphylaxis • Patients should carry and know how to initiate emergency self-treatment for anaphylaxis • Observe patients for an appropriate amount of time after each injection. In clinical trials, patients were observed for 2 hours after the 1st dose and 1 hour for subsequent doses. • Healthcare professionals should be prepared to manage life-threatening anaphylaxis • If a severe hypersensitivity reaction occurs, omalizumab should be discontinued

§ Refer to product package insert or other established resources for dosing recommendations and age specific use

‡ Table is not intended to be inclusive of all cautions and monitoring, but rather to highlight some of the major points

Table D2: Inhaled Steroids^{a,b}

Inhaled steroid (dose/puff)	Dosage forms	Usual dosing interval	Low dose mcg/day ^c	Medium dose mcg/day ^c	High dose mcg/day ^c	PC
Beclomethasone 40mcg 80mcg	MDI (HFA)	12h	≥12 yrs 80-240 5-11yrs 80-160	≥12 yrs >240-480 5-11 yrs >160-320	≥12 yrs >480 5-11yrs >320	C
Budesonide 200mcg (delivered dose 160mcg) 90mcg (delivered dose 80mcg) 180mcg (delivered dose 160mcg) Budesonide suspension 0.25, 0.5, 1mg/2mL ampule Must use with PARI nebulizer or other high-efficiency nebulizer	DPI Nebulizer	12h 24h or 12h	≥12 yrs 200-600 5-11 yrs 180-400 5-11 yrs 0.5 0-4 yrs 0.25-0.5	≥12 yrs >600-1200 5-11 yrs >400-800 5-11 yrs 1.0 0-4 yrs >0.5-1.0	≥12 yrs >1200 5-11 yrs >800 5-11 yrs 2.0 0-4 yrs >1.0	B
Ciclesonide 80mcg 160mcg	MDI (HFA)	24h	≥12 yrs 80-160	≥12 yrs >160-320	≥12 yrs >320-1280	C
Flunisolide ^e 250mcg	MDI (CFC)	12h	≥12 yrs 500-1000 5-11 yrs 500-750	≥12 yrs >1000-2000 5-11 yrs >750-1250	≥12 yrs >2000 5-11 yrs >1250	C
Fluticasone (MDI/DPI) 44mcg /50mcg 110mcg /100mcg 220mcg/250mcg	MDI (HFA) DPI	12h	≥12 yrs 88-264 0-11 yrs 88-176	≥12 yrs >264-440 0-11 yrs >176-352	≥12 yrs >440 0-11 yrs >352	C
Mometasone 220mcg (delivered dose 200mcg) 110mcg (delivered dose 110mcg) ^d	DPI	24h or 12h	≥12 yrs 200	≥12 yrs 400	≥12 yrs >400	C
Triamcinolone ^e 100mcg (delivered dose 75mcg)	MDI with built-in spacer (CFC)	6-8h or 12h	≥12 yrs 300-750 5-11 yrs 300-600	≥12 yrs >750-1500 5-11 yrs >600-900	≥12 yrs >1500 5-11 yrs >900	C

PC = Pregnancy Category

^a Comparative daily doses adapted from the Global Initiative for Asthma 2007 and NHLBI Guidelines for the Diagnosis and Management of Asthma (EPR-3).^b For dosing recommendations, refer to the manufacturer's product package insert.^c Doses for budesonide suspension shown in mg.^d Dose of mometasone for children is 110mcg once daily.^e CFC MDIs are being phased out and will no longer be available in the near future.

Appendix E Environmental Control

House Dust Mite Allergen

The EPR-3 Panel recommends the following mite-control measures. Effective allergen avoidance requires a multifaceted approach:

- Recommended actions to control mites include:
 - Encase the mattress in an allergen-impermeable cover.
 - Encase the pillow in an allergen-impermeable cover or wash it weekly.
 - Wash the sheets and blankets on the patient's bed weekly in hot water.
 - A temperature of >130 °F is necessary for killing house dust mites. Prolonged exposure to dry heat or freezing temperatures can also kill mites but does not remove allergen. If high-temperature water is not available, a considerable reduction in live mites and mite allergens can still be achieved with cooler water using detergent and bleach.
- Actions to consider to control mites include:
 - Reduce indoor humidity to 60 percent or below, ideally between 30 and 50 percent.
 - Remove carpets from the bedroom.
 - Avoid sleeping or lying on upholstered furniture.
 - Remove from the home carpets that are laid on concrete.
 - In children's beds, minimize the number of stuffed toys, and wash them weekly.

