Asthma: Diagnosis and Management

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
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Faculty

Sharon M. Griffin, RN, PhD, specializes in Health Education and Chronic Disease Management especially as it relates to her primary areas of study and research. She has more than 30 years of healthcare experience nationwide and is an accomplished author, presenter and consultant. She frequently lectures on the subjects of Attention Deficit/Hyperactivity Disorder (AD/HD), Obsessive-Compulsive Disorder (OCD) and related disorders. Dr. Griffin is the cofounder of the University Center for Assessment and Learning (UCAL) of Andrews University in Berrien Springs, Michigan. She enjoys writing and teaching and has been listed in Who's Who in American Nursing, Two Thousand Notable American Women, and the eleventh edition of the World Who's Who of Women, Cambridge, England.

Patricia Walters-Fischer, RN, BS, has worked in the healthcare field since 1992. Starting out as a nurse's aide, she worked her way from LVN to ASN while working in several hospital units, including ICU/CCU and adult and pediatric trauma. During her career, she worked at the busiest pediatric emergency center in the country, Children's Medical Center of Dallas Emergency Room. While there, she cared for and educated asthmatic children and their caregivers. Ms. Walters-Fischer is also an honors graduate of Washington University, St. Louis, with a Bachelor's Degree in Communications and Journalism and has been writing for the past ten years in local, national, and international publications.

Faculty Disclosure

Contributing faculty, Sharon M. Griffin, RN, PhD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Patricia Walters-Fischer, RN, BS, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planners

John M. Leonard, MD
Mary Franks, MSN, APRN, FNP-C
Randall L. Allen, PharmD

Senior Director of Development and Academic Affairs

Sarah Campbell

Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for nurses, physicians, physician assistants, pharmacists, and pharmacy technicians who may care for patients with asthma.

Accreditations & Approvals

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INTERPROFESSIONAL CONTINUING EDUCATION

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This program has been pre-approved by The Commission for Case Manager Certification to provide continuing education credit to CCM® board certified case managers. The course is approved for 10 CE contact hour(s). Activity Code: H00057468. Approval Number: 230003916.

Designations of Credit

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This activity has been approved for the American Board of Anesthesiology's® (ABA) requirements for Part II: Lifelong Learning and Self-Assessment of the American Board of Anesthesiology's (ABA) redesigned Maintenance of Certification in Anesthesiology Program® (MOCA®), known as MOCA 2.0®. Please consult the ABA website, www.theABA.org, for a list of all MOCA 2.0 requirements. Maintenance of Certification in Anesthesiology Program® and MOCA® are registered certification marks of the American Board of Anesthesiology®. MOCA 2.0® is a trademark of the American Board of Anesthesiology®.

Successful completion of this CME activity, which includes participation in the activity with individual assessments of the participant and feedback to the participant, enables the participant to earn 10 MOC points in the American Board of Pediatrics' (ABP) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABP MOC credit.

This activity has been designated for 10 Lifelong Learning (Part II) credits for the American Board of Pathology Continuing Certification Program.

Through an agreement between the Accreditation Council for Continuing Medical Education and the Royal College of Physicians and Surgeons of Canada, medical practitioners participating in the Royal College MOC Program may record completion of accredited activities registered under the ACCME's "CME in Support of MOC" program in Section 3 of the Royal College's MOC Program.

NetCE designates this continuing education activity for 10 ANCC contact hours.

If multidisciplinary course, add the following statement here. If not multidisciplinary, keep the original designations of credit for physician and nurse.

This activity was planned by and for the healthcare team, and learners will receive 10 Interprofessional Continuing Education (IPCE) credits for learning and change.

NetCE designates this continuing education activity for 12 hours for Alabama nurses.

NetCE designates this continuing education activity for 5 pharmacotherapeutic/pharmacology contact hours.

AACN Synergy CERP Category A.

NetCE designates this activity for 10 hours ACPE credit(s). ACPE Universal Activity Numbers: JA4008164-0000-24-043-H01-P and JA4008164-0000-24-043-H01-T.

Individual State Nursing Approvals

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This activity is designed to comply with the requirements of California Assembly Bill 1195, Cultural and Linguistic Competency, and California Assembly Bill 241, Implicit Bias.

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The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

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Disclosure Statement

It is the policy of NetCE not to accept commercial support. Furthermore, commercial interests are prohibited from distributing or providing access to this activity to learners.

Course Objective

Asthma is increasingly common, and most healthcare professionals will encounter patients with the condition. The purpose of this course is to provide nurses and pharmacy professionals with up-to-date, accurate information regarding the diagnosis and management of asthma and long-term outcomes for those with the condition.

Learning Objectives

Upon completion of this course, you should be able to:

1. Summarize the history of asthma, including current definitions.
2. Describe the impact of asthma both globally and nationally.
3. Identify risk factors that contribute to the development of asthma.
4. Define the pathophysiology of asthma.
5. Discuss the pathogenesis of an asthma attack in its five phases.
6. Discuss the process of diagnosing asthma, including differential diagnosis and available tests.
7. Outline the appropriate treatment and management of asthma, the medications used, and the application of the various guidelines.
8. Discuss specific population considerations.
9. Explain the importance of patient education when discussing prevention and management of asthma.
10. Identify triggers of asthma attacks.

Pharmacy Technician Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the epidemiology and risk factors for asthma.
2. Define the pathophysiology and pathogenesis of asthma, and recognize the tests used to diagnose the disease.
3. Discuss the appropriate treatment and management of asthma, with special consideration of specific populations and the importance of patient education and trigger identification.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Asthma has existed for thousands of years, but only in the past century has the medical community developed a better understanding of it. Even with the great progress made toward improved treatments and concepts of asthma, the disorder is frequently misdiagnosed and mismanaged in many healthcare settings. Furthermore, the condition is increasingly common, and most healthcare professionals will encounter patients with asthma.

In the United States alone, it is estimated that 8.9% of adults and 6.7% of individuals 18 years of age or younger have asthma, and cases have been trending upward in both age groups for decades [1; 2]. This increase in the number of asthma cases extends globally. In 2019, it was estimated that there were 262 million individuals worldwide with asthma, although exact numbers are difficult to estimate due to differences in diagnosis and reporting methods [3].

Among the general population, 6.3% of patients seen by a physician in the office setting have a diagnosis of asthma in their medical records [2]. In 2021, 939,000 individuals in the United States visited an emergency department and received a primary diagnosis of asthma. In addition, there were 4.9 million office-based physician visits for asthma [2]. The utilization and costs associated with health care related to asthma put a tremendous burden on healthcare systems and professionals as well as on patients and public organizations.

Direct healthcare costs for asthma in the United States total more than $50.3 billion annually; indirect costs (mainly lost productivity) and mortality add an additional $3 billion and $29 billion, respectively [4]. In addition to direct and indirect costs, prescription drugs for the treatment of asthma represented the largest single direct medical expenditure, accounting for more than $17 billion annually [5].

Proper treatment and management can minimize the effects of asthma. Along with pharmacologic treatment, there are many contributing agents (known as triggers or asthmagens) that, once identified, can be addressed with the patient and successfully managed. Reviewing the signs and symptoms, pathophysiology, risk factors, diagnosis, treatment and management, and prevention strategies allows healthcare professionals to be prepared to provide optimal care for the patient with asthma.

HISTORY OF ASTHMA

The first record of asthma-like symptoms was documented in Egyptian manuscripts circa 1500 B.C.E. Hippocrates first referred to asthma as a specific condition, using the Greek word *asthma*, meaning the act of panting or labored breathing . Asthma-like symptoms and their treatments were described thousands of years ago in ancient Chinese writings. The herbal medicine *ma-huang* traditionally used in Chinese medicine to treat asthma-like symptoms, comes from the bark of trees of the genus *Ephedra equisetina*. The modern medication ephedrine, a common ingredient in some asthma medicines, is derived from this plant [6; 7].

In the early 1700s, Bernardino Ramazzini, an Italian physician, noted links between people with asthma and their occupations. Ramazzini documented asthma resulting from mill workers' exposure to mill dust and farmers' contact with animal dander. This was one of the first attempts to identify asthmagens or triggers as causes of asthma attacks. Although most physicians in the 18th century were in agreement that asthma was a new disorder, it remained difficult to auscultate the lungs and examine the patients' lung tissue or secretions. By 1761, Leopold Auenbrugger, an Austrian physician, discovered a new technique for examining the lungs by percussion, or tapping on the patient's chest, to elicit differences in reverberating sounds. Approximately 60 years later, French physician René Laënnec, who had asthma, designed the first crude stethoscope—a rolled piece of paper held to the chest to listen to a patient's heart and lungs. The following decade would also bring improvements in microscopic technology that allowed physicians to examine lung tissue and secretions [6; 7].

British surgeon John Hutchinson developed the first spirometer around 1850. It was originally intended for his research in respiratory physiology, as a tool to measure respiratory flow rates. Soon, smaller devices were being widely used by patients with lung disease in Europe, Australia, and the United States [6; 7].

By the end of the 19th century, many companies were shipping asthma "medications" all over the country and around the world. These were in the form of powders, tablets, and liquids and often labeled as secret formulas. It was not uncommon to find alcohol, cocaine, and/or morphine as active ingredients. Until the late 20th century, inhaling medications via steam or smoke was one of the only ways of introducing medications directly into the bronchial tubes and lungs of a patient with asthma [6; 7].

DEFINITION

Since 1958, several attempts have been made to establish a consensus definition of asthma but thus far have been unsuccessful, and ongoing research continues to evolve the definition. The Global Initiative for Asthma (GINA) defines asthma as a "heterogenous disease, usually characterized by chronic airway inflammation" [8]. It is defined by a history of respiratory symptoms, such as wheeze, shortness of breath, chest tightness, and cough, that vary over time and in intensity, together with variable expiratory airflow limitation [8]. This definition comprises elements set forth by other organizations, including the National Asthma Education Prevention Program (NAEPP), that does not recognize asthma as a specific disease with a single cause, but instead is categorized as a "syndrome composed of multiple phenotypes" [9].

Asthma is considered a chronic, albeit reversible, respiratory disorder. This inflammatory condition produces hyper-reactive and hyper-responsive airway and lungs, causing episodic, reversible airway obstruction through bronchospasms, increased mucus secretions, and mucosal edema. The hyper-reactive lungs of a patient with asthma are more sensitive than most individuals' and may become inflamed or edematous when exposed to specific irritants (e.g., cold air, animal dander, dust, tobacco smoke, care exhaust fumes, grass) or by the respiratory involvement of viral infections, exercise, or laughter . The immune system of an individual with asthma will over-react to these irritants, constricting the airways and filling them with mucus; constricted airways interfere with the movement of air in and out of the lungs, making breathing difficult [8; 9].

Asthma is marked by recurrent episodes of wheezing, breathlessness, chest tightness, and/or coughing. Usually, these periods are associated with widespread but variable airflow obstruction followed by a period of relief, either spontaneously or in response to treatment. Asthma has many puzzling aspects, and its symptoms may wax and wane, especially seasonally. Unlike other respiratory diseases, such as congestive obstructive pulmonary disease (COPD) and emphysema, in which air trapping and hyperinflation of the lungs also occur, asthma is reversible with the use of proper medications and therapies. Long-term lung tissue damage can occur when asthma attacks occur frequently or when the disorder is poorly controlled. Permanent damage would require many instances of severe attacks. In children, whose lungs are still developing, the risk of long-term damage is greater [8; 9].

EPIDEMIOLOGY

GLOBAL IMPACT

As noted, approximately 262 million people worldwide are living with asthma. In 2019, there were approximately 461,000 deaths attributed to asthma [3; 15]. The incidence and severity of the condition varies globally.

Although for many years asthma was characterized as a condition limited to industrialized countries, it is now recognized as a significant health issue in developing countries as well. More than 40 million people in Central and South America and more than 50 million people in Africa have asthma. More than 80% of asthma deaths occur in developing countries [3; 16]. The 2019 Lancet Global Burden of Disease report indicates that countries on the lower and middle parts of the sociodemographic index spectrum sustain the greatest number of asthma deaths, while prevalence of asthma is greatest in countries higher on the sociodemographic index spectrum [15]. Disability-adjusted life-year rates are very high on most of the African continent, as well as in-and-around the Indian subcontinent, southeast Asia, and parts of the United States.

NATIONAL STATISTICS

The global increase in asthma incidence and its impact on public health are also evidenced in the United States. From 2019 to 2022, it was estimated that 8% of Americans had asthma [1; 2]. The number of individuals diagnosed with asthma increased at a rate of 1.5% per year between 2001 and 2010, to a prevalence of 8.4% in 2010, and have remained nearly the same since, with 8% in 2013 and 7.8% in 2019 [1; 2]. Historically, rates of asthma have decreased with age; however, data from 2023 show the prevalence of asthma at 6.7% in children and at 8.9% in adults [1; 17; 18].

The cause of the proliferation of asthma within the last few decades is not yet known, although some have attributed the rise to environmental factors and expansion of the condition's diagnostic criteria. The National Health Interview Survey questions, from which most of the statistics on asthma prevalence are obtained, changed slightly after 1997, causing a shift in how the condition and associated statistics were reported. In 2001, the Centers for Disease Control and Prevention (CDC) introduced a more precise measurement of asthma. Since then, the trend has remained stable at historically high levels [17; 18].

THE PEDIATRIC POPULATION

Asthma remains an important influence on pediatric health. As noted, 6.7% of individuals younger than 18 years of age were reported to have current asthma in 2023, including 7.6% of boys and 5.7% of girls [2; 17]. Childhood asthma contributes considerably to school absenteeism in the United States. In a typical year, school-age children miss 13.8 million school days due to asthma [22]. One study found that among elementary students 5 to 11 years of age in California, approximately 50% reported missing at least one day of school due to asthma. Additionally, it was found that 11% of elementary students met the criteria for excessive absenteeism (defined as 9 to 18 missed school days during the school year) as a result of their asthma [23]. Asthma is the most common chronic disease of childhood, making it a significant threat to pediatric health.

RACE AND GENDER

In 2023, 11% of women in America had asthma, compared with 6.8% of men [18]. The higher incidence of asthma among women may produce additional health consequences during pregnancy and/or childbirth. The CDC has found that the asthma rate is 13.3% among individuals with multiple non-Hispanic race/ethnicity, 9.8% among American Indian/Alaska Natives, and 11.7% among non-Hispanic Black individuals. Among Hispanic individuals, the rates are 6.2% for Mexican/Mexican Americans and 7% for people with other Hispanic heritage. Non-Hispanic White individuals have an asthma prevalence of 8.9%, and Asian Americans have an asthma prevalence of 4.9% [18].

RISK FACTORS

Although experts have been unable to definitively identify the cause or causes of asthma, there are several factors that increase the risk of developing the condition in one's lifetime. The following are some of the most common risk factors and will be addressed throughout this course [8; 15]:

- Environmental allergens (e.g., mold, dander, pollen, dust mites)
- Skin or food allergies
- Overweight/obesity
- Genetic predisposition/family history
- Low birth weight
- Respiratory infections in childhood
- Vitamin D deficiency
- Living in an urban area
- Exposure to secondhand smoke
- Exposure to occupational triggers (e.g., chemicals used in farming, hairdressing)
- Gastroesophageal reflux disease (GERD)

OVERWEIGHT AND OBESITY

There have been many studies illustrating a link between obesity and asthma in adults and children. Research indicates that being overweight or obese significantly increases the risk of developing asthma, worsening asthma symptoms, and poor asthma control [15; 19]. The obesity rate among adults with asthma was significantly higher than the rate among adults without asthma (38.8% vs. 26.8%) [19]. One meta-analysis involving more than 300,000 adults in the United States with asthma found that the prevalence is 7.1% in lean adults, compared with 11.1% in obese adults. In addition, the prevalence of asthma in women with obesity was found to be nearly double that of lean women (14.6% vs. 7.9%). Interestingly, men did not have a statistically significant difference in comorbid overweight/obesity asthma [20]. Patients who are excessively overweight place an additional burden on their bodies, especially on their heart and lungs, decreasing both functional residual capacity (the amount of air left in the lungs after exhalation) and tidal volume.

These decreases were associated with several factors, including changes in lung development and chronic systemic inflammation, that may affect, induce, or exacerbate asthma symptoms. However, weight is a modifiable risk factor, and researchers have found that total weight loss of 5% or greater significantly improves lung function and asthma control [20].

Unless contraindicated, moderate exercise is encouraged for all people with asthma, as it strengthens the lungs and improves respiratory function. Patients whose asthma is triggered by activity may be advised to take a short-acting beta$_2$ agonist or other bronchodilator 30 minutes to one hour prior to exercising. Regular aerobic activity is essential for any person with asthma, taking into consideration contraindications or complications.

Asthma and obesity present a unique problem in pediatric patients. Similar to adults, children with obesity are significantly more likely to develop asthma than other children. This is of particular concern in the United States as nearly one in five children is obese. In addition, studies have found correlation between maternal obesity and weight gain during pregnancy and the development of asthma beginning in utero, with estimates showing that 15% to 30% of children born to mothers with obesity later develop asthma; however, it is important to note that asthma is a heterogenous disease and maternal obesity as a single cause is unlikely [19; 20].

GENETIC PREDISPOSITION/ FAMILY HISTORY

A genetic predisposition to develop immunoglobulin E (IgE) antibodies has been shown to increase the incidence of allergy and asthma. However, since the mapping of the human genome has been completed, more than 100 susceptibility genes contributing to the development of asthma have been recognized. The first gene associated with asthma susceptibility and airway hyper-responsiveness, *ADAM33*, was mapped in 2002. Researchers at Channing Laboratory, Brigham and Women's Hospital in Boston, were able to link variants of this gene to a familial history of asthma and asthma symptoms. In 2003, two more genes relating to asthma, *PHF11* and *DPP10*, were identified [13; 24]. Results have been mixed regarding the role of Clara cell secretory protein gene variants and the asthma phenotype on the development of asthma, but research seems to indicate a positive, but inconsistent link [25; 26].

Although causative chromosomal regions and candidate genes are now being revealed, this has not ruled out the influence of environmental factors in asthma development. In 2013, the results of two studies were analyzed to determine the role of genetic and environmental factors, and the researchers found that variants at the 17q21 locus were implicated in the development of asthma in children with a history of rhinovirus infection with wheezing [27]. This indicates a possible synergistic relationship between genetic and environmental factors in the development of asthma in childhood.

These discoveries opened new avenues for research in asthma and allergy, and advances since the early 2010s in genomics technology and epigenetics now offer expanded methods to link genetic variants, providing important information about the molecular mechanisms underlying the complex (epi)genetics of asthma. Genome-wide association studies have highlighted that the majority of identified gene variants are not associated with altered protein function but are instead controlled by non-coding gene regulatory elements. In these studies, (epi)genetic variants were found to be identified in 25.6% of childhood-onset asthma heritability and 10.6% of adult-onset asthma [28],

Should a family have a history of allergies and asthma, the first two years of a child's life are critical; exposure to potential allergens during this time increases the likelihood that a child will develop asthma. In addition, early contacts to such potential allergens may contribute to the severity of the child's asthma. Genetic tendency toward lung sensitivity may not follow a direct line; asthma may bypass a generation or surface in other family branches. The exact mode of inheritance is unclear [8; 15].

PREMATURE BIRTH

Premature birth and associated low birth weight have been considered a risk factor for asthma for many years. One study found that school-age children (3 to 17 years of age) who had been very low-birth-weight infants (i.e., less than 1,500 grams or 3.3 pounds) experienced several long-term health, educational, and social effects. This included asthma, which was reported in 20.9% of the children of very low birth weights, 10.7% of children with low birth weight (1,500–2,000 grams), and 8.1% of those who had been of normal weight at birth. However, it was found that very low birth weight was only shown to be a risk factor for asthma among Hispanic and Black children between 6 and 12 years of age, demonstrating racial and age disparities [29]. The causal link between low birth weight and premature delivery and asthma development has not been completely determined. Poor intrauterine growth and lung and immune system development have long been believed to be the cause; however, additional factors that are often present in premature infants, including antibiotic use in early life, respiratory syncytial virus (RSV) infection in infancy, vitamin D deficiency, and pneumonia in early childhood, have been associated with the development of asthma and require additional research [29; 30].

Identifying possible risk factors specific to certain patients may allow lifestyle changes or more strenuous observation of symptoms for better control of asthma.

PATHOPHYSIOLOGY

ANATOMY AND PHYSIOLOGY

Asthma most prominently affects the respiratory and immune systems, and knowledge of the structures and workings of these systems is vital to an understanding of the condition.

The most obviously affected structures of the respiratory system are the bronchial tubes. As the bronchi stretch deeper into the lungs, they subdivide into smaller bronchioles. A pale, thin membrane, known as the bronchial mucosa, lines these bronchial tubes. Mucous glands, which keep airways lubricated with watery mucus, are embedded within the many layers of bronchial lining. Harmful substances stick to the mucus or sputum and are propelled out of the lungs by the movement of the cilia; this mucus production is one way the body fights infection [8; 13].

The outer walls of the bronchial tubes are surrounded by smooth muscles; movement of these muscles controls the size of airway openings, permitting air in or out of the bronchioles. When muscles are relaxed, airways remain open, allowing air to pass through without effort. Upon exhalation, the muscles contract. Contraction can occur with amazing rapidity. When the lungs and/or bronchi are irritated, the muscles contract and narrow the diameter of the tubes. As with all muscle, continued contraction will cause growth or hypertrophy. The muscle itself may become chronically thickened even in its resting state, which narrows the tube further. When a stimulus is encountered, profound narrowing of the bronchial tubes due to muscle constriction, or bronchospasm, can occur within just a few seconds. Such narrowing in its most severe form can result in sudden death from asphyxiation. Usually, automatic reflexes control whether muscles contract or relax [6; 13].

Deep inside the lungs, surrounding each bronchiole, are millions of tiny, balloon-like air sacs called alveoli. These structures provide the environment for the exchange of gases, allowing oxygen from inhaled air to pass into the bloodstream through the capillaries within the sacs [13].

Asthma is considered a disorder of exhalation, not inhalation. Patients with asthma are uncomfortable not because they cannot inhale enough air, but because obstructed airways are preventing them from exhaling the air that is already in their lungs. In fact, autopsies of patients who died of asthma complications have revealed lungs full of air. When bron-

chioles narrow during an asthma attack, upstream obstruction causes premature closure of airways with expiration, as pleural pressure becomes greater than the pressure inside the airway (the equal pressure point, or EPP). Downstream airways become compressed with expiration, trapping air in the alveolar sacs. Reduced respiratory muscle efficiency and function can be caused by lung hyperinflation and thoracic hyperexpansion, resulting in air trapping. Respiratory muscle advantage is compromised, and the flattened diaphragm is forced to contract with shortened muscle fibers, resulting in a feeling of chest tightness. This can lead to airway rupture, manifested as pneumothorax, pneumomediastinum, or subcutaneous emphysema [13].

INFLAMMATION AND THE IMMUNE SYSTEM

The most common features of asthma are inflammation and edema (swelling) of the airways, and treatments have focused on the connection between inflammation and asthma since the mid-1980s. At that time, researchers developed fiber-optic bronchoscopes with which they were able to view the lungs (and take samples of airway tissues) of those with chronic asthma. With this advancement, researchers concluded that airway inflammation in individuals with asthma never clears, even with mild asthma; therefore, treatment focusing on inflammation reduction was determined to be the most effective for long-term management. When the inflammatory cascade, the physiologic process of an asthma attack, is not treated, rebound of acute symptoms can occur, resulting in extreme damage and potentially permanent scarring [8; 13].