Animal Allergens

The EPR-3 Panel recommends the following actions to control animal antigens:

- If the patient is sensitive to an animal, the treatment of choice is removal of the exposure from the home.
- If removal of the animal is not acceptable:
 - Keep the pet out of the patient's bedroom.
 - Keep the patient's bedroom door closed.
 - Remove upholstered furniture and carpets from the home, or isolate the pet from these items to the extent possible.
 - Mouse allergen exposure can be reduced by a combination of blocking access, low-toxicity pesticides, traps, and vacuuming and cleaning.

Cockroach Allergen

The EPR-3 Panel recommends that cockroach control measures be instituted if the patient is sensitive to cockroaches and infestation is present in the home:

- Patients should not leave food or garbage exposed.

- Poison baits, boric acid, and traps are preferred to other chemical agents, because the latter can be irritating when inhaled by persons who have asthma.
 - If volatile chemical agents are used, the home should be well-ventilated, and the person who has asthma should not return to the home until the odor has dissipated.
 - Care should be taken so that young children do not have access to cockroach baits and poisons.

Indoor Fungi (Molds)

The EPR-3 Panel recommends consideration of measures to control indoor mold:

- Measures to control dampness or fungal growth in the home may be beneficial.

Outdoor Allergens (Tree, Grass, and Weed Pollen; Seasonal Mold Spores)

The EPR-3 Panel recommends that measures be taken to reduce exposure to outdoor allergens if the patient is sensitive to outdoor allergens and has symptoms that correlate with exposure:

- Patients who are sensitive to seasonal outdoor allergens should consider staying indoors, if possible, during peak pollen times—particularly midday and afternoon.
- Patients can reduce exposure during peak pollen season by staying indoors with windows closed in an air-conditioned environment, particularly during the midday and afternoon when pollen and some spore counts are highest.
- Conducting outdoor activities shortly after sunrise will result in less exposure to pollen.
- These actions may not be realistic for some patients, especially children.

Appendix G Acronym List

ABG	Arterial Blood Gas
ABPA	Allergic Bronchopulmonary Aspergillosis
ACT	Asthma Control Test
ALT	Alanine Aminotransferase
ATS	American Thoracic Society
BNP	Brain Natriuretic Peptide
BPD	Bronchopulmonary Dysplasia
CAD	Coronary Artery Disease
CAM	Complementary and Alternative Medicine
CHF	Congestive Heart Failure
COPD	Chronic Obstructive Pulmonary Disease
CPAP	Continuous Positive Airway Pressure
CT	Computed Tomography
CXR	Chest X-Ray
DLCO	Carbon Monoxide Diffusing Capacity
DPI	Dry Powder Inhaler
ED	Emergency Department
EIB	Exercise-Induced Bronchospasm
ETS	Environmental Tobacco Smoke
FEV1	Forced Expiratory Volume in 1 Second
FVC	Forced Vital Capacity
GERD	Gastroesophageal Reflux Disease
ICS	Inhaled Corticoid Steroids
ICU	Intensive Care Unit
LABA	Long-Acting Beta Agonists
LTRA	Leukotriene Receptor Antagonist
MDI	Metered Dose Inhalers
NAEPP-3	National Asthma Education and Prevention Program Expert Panel Report 3
OSA	Obstructive Sleep Apnea
PEF	Peak Expiratory Flow
PFT	Pulmonary Function Test

PND	Post Nasal Drip
PPI	Proton Pump Inhibitor
SABA	Short-Acting Beta Agonists
SOB	Shortness of Breath
VCD	Vocal Cord Dysfunction
VHC	Valved Holding Chamber