Inflammation is a process involving the immune system's reaction to what it identifies as foreign or harmful items. The immune system consists of three primary components: the thymus gland, lymph nodes, and bone marrow. These parts produce two major types of blood cells: red blood cells, which transport oxygen from the lungs to the tissues of the body, and white blood cells, which defend the body against invasion and infection.

Lymphocytes, a type of white blood cell, are divided into two categories: B cells, which manufacture antibodies or immunoglobulins that identify foreign contacts as harmful agents, and T cells (from the thymus gland), which release chemicals known as cytokines that kill the invading antigen. Antibodies aid the immune system in recognizing organisms that have infected the body in the past, allowing the immune system to fortify and strengthen the body against future invasions by the recognized antigen [8; 13].

PATHOGENESIS OF ASTHMA

The pathogenesis of an asthma attack can be described as an inflammatory cascade composed of triggered, acute inflammation and chronic inflammatory changes. In the body of a person without asthma, the immune responses in the bronchi (e.g., swelling, excretion of mucus, recruitment of inflammatory cells) are present in a lesser degree to protect the body against any infectious agents or foreign objects. However, a person with asthma produces an extreme reaction to otherwise relatively harmless irritants, referred to as asthmagens or triggers. Exposure to a trigger causes inflammatory mast cells to release specific inflammatory mediators, including histamine and interleukins, resulting in an acute response. Histamine causes local tissue edema; interleukins generally act as chemotactic factors and activate other inflammatory cells. Studies reveal that leukotrienes, another chemical released by mast cells, prolong bronchial muscle and airway constriction [8; 12].

After the inflammatory cells are activated, bronchospasm occurs. Bronchospasm and local tissue edema cause narrowing of the airways. Release of interleukins and other chemotactic substances causes migration of other inflammatory cells, including eosinophils, airway macrophages, and neutrophils. The physical presence of these cells can also cause airway narrowing. The migration of the inflammatory cells starts within 30 minutes of exposure and may take hours to reach peak levels.

Several different types of antibodies contribute to the inflammation process. One group of antibodies has evolved to be particularly harmful: IgE. Researchers believe that IgE once helped individuals ward off common ancient parasites; although IgE is not needed today, the body continues to manufacture it. Most individuals are unaffected by the presence of IgE, as it only accounts for about 1% of all antibodies. However, millions of individuals have inherited the genetic predisposition to overproduce IgE; in some cases, B cells release up to 20 times the normal amount of IgE. If an excess of the antibody is produced, the immune system may overreact to routine substances. Each substance to which an individual is sensitive triggers a different IgE antibody; any one of these substances could result in allergies that can trigger asthma [8; 12].

CAUSES OF HYPER-RESPONSIVENESS IN PERSONS WITH ASTHMA

The actual cause of the hyper-reaction by the immune system in persons with asthma is unclear. While many cases may be attributed to a reaction in response to exposure to an asthmagen, the possibility of nervous system involvement is also an accepted theory. Generally, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS) work in harmony to balance the body's functions; the PNS stimulates the bronchial tubes to constrict while, at the same time, the SNS stimulates the bronchial tubes to dilate. Ideally, these two systems coordinate to maintain open airways, allowing an effortless flow of air during inhalation and exhalation. In the lung of a person with asthma, it is thought that the balance may be tipped toward the PNS and that this imbalance may result in narrowed bronchial tubes and asthma symptoms. There was once a belief that the PNS was solely responsible for airway sensitivity; however, studies now seem to indicate that, although the PNS is involved, it is not the major reason for inflammation in asthma[12; 13]. Researchers continue to study the importance of these neurotransmitters relative to bronchial muscle tone.

Additionally, there is a proposed theory that some people with asthma have abnormal beta receptors and the proper neurotransmitters are blocked from reaching the appropriate receptors. When the nervous system becomes unbalanced due to this blockage, the parasympathetic nerves overreact and constrict the bronchial tubes. For some researchers, the "beta blockage theory" offers a better explanation of the cause(s) of asthma symptoms present in some patients after exposure to what are known as nonspecific triggers, such as viruses and extreme weather changes [12; 13]. However, it is still not understood how and when beta receptors would become defective.

ELEMENTS OF AN ASTHMA ATTACK

There are essentially five key elements of an asthma attack: muscle spasm, excess mucus, coughing, wheezing, and fatigue. While not all five elements are present for all patients, they are the most common physical manifestations of an episodic attack of the condition and should be evaluated and treated urgently.

Muscle Spasm

In response to irritation and immune response, muscles on the outer layer of the bronchi contract, causing a bronchospasm. Tightened muscles restrict the movement of air. Depending on the degree of airway narrowing, which differs for each patient and with the severity of the attack, the characteristic breathing difficulty, chest tightness, wheezing, and coughing will follow [13].

Excess Mucus

Inflammation can produce excess mucus as a protective mechanism. During an asthma attack, glands secrete excessive amounts of thick mucus to compensate for the increased amount of irritants or allergens. The excess mucus clumps together in the airways, further narrowing the bronchial tubes by partially blocking the passageway and hindering breathing. This increased amount of mucus can also form plugs that clog very small airways. During an asthma episode, some patients attempt to clear their airways by coughing up what seems to be a mucus

plug. However, patients may produce many plugs; consequently, they may have a continuous, irritating hacking cough. If left untreated, mucus plugs can prolong asthma episodes and increase the risk of infection [13].

Coughing

When secretions become too thick for cilia to handle, the system responds by coughing to remove the unwanted substance. Dry coughs in patients with asthma are generally the product of extra-thick mucus plugs or bronchioles so blocked that the mucus cannot be removed or moved through. Nasal and sinus drainage, a common symptom of allergies, may also irritate airways and produce a nagging, unproductive cough [13]. If a patient has been mouth breathing, the airways may become dry and have decreased elasticity, making it more difficult to clear them. If this is the case, the patient should be encouraged to take frequent sips of water or isotonic fluids (e.g., electrolyte replacement drinks).

Wheezing

Wheezing is considered to be a trademark of asthma, but it is not a definite indicator. The wheezing sound associated with asthma results from a forceful rush of air pushing through narrowed, constricted airway lumens. The surge of air causes vibrations that make the wheezing sound. In some cases, airways can be so constricted that the air flowing past a blockage is not sufficient to produce a wheeze. In very severe attacks, the absence of wheezing is a worrisome sign.

It is important to note that patients with severe asthma have acute airway inflammation during an episode, and as stated previously, patients with chronic asthma have continuous symptoms of airway inflammation, which can eventually destroy airway tissue and alter lung function. Prolonged inflammation may result in permanent obstruction as a result of alteration of the bronchial walls. Unfortunately, after this change occurs, the airways may not respond to common treatment as quickly or at all. This is why it is important to use medication to reduce airway inflammation, subsequently preventing permanent obstruction [13].

Fatigue

Breathing with asthma can fatigue the body. As exhalation is blocked and air is trapped in the lungs, more force is required to maintain adequate oxygen supply. To aid in exhalation, accessory muscles become involved, which can deplete the body of energy. Untreated asthma can produce severe degrees of fatigue for the patient, and this can become a critical situation warranting immediate intervention [13]. Lethargy, decreased response time, and weakness are all late signs of fatigue.

DIAGNOSIS

PHYSICAL EXAMINATION AND PATIENT HISTORY

In some instances, a physical examination and a thorough exploration of a patient's medical history offer enough information for an accurate asthma diagnosis. There are several main criteria that should be present for a diagnosis of asthma to be ascertained. It is vital that a history of episodic asthma symptoms, characterized by airflow obstruction, be established. Symptoms that increase the probability of an asthma diagnosis include episodic wheeze, chest tightness, allergic rhinitis, atopic dermatitis, shortness of breath, and cough. It should also be noted if symptoms worsen at night or in the presence of aeroallergens, irritants, or exercise. A family history of asthma, allergies, sinusitis, or rhinitis is also an indication of potential asthma. According to the National Institutes of Health (NIH), most recurrent episodes of coughing and/or wheezing may be attributed to asthma [9; 10]. Clinical signs of airway narrowing generally consist of wheezing, increased respiratory rate, retractions, nasal flaring, and grunting. Later signs can include tripoding (using accessory muscles to breathe) and altered mental status. In general, asthma symptoms are revealed in different combinations and varying intensities. Due to the fact that asthma symptoms can vary throughout a day, month, or even year, absence of the symptoms during the examination does not exclude a diagnosis.

The physical examination should include an assessment of the upper respiratory tract, chest, and skin. One presenting sign is hyperexpansion of the thorax. Patients with severe asthma often develop a barrel-shaped chest due to the forced inhalation and exhalation, which may cause chest and rib muscles to overdevelop. In time, the chest walls stretch out of shape, assuming a rounded appearance. As the patient inhales and exhales deeply, the quality of the breath sounds can be assessed. Sounds of wheezing during normal breathing or a prolonged phase of forced exhalation may indicate asthma. Observing increased nasal secretions, mucosal swelling, sinusitis, rhinitis, nasal polyps, or edema under the eyes are possible signs of allergic asthma. Any of these indications should be noted. Lastly, the skin should be examined for evidence of atopic dermatitis, eczema, or other allergic skin reactions. Red, scaly skin with pruritus may indicate eczema and can signal other forms of allergy and possibly allergy-related asthma.

PULMONARY TESTS

Most physicians order tests to confirm an asthma diagnosis or to rule out any complications and evaluate the severity of the condition. The objectivity of pulmonary tests allows for a reliable analysis of lung function that patient history and physical examination may not provide; this information may be valuable to the diagnosis process. The most critical tests for evaluating asthma assess pulmonary function, which measures lung performance. Pulmonary tests calculate the amount and rate of air expelled during a single breath, helping to discern whether constricted airways are responsible for blocked airflow [10; 21]. Guidelines for normal breathing are based on analysis of data obtained from large segments of the population. A patient's information is plotted on a continuum, allowing comparison to average breathing patterns for healthy individuals of the same sex, age, and size. Two common methods of measuring airflow assess forced expiratory volume (FEV_1) and peak expiratory flow (PEF) [9; 10; 21].

Spirometry

A spirometer is a simple machine used to determine both the total amount of air that can be forcefully exhaled after maximum inspiration, referred to as forced vital capacity (FVC), and how fully air can be expelled from the lungs, measured by the amount of air forced from the lungs in one second, which is expressed as FEV_1 [9; 21]. The spirometer is generally used in diagnosis to establish airflow obstruction and reversibility. Obstruction may be ascertained if the FEV_1 is less than 80% of the predicted value or if FEV_1 divided by FVC is less than 65%. Normally, the FEV_1 should account for more than 75% of the FVC; anything less than 75% indicates a possible obstruction and 65% or less may indicate a diagnosis of asthma [9; 10; 21].

Peak Flow Meter

A peak flow meter measures the speed of exhalation. The highest speed or best flow is PEF or peak flow. The peak flow meter is less sophisticated than a spirometer, which provides a more thorough assessment of lung function. However, the meter has the advantages of being less expensive, portable, and easy to use. The severity of a patient's asthma can be determined by careful and consistent monitoring of peak flow and comparison to a patient's best peak flow and to standard measurements. Studies confirm that short-term peak flow measurements assist healthcare providers in assessing asthma severity [8; 9; 21].

Exhaled Nitric Oxide

Studies have shown that measuring exhaled nitric oxide (FeNO) is helpful in evaluating and diagnosing asthma, particularly in cases of an uncertain diagnosis of asthma using history, clinical course, clinical findings, and spirometry (including bronchodilator responsiveness testing) or when spirometry cannot be performed [9; 10; 13]. Nitric oxide is a mediator for the inflammation that occurs during an asthma episode; the amount of nitric oxide measured during exhalation will directly correlate with the

inflammation in the bronchial tubes. In general, higher concentrations of nitric oxide are a sign of more severe forms of asthma. However, the NAEPP notes that increased FeNO levels can be caused by allergic rhinitis and atopy, which can be present in individuals with and without asthma; taking these factors into consideration is important for accurate interpretation of FeNO test results [9; 10].

Monitoring the concentration of nitric oxide in expired breath may allow healthcare providers to confirm the reversible nature of the inflammation and assess the effectiveness and adherence to the prescribed therapeutic treatment. It is not recommended, however, that asthma treatment be routinely tailored based on exhaled nitric oxide levels alone [9; 10; 13].

ASTHMA CHALLENGE TESTS

When an asthma condition is difficult to confirm or treat, asthma challenge tests may be undertaken to verify the diagnosis. Of course, any challenge test is potentially dangerous, as there is a risk that the test may induce a serious asthma emergency or unpredicted delayed reaction. So, preferably, challenge tests should be performed in a hospital setting under controlled conditions.

There are two main challenge tests that are useful in assessing a patient for a possible asthma diagnosis. The first is an inhalational or chemical challenge (i.e., direct challenge), whereby patients inhale a small amount of either a suspected asthma trigger or one of two chemicals: histamine, which occurs naturally in the body and may induce asthma-like symptoms, or methacholine, which is known to cause airway constriction only in people with asthma. After exposure, spirometry is performed. If a reaction does not occur initially, the concentration of the substance is increased and spirometry is repeated. The procedure is repeated until it is determined that there is no sensitivity or until FEV_1 decreases by 20%, which would be indicative of asthma [9; 13].

Second, if respiratory distress increases with exercise, an exercise challenge (i.e., indirect challenge) may be recommended. Spirometry is performed before, during, and after the patient engages in moderate-to-strenuous activity, such as running on a treadmill or riding a stationary bicycle, in a controlled laboratory setting. If peak flow or FEV_1 drops more than 12% to 15% during or after the activity, the diagnosis will most likely be exercise-induced asthma [9; 13].

ALLERGY TESTING

Because the comorbidity rate associated with asthma and allergies is so high, it is advisable to engage those patients suspected of having asthma in standard skin and blood tests to determine if they are atopic. The most common allergy tests involve introducing the suspected allergen into the skin's surface and monitoring the area for a reaction. This skin testing can be expensive, time consuming, and, if conducted improperly, results may be misleading. Nonetheless, skin testing can be useful in confirming suspected allergies. The three types of skin tests are prick, scratch, and intradermal, each of which involves adding small amounts of a given allergen to the skin, either percutaneously or intradermally. The test site should be assessed after approximately 15 to 20 minutes to determine if a reaction has occurred. A positive allergic reaction is characterized by a wheal at least 3 mm in diameter greater than the negative control. A few patients may experience delayed anaphylactic reactions to even the smallest amounts of allergen; untreated, these reactions can result in asthma attacks of increasing severity, especially in sensitive individuals [9; 10; 14]. Therefore, many physicians and allergists favor elimination diets over skin tests for differentiating food sensitivity.

In addition to elimination diets and skin testing, there are various blood tests that may be used to assess allergy or allergic reactions in a patient. These tests are able to calculate the proportion of the antibody IgE in the body. In infancy, IgE levels tend to be low, rising gradually over the following decades and decreasing beginning around 40 years of age.

Lowest levels are recorded when an individual is 70 years of age. Therefore, high IgE levels can imply that allergies may be triggering the asthma. Elevated IgE levels in infants and young children are one test used to help predict future allergies. Although the analysis is fairly common, it is rarely used as a sole indicator of allergy or allergic asthma. A group of tests, the radioallergosorbent test (RAST), the multiple allergosorbent test (MAST), and the fluorescent allergosorbent test (FAST), evaluate blood levels of IgE for sensitivity to specific allergens [9; 10; 14].

Although the connection between asthma and allergies is compelling, it is vital to remember that not all people who develop asthma have allergies. Whereas allergies play a part in asthma for 80% to 90% of children, the figure is thought to be lower for adults [14; 24]. Nevertheless, it is worth investigating the possible role of allergens in asthma because, quite simply, knowledge of allergic triggers associated with asthma will allow patients to avoid the harmful agents and better manage the condition. Allergen and asthmagen avoidance is one of the most effective treatments for asthma and allergy patients [9; 10].

DIFFERENTIAL DIAGNOSIS

Because the signs and symptoms of asthma are similar to several other diseases and disorders, it is important to rule out other conditions that may have a similar outward appearance of asthma. This is particularly imperative for patients unable to express symptoms or history verbally.

In particular, panic disorders, physical airway obstructions, congestive heart failure (CHF), GERD, and other pulmonary conditions, such as COPD, pneumonia, and bronchitis, may either exacerbate or mimic the signs and symptoms of asthma. Shortness of breath, decreased exercise tolerance, chest tightness, and wheezing may occur with any of these conditions.

Although not all individuals with asthma wheeze, it is one of the characteristic symptoms of asthma, occurring either during episodic attacks or quite regularly, depending on the severity of the condition. However, there are several other potential causes of wheezing that should be investigated as part of the diagnosis process. For example, wheezing in children may be attributed to acute infections, including bronchiolitis or pneumonia. If these diseases are suspected, chest x-rays and/or blood gas tests may be ordered.

Pediatric Concerns

Differential diagnosis for children presenting with wheezing and recurrent lower respiratory infections should include cystic fibrosis, bronchopulmonary dysplasia (prevalent in premature infants), dysmotile cilia syndrome, alpha-1-antitrypsin deficiency, and immunodeficiencies [9; 31].

Cystic Fibrosis

Cystic fibrosis is the leading cause of chronic debilitating pulmonary disease and pancreatic exocrine deficiency in the first three decades of life. The median age at diagnosis is 6 to 8 months; more than 75% of patients are diagnosed by 2 years of age. It occurs most often in White children, and it is estimated that 1 in every 20 White Americans is a carrier of the cystic fibrosis mutation. Among Black individuals, the incidence is approximately 1 in 16,000, and in Asian Americans, it is 1 in 31,000 [31; 32]. Although cystic fibrosis can be a multisystem disorder, the respiratory system is almost always involved and tends to dominate the clinical picture. Common respiratory complications include air trapping and wheezing, chronic cough and sputum production, retractions, tachypnea, and recurrent or chronic pneumonia. However, the earliest signs of cystic fibrosis can be gastrointestinal and pancreatic, not respiratory. Signs of cystic fibrosis include radiograph abnormalities such as bronchiectasis, atelectasis, infiltrates, and hyperinflation. Therefore, a chest x-ray or computed tomography scan may be useful in determining the correct diagnosis, especially in children [9; 31].

GERD

Excessive mucosal secretion secondary to GERD or gastrointestinal malformation may cause wheezing in both children and adults and should be considered during evaluation. It is reported that 34% of patients with GERD experience chronic cough and/or wheezing as part of their symptomatology. Additionally, bronchiole irritation resulting from repeated exposure to gastric acid may trigger asthma symptoms. Generally, asthma-like symptoms that stem from GERD can be controlled with initiation of reflux medications and lifestyle modification [9; 31].

Structural Issues

If respiratory difficulties are suspected to be more of a structural issue, a bronchoscopy may be performed. This is especially important if congenital abnormality, such as laryngomalacia or tracheobronchomalacia, or tumors or growths are suspected. It can also rule out foreign body aspiration. Samples of tissue and sputum to be used in additional testing may be taken during the procedure, if necessary [9; 31].

Adult and Geriatric Concerns

In adults, CHF and other cardiac conditions, such as mitral valve disease, should be considered in the differential diagnosis of asthma. Establishing an asthma diagnosis is difficult for patients older than 55 years of age due to the increased incidence of CHF and respiratory difficulties resulting from cardiac problems, or "cardiac asthma." Conversely, asthma can aggravate heart disease when oxygen supplied by the lungs is inadequate for the reduced blood supply to the heart. Any diseases or conditions that may cause dyspnea should be considered when determining a differential diagnosis of asthma [9; 33].

A particular form of an infection-plus-allergy condition known as allergic bronchopulmonary aspergillosis, often shortened to aspergillosis or ABPA, should also be considered. The condition initiates with the introduction of the fungus *Aspergillus fumigatus*, a mold that is abundant in damp straw, compost heaps, birdcages, and any decomposing material. *A. fumigatus* does not usually have an adverse effect on those with normal immune systems. However, in individuals with asthma or immunocompromise, the spores from this mold may begin to grow in the lung tissue. An allergic reaction may then occur in response to the fungus. This is an important consideration for those who work in agricultural occupations and is one example of the usefulness of a thorough history and lifestyle questionnaire in the diagnosis and management of asthma [9; 33].

ABPA may present comorbid with asthma or the similar symptoms may result in a false asthma diagnosis. The signs and symptoms of ABPA include rubbery plugs of golden-brown or green sputum; a fever apparent only when the asthma symptoms are severe; worsening symptoms despite treatment; dependence on steroid medications; and very high levels of serum IgE. ABPA is normally treated with steroids to control the allergic reaction and with physiotherapy to clear the mucus from the lungs [9; 33].

There are also certain medications that may induce asthma-like symptoms. Specifically, there are two conditions, aspirin-sensitive triad and nonallergic rhinitis with eosinophilia syndrome (NARES), known for their similar presentation to asthma. The diagnosis of aspirin-sensitive triad is based on three distinct symptoms: perennial rhinitis, nasal polyps, and asthma. Patients with an aspirin-sensitive triad diagnosis tend to collect all three symptoms gradually, in no particular order, over a period of years or decades. Although it is not known how common nonsteroidal anti-inflammatory drug (NSAID) sensitivity is for adult patients with asthma, various reports site frequencies from 3% to approximately 40%. It is far less common in pediatric patients with asthma; women in their third decade are most commonly affected [9; 33].

Quite often, aspirin-sensitive patients with asthma have other related respiratory conditions, including sinusitis, severe rhinitis, and nasal polyps. Nasal polyps are benign inflammatory growths that begin in the sinuses but protrude into the nostril. However, the absence of sinusitis and nasal polyps does not automatically rule out the presence of aspirin sensitivity. Aspirin sensitivity can develop suddenly and produce a reaction similar to anaphylaxis, but it usually builds over many years. Patients with asthma found to have a sensitivity, usually by an aspirin challenge test, are advised to avoid all NSAIDs even if they have not reacted to these medications in the past. Also, patients with aspirin-sensitive triad will often have cross intolerances with sulfides, particularly wine and other alcoholic beverages containing sulfides, and naturally occurring salicylates, which are found in citrus fruit, nuts, and grapes. Food additives may also be problematic [9; 33].

NARES is caused by the invasion of eosinophils into the nasal passages, resulting in severe inflammation. Nasal secretions testing positive for the presence of eosinophils (usually greater than 20% of the cells on nasal smears) are used to confirm a positive diagnosis of NARES. NARES may develop as part of aspirin-sensitive triad or completely separately from any aspirin sensitivities. The cause of the eosinophil infiltration is not clear [9; 33].

In general, a diagnosis of asthma may be reached if a patient has a strong family history, has repeated episodes of wheezing or other breathing difficulties, and responds to bronchodilators. However, because a wide spectrum of diseases and disorders have strikingly similar symptomatology, it is vital that those avenues are exhausted prior to establishing an asthma diagnosis [9; 33].

MEDICAL TREATMENT AND MANAGEMENT

The treatment of asthma is generally divided into one of two categories, either short- or long-term management. Short-term treatments are used only in the case of an asthma attack for immediate relief from the devastating symptoms. The focus of treatment for stable asthma is long-term prevention, planning ahead for emergencies, and being alert to increased symptoms [11]. Asthma may be controlled with early, accurate diagnosis and a treatment plan that involves a patient's, and perhaps an entire family's, active participation.

Asthma exacerbations can be frightening experiences for both patients and their caregivers, especially the first time an attack occurs. A thorough explanation of all the treatments administered will better educate patients for future attacks and prepare them for future treatment.

CREATING A TREATMENT PLAN

The NAEPP advocates the use of a stepwise approach to asthma management [9; 10]. In this program, the asthma classifications are treated as separate steps, beginning with mild intermittent at step 1 and advancing to severe persistent at step 6.

Asthma is classified based on symptom severity and frequency (***Table 1***) [9; 10]. Patients for whom symptoms occur more frequently (i.e., more than two times per week) and who experience interference with normal activity as a result of asthma symptoms are classified as having persistent asthma. Patients who experience asthma less than two times per week, have less than two night-time awakenings due to asthma per month, use rescue inhalers less than two times per week, have no interference with normal activity, and have "normal" peak FEV_1 are categorized as having intermittent asthma. The asthma is then further classified as mild, moderate, or severe based on the extent of interference in daily life, lung function tests, and use of rescue medications. After asthma severity has been classified, the treatment step is determined and initiated (***Table 2***) [9; 10].

CLASSIFICATION OF ASTHMA SEVERITY IN PATIENTS 12 YEARS OF AGE OR OLDER				
Component	**Intermittent**	**Persistent**		
		Mild	**Moderate**	**Severe**
Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
Nighttime awakenings	≤2 times/month	3 to 4 times/month	>1 time/week but not nightly	Often every night
Short-acting $beta_2$ agonist use for symptom control	≤2 days/week	>2 days/week but not daily and not more than once per day	Daily	Several times per day
Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Lung function	Normal FEV_1 between exacerbations FEV_1 >80% predicted FEV_1/FVC normal[a]	FEV_1 ≤80% predicted FEV_1/FVC normal[a]	FEV_1 >60% predicted but <80% predicted FEV_1/FVC[a] reduced 5%	FEV_1 <60% predicted FEV_1/FVC[a] reduced >5%
Recommended step for initiating treatment	Step 1	Step 2	Step 3 or 4	Step 5 or 6
[a]Normal FEV_1/FVC values are 85% for individuals 8 to 19 years of age; 80% for those 20 to 39 years of age; 75% for those 40 to 59 years of age; and 70% for those 60 to 80 years of age.				
Source: [9; 10]				*Table 1*

The goal of each step of treatment is to prevent asthma symptoms and provide the best therapy for the patient. Physicians and other healthcare providers may differ in their "step" approach to medication prescriptions. Some may treat symptoms with the weakest medications for a specific step and add stronger medications if symptoms are difficult or persist; others may prefer to rapidly control symptoms and then reduce medications to the smallest effective doses. The NAEPP recommends the step-down approach to managing asthma symptoms (if asthma is well controlled for at least three consecutive months) [9; 10]. In any case, the goal of the treatment plan should be expressed to the patient and outlined clearly, to ensure the best patient adherence possible.

Each step of the management plan requires a short-acting inhaled $beta_2$ agonist or combination inhaled corticosteroid/formoterol for relief of sudden onset and/or infrequent symptoms. Steps 2 (mild persistent classification) and above include long-term control measures. There are separate step plans for children 0 to 4 years of age and children 5 to 11 years of age, as will be discussed later in this course [9; 10]. Adolescents 12 years of age and older follow the plan established for adults.

Regular follow-ups are vital to monitor the progress in the management of asthma symptoms. A review of current symptoms and improvements should be undertaken every two to six weeks initially and then every three months, depending on the patient's condition, stage in treatment, and management process. If symptoms start to subside and appear controlled after 3 months, consider stepping down to less intense treatment [9; 10].

The NAEPP also recommends that any patients who require treatment for steps 4 or above be referred to an asthma specialist. Other factors that may require referral include initiation of immunotherapy, difficulty achieving or maintaining control of asthma symptoms, or the presence of life-threatening asthma episodes. Referral to a specialist may also be considered for those who require step 3 treatment [9; 10]. Asthma biologic therapies should be considered for patients who require treatment at step 5 or 6.

STEPWISE APPROACH FOR MANAGING ASTHMA IN PATIENTS 12 YEARS OF AGE AND OLDER			
Treatment Step	**Preferred Treatment**	**Alternative Treatment**	**Considerations**
Step 1	SABA	—	Use SABA as needed for symptoms in any step (as indicated), up to three treatments at 20-minute intervals depending on severity of symptoms. Caution: Increasing use of SABA or use ≤2 days a week for symptom relief generally indicates inadequate control and may require a step up in treatment.
Step 2	Daily low-dose ICS and SABA OR Concomitant ICS and SABA	Daily LTRA[a] and SABA OR Cromolyn[a]; or nedocromil[a]; or zileuton[a]; or theophylline[a]; and SABA	Steps 2–4: Conditionally recommend subcutaneous allergen immunotherapy as an adjunct treatment to standard therapy in individuals 5 years of age and older with asthma controlled at initiation, build up, and maintenance phases of immunotherapy Steps 3–4: Preferred use of ICS/formoterol is 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 12 puffs (54 mcg)
Step 3	Daily and as needed combination low-dose ICS/formoterol	Daily medium-dose ICS and SABA OR Daily low-dose ICS/LABA; or daily low-dose ICS + LAMA; or daily low-dose ICS + LTRA[a]; and SABA OR Daily low-dose ICS + theophylline[a] or zileuton[a]; and SABA	
Step 4	Daily and as needed combination medium-dose ICS/formoterol	Daily medium-dose ICS/LABA; or daily medium-dose ICS + LAMA; and SABA OR Daily medium-dose ICS + LTRA[a]; or daily medium-dose ICS + theophylline[a]; or daily medium-dose ICS + zileuton[a]; and SABA	
Step 5	Daily medium-high dose ICS/LABA + LAMA and SABA	Daily medium-high dose ICS/LABA and SABA OR Daily high-dose ICS + LTRA[a] and SABA	Steps 5–6: Consider adding asthma biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)
Step 6	Daily high-dose ICS/LABA + oral systemic corticosteroids + SABA	—	
Steps 1–6	In each step, assess environmental factors, provide patient education, and manage comorbidities, then: **Step up** if needed; reassess in 2 to 6 weeks **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)		

ICS=inhaled corticosteroid; LABA=long-acting beta$_2$-agonist; LAMA=long-acting muscarinic antagonist; LTRA=leukotriene receptor antagonist; SABA=inhaled short-acting beta$_2$-agonist

Note: Medications linked with a slash (/) indicate combination formulations in a single inhaler.

[a]Cromolyn, nedocromil, theophylline, and LTRAs including zileuton and montelukast were not considered in the 2022 update of the NAEPP guidelines, have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a boxed warning for montelukast in March 2020 due to the risk for serious neuropsychiatric events, including suicide.

Source: [9; 10] *Table 2*

In each of the six steps, the NAEPP recommends assessment of environmental factors to provide applicable patient education and manage comorbidities.

PHARMACOLOGIC INTERVENTIONS

When considering pharmacologic treatment of asthma, the dosage, timing, and type of medication should be tailored to individual needs. Optimal treatment should include methods to reverse airflow barriers, stop symptoms from occurring, prevent serious attacks and need for emergency care and hospitalization, keep asthma from interfering with activities of daily living, minimize side effects, and control symptoms with the least amount of medication. As with the approach to management, medication therapy generally adheres to two possible uses: to relieve symptoms quickly with the use of bronchodilators or to reduce chronic airway inflammation with anti-inflammatory medications, preventing asthma from recurring in the future [9; 10].

Medication Administration

Asthma medications may be inhaled, taken orally in pill, granule, or liquid form, or in emergency situations, injected intravenously.

Inhalers

There are several types of inhalers available including aerosol, dry powder, and nebulizers. Metered-dose inhalers (MDIs) rely on a mixture of medication, preservatives, and liquid propellant gas to deliver medicine into the lungs in aerosol form. As of 2008, inhalers that contain chlorofluorocarbon propellants are no longer permitted to be sold [34].

Some short-acting inhaled medications begin to reverse airway constriction within five minutes; however, long-acting medications have been developed in inhalant form as well. Inhaled medications have advantages over oral administration because the medication is able to enter directly into the lungs rather than through the circulatory system. Some MDIs discharge medication after a trigger is pressed, but newer versions are breath activated. For patients with poor coordination or impaired hand function, such as those with arthritis or with a history of stroke, breath-activated devices may improve medication delivery. The drawback of the breath-activated inhalers is that, during a severe attack, a lack of air may make device triggering difficult [9; 11].

Some patients require the assistance of a spacer when using an inhaler. A spacer is a plastic tube that attaches to an MDI; its function is to momentarily trap medication as it exits the inhaler, allowing the medication to be inhaled more easily and preventing it from being lost. Spacers may benefit patients who find it difficult to squeeze the trigger and inhale at the same moment, such as young children or older adults. As medicine deposited in the mouth area can produce side effects, spacers can help limit this and ensure that more medication reaches the lungs instead of the tongue or back of the throat [9; 11].

A major problem with MDIs is knowing when they are empty. Usually, a patient cannot see, hear, or taste when a canister is empty or delivering less medication than intended; in fact, at times, inhalers may feel heavy enough to hold medication but only contain propellant and preservatives. In some cases, empty inhalers may leave a strange taste or heavier spray in the patient's mouth [9; 11].

Each inhaler should have a label that indicates how many measured metered doses the canister holds. For regularly scheduled medications, it is best to calculate the number of usable doses before a new inhaler is needed. Patients may mark calendars or the canister to remind themselves when to reorder another inhaler. In the past, some patients have used the so-called "float test" to determine the amount of medication remaining in the canister. This has been proven to be inaccurate and should not be recommended. Some canisters may require cleaning to prevent the accumulation of bacteria [9; 11].

Breath-activated dry powder inhalers incorporate the same benefits as other breath-activated inhalers; patients are not required to coordinate inhaling with releasing medication. Some dry powder inhalers have a different delivery system involving the insertion of a capsule with medicated, fine powder into the canister. In general, each capsule contains a single dose that equals two sprays of medication (although double doses are available). One disadvantage of the dry powder is the amount of coordination needed to load the capsule into some inhalers. This can be a problem for the young or elderly or for people with arthritis, Parkinson disease, or other diseases affecting coordination or dexterity. Furthermore, depending upon the patient's ability to breathe in deeply, variable amounts of medication may be inhaled. Another concern involves the effect of humidity on dry powder, which may influence dose strength [9; 11].

The nebulizer is a form of inhaler that acts as a vaporizer or humidifier, delivering microdroplets of asthma medication in spray form and allowing a patient to breathe it in through a mouthpiece or face mask. Larger doses from nebulizers may increase the risk of side effects, and studies have shown MDIs to be as effective as nebulizers in delivering medication to the lungs. Nebulizers are used frequently in children as they are easier to administer and provide more accurate dosing. In the past, hospitals frequently provided medication in nebulizers to treat emergency asthma episodes, but now many facilities have converted to the use of MDIs [9; 11].

Oral Administration

In addition to inhalers, many asthma medications are manufactured as pills, granules, or liquids to be ingested orally. Oral medications benefit patients by reaching the small bronchial tubes that most inhaled medication cannot reach. Newer developments in longer-acting, timed-release oral medications adapt to the needs and lifestyles of many patients. However, the amount of medication absorbed over a given time period can vary. Some medications may take up to six times longer than others to reach peak concentrations, which means each patient may require a different dose and frequency of administration to reverse breathing problems [11; 13].

The disadvantage associated with oral medications is the systemic distribution. If negative or unpleasant side effects occur, they last the entire time the medication is active in the body. Depending upon the form and dose, oral medication may be more difficult for the system to balance throughout a 12- or 24-hour period than inhaled formulations [11; 13].

Bronchodilators

Bronchodilators are used to address the acute symptoms of an asthma attack. They act by relaxing the muscles surrounding airways, thereby dilating bronchial tubes. The primary categories of bronchodilators are beta$_2$ agonists, theophylline derivatives, and anticholinergics. Most often, bronchodilators are prescribed in inhaler or aerosol form. They are also available in liquid, tablet, and capsule forms, but these are generally not used due to gastrointestinal side effects. The bronchodilator inhaler is usually the first line of defense in an asthma attack [11; 13].

Epinephrine

The first oral medication to become available for the relief of an acute asthma episode was epinephrine, a hormone produced by the sympathetic nervous system. Epinephrine was once the first choice for treating acute asthma, but it has proved to be a weak bronchodilator with quickly diminished action. Moreover, epinephrine has very potent systemic effects, causing tachycardia, high blood pressure, nervousness, headache, and in some cases, panic attacks. However, this medication may still be used intravenously or subcutaneously in severe asthma emergencies. Epinephrine can be described as nonselective; that is, the medication acts on both the lungs and the heart [9; 13].

Despite its limitations, epinephrine remains the treatment of choice for severe asthma and airway constriction related to allergy. There is agreement that self-injectable epinephrine should be prescribed for patients who have had a previous allergic reaction involving the respiratory or cardiovascular system. The patient, as well as caregivers and all members of the family, should be instructed in how to administer the injection. Parents of children who have been prescribed self-injectable epinephrine should inform school personnel about the allergy and the availability of the medication. Instructions regarding the proper use of self-injectable epinephrine should be repeated frequently to ensure proper use during emergency situations [9; 31].

Beta$_2$ Agonists

Bronchodilators that selectively act on the lungs have largely replaced the routine use of epinephrine. These drugs are called beta$_2$ agonists. Beta$_2$ agonists stimulate the sympathetic nervous system, similar to epinephrine. However, they only act on receptors located in nerve endings inside the lungs. These medications provoke specific beta$_2$ receptors in the muscles encasing the bronchial tubes to reverse; when the drug stimulates these receptors, bronchial muscles relax and bronchial tubes dilate. Beta$_2$ agonists last longer in the body than epinephrine and result in less risk of cardiovascular side effects, making them the drugs of choice for safe, short-acting bronchodilation [9; 11; 35].

Beta$_2$ agonists may cause negative side effects, especially if fast-acting forms are taken too frequently for too long. Overuse can lead to poor asthma control and possibly desensitization. Inhaling more than one canister a month indicates an excessive reliance on bronchodilators to improve asthma. Patients with severe asthma may prefer a beta$_2$ agonist for quicker action than anti-inflammatory medications, which take days to act. However, patients may then expose themselves to potentially fatal attacks due to decreased beta$_2$ agonist effectiveness if the asthma flares out of control [9; 11].

Inhaled beta$_2$ agonist medications are associated with fewer major side effects than orally administered preparations. However, patients who use inhalers may report problems as well. The most common complaint is shakiness; other noticeable side effects may include tachycardia, heart palpitations, headache, dizziness, and increased serum glucose [35]. These side effects tend to diminish over time. Patients using oral beta$_2$ agonists have reported tremors, nervousness, tachycardia, muscle cramps, and sleeplessness [9; 11].

There are several beta$_2$ agonists approved by the U.S. Food and Drug Administration (FDA) for use as bronchodilators. Beta$_2$ agonists come in every administration form, which can assist in individualizing treatment. Injections may work quickly in case of emergency, although the effect lasts only about 20 minutes. Two to four puffs of an inhaled beta$_2$ agonist taken before exercise or travel in cold air can block wheezing for up to four hours [11; 35]. Long-acting beta$_2$ agonists are usually taken twice a day and last up to 12 hours. Their longer action can help prevent interruptions from night-time symptoms and/or allow patients to engage in activities that they would otherwise be advised to avoid.

However, even longer-acting beta$_2$ agonists cannot control unstable asthma. These medications are unable to reverse the chronic airway inflammation found in patients with asthma, necessitating the additional use of an anti-inflammatory drug to prevent symptoms in the long-term. And, as discussed, overuse of these medications can lead to poor asthma control, possible desensitization, and even death. FDA analyses of clinical trials have shown that use of long-acting beta$_2$ agonists without concurrent use of an inhaled corticosteroid is associated with an increased risk of severe worsening of asthma symptoms, leading to hospitalization and death in some patients with asthma, including children [9; 36; 37].

Theophylline Derivatives

Before inhalers became widely available, methylxanthines were the leading asthma medications. They could be administered intravenously or orally. Theophylline was formerly the most widely prescribed bronchodilator in the methylxanthine category and a keystone of asthma treatment in the United States. Theophylline reduces airway responsiveness to histamine, adenosine, methacholine, and allergens, and also relaxes airway muscles and pulmonary blood vessels, allowing the tubes to open and airflow to continue [35]. However, controversies over the medication's benefits and action, and higher efficacy of newer drugs have led to a decline in use [11; 35].

Theophylline provides both a short- and a long-term alternative for patients who cannot tolerate $beta_2$ agonists. The drug reduces mucus buildup and blocks night-time symptoms in mild-to-moderate asthma. Its long-term benefits for preventing symptoms are well documented for up to 12 hours, although theophylline is generally less effective than $beta_2$ agonists. It should be noted that caffeine is considered a methylxanthine drug, so patients should be advised to monitor coffee, tea, and chocolate intake while using this medication. Many factors may affect the metabolism or serum concentration of theophylline, including diet, viral infections, hypoxia, age, some antibiotics, and smoking [11; 35]. In addition, studies have shown that theophylline for asthma management is not as effective in patients with obesity [20].

Anticholinergics

Anticholinergics such as ipratropium bromide, atropine, and tiotropium are shown to be effective in relieving breathing disorders, including asthma. When used for asthma, these medications are not usually the first line of defense but rather are used to supplement $beta_2$ agonists. Anticholinergics act on different nerves than $beta_2$ agonists, although both block nerve pathways to the lung and alter muscle tone in the bronchial wall. Anticholinergics affect specific lung nervous system receptors, or cholinergics, in the vagus nerve; this nerve branches into the smooth muscles responsible for airway opening and the mucous glands that discharge thick secretions. The result is reduced inflammation and relaxed bronchial muscles. Throughout the respiratory tract, the drug stimulates nerve activity in other reactive cells to decrease mouth and lung secretions [9; 11].

Anti-Inflammatory Medications

In 2007, a panel of experts, under the guidance of the NAEPP, noted that the critical role of airway inflammation in asthma has been further substantiated since the 1990s, when this inflammatory role was first acknowledged and treatment was shifted away from calming acute flare-ups to engaging in preventative measures. The NAEPP also noted that bronchodilators work best for acute asthma situations and for preventative treatment before exertion or exercise, but it emphasized anti-inflammatory medications as the foundation for long-term treatment of asthma; this was reaffirmed in the NAEPP 2020 Focused Updates to the Asthma Management Guidelines and in the 2024 GINA guidelines. This approach relies on daily medication to maintain healthy lungs. Patients who require regularly administered bronchodilators should switch to longer-acting drugs designed to reduce airway inflammation [8; 9; 10].

Anti-inflammatory medications block production of substances from cells involved in inflammation, such as mast cells; this action reduces or reverses the swelling that causes asthma symptoms. Equally important, these medications lessen airway sensitivity, which prevents edema. If asthma symptoms appear more than once or twice a week and less powerful options cannot control them, anti-inflammatory medication is indicated. Before newer drugs were developed, the only anti-inflammatory asthma medication available was an oral corticosteroid, such as prednisone. Long-term treatment with oral corticosteroids is associated with serious side effects, including stunted growth in children, hyperlipidemia, thinning skin, and immune system impairment, making patient compliance difficult. As a result, several inhaled anti-inflammatory drugs were developed, which greatly reduced negative reactions.

The four primary types of anti-inflammatory drugs are corticosteroids, mast cell stabilizers, antiallergic medications, and antileukotriene medications [9; 11; 13].

Corticosteroids

The most common group of anti-inflammatory medications is oral corticosteroids. Oral corticosteroids are powerful anti-inflammatory medications. They are easy to administer and offer dramatic reversal of symptoms during life-threatening asthma situations. Although some corticosteroids take a few hours to work, their protection is long-lasting. Oral corticosteroids can be used for a brief period to gain control of asthma before moving to other long-term treatments that have fewer side effects, such as inhaled corticosteroids. Although reports about side effects from steroids may concern some patients with asthma, oral or inhaled corticosteroids can be a promising remedy for severe, uncontrolled asthma [9; 11]. Patients and/or parents may require reassurance that these are not the same class of steroids used illegally by athletes.

Corticosteroids used in the treatment of asthma are adrenal hormones. Oral corticosteroid medications are absorbed into the circulatory system and are distributed throughout the body. In the lungs, they prevent the development of airway edema. Significant amounts of corticosteroids for prolonged periods can adversely affect other organ systems, such as bones and skin [9; 11].

Severe asthma may require higher doses for longer periods, which may then be tapered off over a period of one to three weeks. Patients should be reminded that it is dangerous to abruptly discontinue oral corticosteroids. Corticosteroids are usually taken upon awakening, mimicking the body's natural steroid production schedule. Night-time symptoms may be managed with split doses taken in the morning and at night [9; 35].

A major disadvantage of oral corticosteroids is the array of negative side effects associated with taking large doses over long periods of time. Because these medications enter the circulatory system, there is potential for damage to other organs. If taken for severe asthma, patients should be diligent about identifying and reporting any side effects [9; 11].

Inhaled corticosteroids are the most consistently effective long-term control medication for both children and adults with persistent asthma, and the NAEPP recommends the use of inhaled corticosteroids, either alone or in combination, for most individuals with persistent asthma [9; 10]. Inhaled corticosteroid therapy concentrates on reducing airway edema and improves results obtained from bronchodilators while eliminating extraneous effects to other systems. A $beta_2$ agonist may be prescribed in conjunction with an inhaled corticosteroid; the $beta_2$ agonist is used first to unblock airways so the corticosteroid can penetrate deeper. Common inhaled corticosteroids include beclomethasone, flunisolide, triamcinolone, and budesonide (available in a dry powder inhaler) [11]. Corticosteroids are often combined with formoterol in a single inhaler for ease of use and better asthma control [9]. In 2023, the FDA approved an albuterol/budesonide combination inhaler; this is the first inhaler combining both a corticosteroid and a $beta_2$ agonist [53].

In 2010, the FDA required a boxed warning for drugs that include both a long-acting $beta_2$ agonist and inhaled corticosteroid due to an increased risk of severe exacerbation of asthma symptoms that led to hospitalization and death in some patients using these drugs for the treatment of asthma. In 2011, the FDA required post-market safety trials for these drugs [36]. In 2017, clinical trials were concluded, and it was determined that there was no significant increase of serious risks in patients taking $beta_2$ agonists in conjunction with an inhaled corticosteroid; however, it was noted that taking a long-acting $beta_2$ agonist alone to treat asthma without an inhaled corticosteroid to treat lung inflammation increases the risk of asthma-related death. The boxed warning, therefore, only pertains to single-ingredient long-acting $beta_2$ agonists [37].

Patients who take inhaled corticosteroids may complain about the lack of immediate symptom relief and cite it as a reason for not taking the medication. It is important to stress the long-term benefits when discussing this therapy with patients. Although risks of corticosteroid side effects are greatly reduced with inhalers, they do exist; prolonged use of high doses can increase chances for the same types of unpleasant symptoms attributed to the oral or injected forms [9; 11].

The doses of the inhaled corticosteroid must be very high to equal the risk of side effects associated with oral corticosteroids. Two more common adverse reactions to inhaled corticosteroids are throat irritation and candidiasis. Candidiasis can develop when a patient is taking antibiotic medications in addition to the corticosteroid inhaler or if other medical problems, such as diabetes, exist. To prevent candidiasis, advise patients to rinse their mouths after each inhaler treatment and to gargle with warm water to remove any medication left in the throat. The use of a spacer may also be advisable, as it should ensure that medicine particles are delivered to the lungs rather than to the mouth and throat [9; 11].

Mast Cell Stabilizers

Mast cell stabilizers or inhibitors are considered mild-to-moderate anti-inflammatory agents and are most effective in the treatment and prevention of exercise- or allergen-induced asthma. Mast cell stabilizers interfere with the inflammatory process by stabilizing mast cell membranes and inhibiting the activation and release of mediators such as histamine and leukotrienes. They may also restrain the development of early and late bronchoconstriction responses to inhaled antigens. Mast cell stabilizers used to treat asthma are generally administered by inhalation, but eye and nasal drops are also available. One mast cell inhibitor available for the long-term management of asthma is cromolyn. However, this medication is considered less effective than inhaled steroids in the treatment of moderate-to-severe persistent asthma in adults and children and is not effective for immediate relief of acute asthma attacks [11; 35]. The NAEPP recommends that they may be considered for treatment of persistent asthma for patients of all ages, but their use is not preferred [9; 10].

Other Antiallergic Medications

Similar to mast cell stabilizers, the concept of antiallergic medications as a separate category is under intense study. The idea behind antiallergic drugs is simple—eliminate the allergic reaction so allergic asthma symptoms are greatly reduced. Particularly, some studies have been undertaken to research the effectiveness of antihistamine medications on the long-term control of asthma symptoms. However, research generally shows that the effect of antihistamines for the control of asthma is modest, especially if the patient is receiving the recommended treatment with corticosteroids. If the patient also has allergic rhinitis, as many patients with asthma do, antihistamine medications may help to control the rhinitis with secondary benefits to asthma symptoms. While second-generation antihistamines (e.g., loratadine, cetirizine) have been reported to decrease emergency department visits, the NAEPP recommends against their routine use for home management of asthma, as patient delays in seeking treatment have been associated with home use of antihistamines. Data on the use of second-generation antihistamines suggest that they are safe for use during pregnancy [9; 10]. There are also some preliminary data that suggest that asthma and allergies may provide protection against adult malignant gliomas; however, it was also found that the long-term use of immune mediators such as antihistamine medications may be a cancer risk for developing gliomas [38; 39; 40]. Research is ongoing to determine the link between antihistamine response and cancer.

Antileukotrienes

Antileukotriene medications, introduced in 1996, were the first new class of asthma medications released in decades. Leukotrienes act as a communication system for the inflammation process. Antileukotrienes disrupt this communication process, reducing the effects of hyper-responsiveness in patients with asthma. There are two types of antileukotriene drugs: leukotriene synthesis inhibitors, which prevent these chemicals from being generated, and leukotriene receptor antagonists, which prevent the chemicals from delivering their messages by blocking their receptors [9; 11].

Antileukotrienes are strong and very effective in preventing exercise-induced asthma; they can also prevent the development of bronchospasm caused by aspirin and may be useful in milder forms of asthma. These medications may be useful in the management of moderate-to-severe asthma when combined with an inhaled corticosteroid but may not be as effective as other approaches.

Common antileukotriene medications approved in the United States include montelukast, zafirlukast, and zileuton. Compared to other anti-inflammatory drugs, antileukotrienes may produce more serious side effects, including reversible liver problems, headache, and nausea. Healthcare providers should caution pregnant women against taking these medications. For patients receiving antileukotrienes, serum levels of the agent(s) should be checked regularly to monitor for potential liver problems. The use of antileukotrienes has been associated with the rare condition Churg-Strauss syndrome. This condition usually occurs in adult patients with asthma, with an initial presentation of flu-like symptoms and blood vessel inflammation. Other signs include eosinophilic rash, nasal polyps, and pulmonary infiltrates. Left untreated, Churg-Strauss syndrome can result in major organ damage and even death. The FDA issued a boxed warning for montelukast in 2020 [9; 10; 35].

Other Medications

Mucolytics may be prescribed to patients with asthma to destroy or dissolve mucus buildup in airways; expectorants may be used to thin and loosen mucus. With mucus thinned, coughing and clearing the airways should become easier. However, the value of mucolytics and expectorants for patients with asthma is the subject of debate, as they do not halt the production of excess mucus or treat the underlying causal factors [9; 11].

Antibiotics are useful for combating bacterial infections throughout the respiratory system; most respiratory infections, however, are viral, and antibiotics would not be useful in these cases. In general, antibiotics do not eliminate common asthma triggers, nor do they contribute to shorter hospital stays after severe attacks [9; 11]. The NAEPP and GINA recommend against the routine use of antibiotics for asthma [8; 9].

Decongestants are found in over-the-counter cold remedies and can produce side effects of nervousness, nausea, and headache; these side effects increase when compounded with asthma medications with similar side effect profiles. Decongestants are usually not recommended for patients who have cardiac or prostate problems and should be carefully monitored if taken in conjunction with other asthma medications [11]. Research continues for new, improved decongestants.

NONPHARMACOLOGIC MANAGEMENT

The most effective nonpharmacologic intervention for the treatment and/or prevention of asthma at this time is trigger avoidance, which will be discussed in detail later in this course. Knowing and eliminating any possible asthma triggers is one of the most important elements of any management plan. Additionally, peak flow meter use and increased patient education contribute to an enhanced understanding and control of asthma symptoms. Immunotherapy and complementary medicine modalities have also been used by patients with asthma. Strong patient education and communication is vital to the successful management of asthma.

Immunotherapy/Biologics

For some patients, particularly those with allergy-induced asthma, immunotherapy may result in a reduction of airway sensitivity, which should help prevent asthma attacks. With immunotherapy, small amounts of diluted allergen are injected, causing the patient's immune system to produce the antibodies associated with an allergic reaction. This process is repeated once or twice a week for three to four months, sensitizing the patient with gradually higher concentrations of allergen, until the body is able to tolerate the trigger without reaction. The frequency of injections may be reduced, but the allergen dose may be increased for up to three to five years. Successful immunotherapy results in fewer symptoms and decreased need for medication to control allergies and allergy-related asthma. Immunotherapy is generally more successful in children than adults. Studies report that this preventive treatment is effective in reducing symptoms of allergic asthma if the allergies involve animal dander, house dust mites, pollen, or fungi; to date, research has not confirmed that the positive effects are lasting. Also, immunotherapy may be costly and time-consuming and may not result in a complete cure. Even without cure, lessening an allergic reaction can result in better control of asthma and asthma-like symptoms. It may also provide additional time for medical interventions in cases of severe asthmatic reactions [8; 9; 13].

Several biologics for moderate-to-severe allergic and/or eosinophilic asthma are currently approved by the FDA. Omalizumab has become a widely used option for patients with persistent allergic asthma not adequately controlled with inhaled corticosteroids, either alone or in combination with inhaled long-acting beta$_2$ agonist bronchodilators. Omalizumab is a humanized monoclonal antibody that binds circulating IgE antibody, which leads to a decrease in the release of mediators in response to allergen exposure. It is approved for the treatment of adults and children older than 12 years of age in conjunction with inhaled corticosteroids and long-acting beta$_2$ agonists. The agent is administered subcutaneously every two or four weeks (depending on the dosage schedule), and the dose used is based on pretreatment IgE serum levels and body weight. Possible adverse effects of omalizumab use include injection site pain and bruising, viral infection, headache, and sinusitis. Allergic reactions (e.g., urticaria, anaphylaxis) occur in 0.1% to 0.2% of patients [9; 35; 41].

Several other biologics have been approved to treat moderate-to-severe allergic and moderate-to-severe asthma with levels of blood eosinophils (i.e., eosinophilic asthma). These therapies include three monoclonal antibodies that treat eosinophilic asthma by targeting IL-5 pathways (mepolizumab, reslizumab, and benralizumab), and one that treats both eosinophilic and allergic asthma by targeting IL-4/IL-13 pathways (dipilumab). Patients with eosinophilic asthma should have their blood eosinophils tested several times per year, as studies have shown that eosinophil count may shift over time into a range that may warrant immunotherapy [11; 35; 42].

Another novel monoclonal antibody (tezepelumab-ekko) binds to human thymic stromal lymphopoietin (TSLP) and blocks the interaction with the TSLP receptor. The interaction reduces the biomarkers and cytokines associated with inflammation, including blood eosinophils, airway submucosal eosinophils, IgE, IL-5, and IL-13. Tezepelumab-ekko is the first biologic approved for all types of severe asthma [35; 43]

Mepolizumab was approved in 2015 for use in patients 12 years of age and older. Patients with uncontrolled asthma who are receiving NAEPP step 5 or 6 treatment, with an initial blood eosinophil count of ≥150 cells/mcL and at least two asthma exacerbations requiring systemic corticosteroids in the past year are good candidates for therapy]. Mepolizumab is administered as a subcutaneous injection every four weeks at a fixed dose of 100 mg [9; 35; 42].

Reslizumab is approved for patients 18 years of age and older. Patients with severe eosinophilic asthma (initial blood eosinophil count of ≥400 cells/mcL) that is not controlled with high-dose corticosteroids and inhalers and who have a history of exacerbations may be good candidates. Reslizumab is administered as an IV infusion every four weeks at a dose of 3 mg/kg [35; 42.

Benralizumab is approved for patients 12 years of age and older as add-on maintenance treatment for uncontrolled severe eosinophilic asthma (recommended for blood eosinophil count of ≥300 cells/mcL). Benralizumab is administered at a dose of 30 mg subcutaneous every four weeks for the first three doses and then once every eight weeks [35; 42].

Dupilumab is also approved for patients 12 years of age and older as an add-on maintenance treatment for moderate-to-severe allergic and/or eosinophilic asthma. Indications for use include NAEPP steps 5–6, inflammation characterized by increased blood eosinophils and/or elevated FeNO. Dupilumab is initially administered as two 200-mg (total: 400 mg) or two 300-mg (total: 600 mg) subcutaneous injections, followed by one 200-mg or 300-mg injection (depending on initial dose) every other week [35; 42].

Tezepelumab-ekko was approved in 2021 for patients 12 years of age and older as an add-on maintenance treatment for patients with severe asthma (with or without inflammatory markers) and a history of severe exacerbations. Tezepeluab-ekko may be used for any type of asthma and is administered subcutaneously at a dose of 210 mg once every four weeks [35; 43]

Complementary or Alternative Treatments

There are many alternative or complementary therapies available to patients with asthma. In general, these therapies should be regarded as adjuncts, not replacements, to conventional treatment. The most common complementary therapies used in the management of asthma include breathing exercises, acupuncture, yoga, postural drainage, massage therapy, homeopathy, and herbal medications. There has been relatively little research into the effectiveness of complementary treatments in the management of asthma. However, some inconclusive, small trials support the further investigation of these treatment modalities. For example, studies focusing on magnesium's role in lung function have found that the element appears to block chemicals that inflame the lungs by stabilizing mast cells and T cells released during exposure to allergens. The results are relaxed airway muscles and open bronchioles, which contribute to improved lung function and a reduction in wheezing and other allergy-induced asthma symptoms. Magnesium is often used in the emergency department, but it is not recommended in the management of chronic asthma. Patients and/or their caregivers should be cautioned not to self-prescribe these and other agents without consent or supervision by a qualified healthcare provider [8; 11].

SPECIAL POPULATIONS

ASTHMA IN PEDIATRIC PATIENTS

Asthma in pediatric patients may be difficult to diagnose, as children are more susceptible to respiratory viruses and reaction from allergens. Parents or caregivers of children with asthma may suspect the condition is present if the child begins to have repeated episodes of wheezing and coughing with or without illnesses. This is especially true if there is a strong family history of asthma and/or allergies.

CLASSIFICATION OF ASTHMA SEVERITY IN CHILDREN YOUNGER THAN 12 YEARS OF AGE								
Components	**Intermittent**		**Persistent**					
			Mild		**Moderate**		**Severe**	
	0 to 4 Years	**5 to 11 Years**	**0 to 4 Years**	**5 to 11 Years**	**0 to 4 Years**	**5 to 11 Years**	**0 to 4 Years**	**5 to 11 Years**
Symptoms	≤2 days/week		>2 days/week but not daily		Daily		Throughout the day	
Nighttime awakenings	0	<2 times/ month	1 to 2 times/ month	3 to 4 times/ month	3 to 4 times/ month	>1 time/ week but not nightly	>1 time/ week	Often nightly
Short-acting $beta_2$ agonist use for symptom control	≤2 days/week		>2 days/week but not daily		Daily		Several times per day	
Interference with normal activities	None		Minor limitation		Some limitation		Extremely limited	
Lung function	N/A	Normal FEV_1 between exacer-bations FEV_1 or peak flow >80% predicted FEV_1/FVC >85%	N/A	FEV_1 or peak flow >80% predicted FEV_1/FVC >80%	N/A	FEV_1 >60% predicted but <80% predicted FEV_1/FVC 75% to 80%	N/A	FEV_1 <60% predicted FEV_1/FVC <75%
Recommended step for initiating treatment	Step 1		Step 2		Steps 3–4		Steps 5–6	

Source: [9; 10] *Table 3*

Parents or caregivers should be encouraged to keep an asthma journal detailing asthma symptoms, triggers, and response to treatments.

The treatment plan for infants and children younger than 5 years of age is modified according to the specific condition manifestations and treatment limitations specific to pediatrics (***Table 3***). In this population, lung function tests are difficult to impossible to administer; therefore, information regarding the severity and frequency of symptoms as observed by healthcare practitioners or caregivers may be used to determine the classification of each child's asthma [9; 10; 31]. As with patients 12 years of age and older, the NAEPP recommends the stepwise management plan be followed according to age groups (0 to 4 years of age and 5 to 11 years of age) (***Table 4*** and ***Table 5***) [9; 10]. However, the medications and/or dosages may vary for this population due to compliance, history, family dynamics, environmental triggers, physiologic response, or medical coverage.

STEPWISE APPROACH FOR MANAGING ASTHMA IN PATIENTS 0 TO 4 YEARS OF AGE			
Treatment Step	**Preferred Treatment**	**Alternative Treatment**	**Considerations**
Step 1	SABA AND At the start of respiratory tract infection, add a short course of ICS	—	Use SABA as needed for symptoms in any step (as indicated), up to three treatments at 20-minute intervals depending on severity of symptoms. **Caution**: Increasing use of SABA or use >2 days a week for symptom relief generally indicates inadequate control and may require a step up in treatment. Consider short course of oral systemic corticosteroid if exacerbation is severe or individual has history of previous severe exacerbations.
Step 2	Daily low-dose ICS and SABA	Daily cromolyn[a]; or montelukast[a]; and SABA	
Step 3	Daily medium-dose ICS and SABA	—	For children 4 years of age only, see Step 3 and Step 4 in ***Table 5***
Step 4	Daily medium-dose ICS/LABA and SABA	Daily medium-dose ICS + montelukast[a] and SABA	
Step 5	Daily high-dose ICS/LABA and SABA	Daily high-dose ICS + oral montelukast[a] and SABA	
Step 6	Daily high-dose ICS/LABA + oral systemic corticosteroid and SABA	Daily high-dose ICS + montelukast[a] + oral systemic corticosteroid and SABA	
Steps 1-6	In each step, assess environmental factors, provide patient education, and manage comorbidities, then: **Step up** if needed; reassess in 2 to 6 weeks **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)		

ICS=inhaled corticosteroid; LABA=long-acting beta$_2$-agonist; LAMA=long-acting muscarinic antagonist; LTRA=leukotriene receptor antagonist; SABA=inhaled short-acting beta$_2$-agonist

[a]Cromolyn and montelukast were not considered in the 2022 update of the NAEPP guidelines, have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a boxed warning for montelukast in March 2020 due to the risk for serious neuropsychiatric events, including suicide.

Source: [9; 10] *Table 4*

In school-aged children (5 to 11 years of age), it is recommended that the same stepwise treatment and management principles established for adults be followed, with some modification [9]. Healthcare providers should prepare and make available a written asthma plan for pediatric patients, not only for the patient and the patient's caretaker(s), but also for the child's school. This plan should detail any medications that may be appropriate (both short- and long-term medications), identify any known asthma triggers, and establish an action plan (including preferred or required medication usages) for any asthma attack [9; 10]. Additionally, if the use of a bronchodilator prior to outdoor exercise or activity, especially in cold weather, is indicated, this should be noted in the action plan. Annual influenza and pneumococcal vaccination, particularly in pandemic years, can assist in preventing respiratory inflammation in an already compromised system.

STEPWISE APPROACH FOR MANAGING ASTHMA IN PATIENTS 5 TO 11 YEARS OF AGE			
Treatment Step	**Preferred Treatment**	**Alternative Treatment**	**Considerations**
Step 1	SABA	–	
Step 2	Daily low-dose ICS and SABA	Daily LTRA[a]; or cromolyn[a]; or nedocromil[a], or theophylline[a]; and SABA	Steps 2–4: Conditionally recommend subcutaneous allergen immunotherapy as an adjunct treatment to standard therapy in individuals 5 to 11 years of age and older with asthma controlled at initiation, build up, and maintenance phases of immunotherapy
Step 3	Daily and as needed combination low-dose ICS/formoterol	Daily medium-dose ICS and SABA OR Daily low-dose ICS/LABA; or daily low-dose ICS + LTRA[a]; or daily low-dose ICS + theophylline[a]; and SABA	Steps 3–4: The preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 8 puffs (36 mcg).
Step 4	Daily and as needed combination medium-dose ICS/formoterol	Daily medium-dose ICS/LABA and SABA OR Daily medium-dose ICS +LTRA[a]; or daily medium-dose ICS + theophylline[a]; and SABA	
Step 5	Daily high-dose ICS/LABA and SABA	Daily high-dose ICS + LTRA[a]; or daily high-dose ICS + theophylline[a]; and SABA	Steps 5–6: Consider omalizumab
Step 6	Daily high-dose ICS/LABA + oral systemic corticosteroid and SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid; or daily high-dose ICS + theophylline + oral systemic corticosteroid; and SABA	
Steps 1-6	In each step, assess environmental factors, provide patient education, and manage comorbidities		

[a]Cromolyn and montelukast were not considered in the 2022 update of the NAEPP guidelines, have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a boxed warning for montelukast in March 2020 due to the risk for serious neuropsychiatric events, including suicide.

Medications linked with a slash (/) indicate combination formulations in a single inhaler.

Source: [9; 10] *Table 5*

Asthma is a highly individual condition, and treatment and management will be specifically tailored to each patient's symptoms and needs. Emphasizing compliance with the prescribed treatment and management plan and establishing good communication with the parent or caregiver of the pediatric patient will contribute greatly to the successful control of asthma symptoms. In some states, law requires a child's physician or healthcare provider to provide written instructions and an asthma plan to the child's school and/or childcare center.

Asthma and obesity present a unique problem with pediatric patients. In recent decades, studies have found that children with obesity are at increased risk of asthma. In addition, children with obesity who have asthma have greater severity and poorer control of their asthma symptoms, more frequent asthma exacerbations, and overall lower asthma-related quality of life than children with asthma who have a healthy weight. The causative link between childhood obesity and asthma remains unclear, but sedentary lifestyle may be a risk factor for both. Fur-

ther research is underway to determine the impact of obesity on pediatric lung development and possible implications in the development of asthma.

Some learning and behavioral disorders have been found to coexist with asthma. One of these disorders is attention deficit hyperactivity disorder (ADHD), a chronic neurobiochemical condition that normally presents at an early age and includes primary behavior characteristics such as impulsivity, distractibility, short attention span, difficulty concentrating, extreme tempered mental characteristics, and in some cases, hyperactivity. Studies suggest an association between asthma and ADHD, but this association is likely the result of complex and possibly multiple pathways [44]. Results of a systematic review of literature and meta-analysis published in 2018 continued to show a positive association between ADHD and asthma after controlling for possible confounders. More research is needed to determine the cause of the association [45].

Case Study

Patient J is a boy, 5 years of age, residing in Southwest Michigan. One March evening, Patient J was home with a conscientious babysitter. He had experienced several coughing episodes during the previous days and began to cough while playing hide-and-seek with the babysitter. She noticed that the coughing was continuing and that the more he coughed, the more he cried. She was not able to calm the patient and telephoned his parents at a nearby restaurant. Within 20 minutes, the parents returned home and found Patient J upset, crying, and coughing. They could hear audible wheezing on exhalation and could see the young boy's chest retract on inspiration. A physician was called immediately, and the parents were instructed to meet the pediatrician at his office located next to the area's hospital; they arrived within 30 minutes. The pediatrician administered a nebulizer treatment with albuterol in a 0.083% solution for inhalation, which seemed to resolve the cough, wheeze, and labored breathing after 15 to 20 minutes.

The patient's history was reviewed. According to his parents and office records, Patient J's first few years of life were essentially medically uneventful with the exception of occasional benign rashes, several that were specifically found to be related to a wood sensitivity. By 4 years of age, Patient J had experienced a number of cold viruses and allergies, with severe bouts of nasal and chest congestion. He had no history of medical emergencies related to labored breathing or otherwise.

As a precaution, the physician was prepared to recommend hospital admission to provide intensive respiratory tent therapy in the event that the symptoms did not improve. However, the symptoms seemed to resolve completely, and Patient J was sent home with his parents and placed on a 10-day period of antibiotic therapy and an albuterol aerosol inhaler, one or two inhalations every four to six hours as needed. It was also recommended that a nebulizer be kept at home, for faster results in case of sudden onset of moderate-to-severe coughing, chest congestion, wheezing, and/or tightness in the chest.

Patient J was subsequently diagnosed with an extrinsic, mild-intermittent asthma, triggered by several sensitivities, specifically to wood, dust, pollen, and cold weather. Recommendations for control of the patient's asthma symptoms were made to the patient and his family in an effort to manage the condition. He was encouraged to sleep with his head propped up with pillows about 30 degrees. Outdoor play and activities at home or at school were evaluated for appropriate participation based on severe weather, particularly when accompanied by wind. On very cold days or days with high mold or pollen counts, Patient J was instructed to wear a mask. Spring and fall proved to be difficult times for outdoor activities. His lungs became sensitive to the smoke from burning leaves and the mold-infested fallen leaves in autumn.

At home, Patient J's room was evaluated for sources of asthma triggers. Stuffed animals, carpeting, and heavy draperies were kept to a minimum. He had no feather-filled pillows, and his bedding was washed weekly in hot water. He slept with a room air purifier. When his asthma flared up, the patient was given his prescribed medications and warm liquids. A soothing bath or shower allowed him to be in an area of humidified, misty air, which often relaxed and dilated the bronchial airways.

One decade later, Patient J's asthma remains in control. At 15 years of age, he continues to take his medication and stays aware of his asthma triggers. The frequency and severity of asthma episodes have gradually lessened over time. He and his family, however, are aware that the condition is capable of changing or worsening at any time and may return with increased frequency and severity in later years. For now, Patient J is living a normal, healthy, active adolescent life.

ASTHMA IN ELDERLY PATIENTS

The management and diagnosis of asthma in the elderly population may be difficult due to the frequency of additional medical complications or diseases, any of which may aggravate or be aggravated by asthma and/or asthma medications. Specifically, the high incidence of other obstructive lung diseases makes it vital to fully explore possible causes of airway obstruction. Asthma may usually be diagnosed if the obstruction is determined to be reversible. Also, due to the higher prevalence of co-existing diseases, healthcare providers should be aware of possible drug interactions. As mentioned, theophylline in particular has several possible interactions, as well as reduced clearance in the elderly, all of which should be considered. Use of the asthma classification standards and the NAEPP treatment plan is also approved for elderly patients, but individual condition and drug interactions should be closely monitored [9; 10]. Many medications may also trigger asthma symptoms; this may be more prevalent in the elderly population, as more medications may be prescribed.

Various asthma medications can adversely affect elderly patient health. Corticosteroids have been shown to cause confusion and agitation in older patients [35]. There also appears to be a reduction in bone mineral concentrations in patients taking inhaled corticosteroids, particularly in those with pre-existing osteoporosis. However, in low-to-moderate doses, there seems to be no major adverse effect. The NAEPP recommends concurrent treatment with calcium supplements and vitamin D, if appropriate [9; 10].

ASTHMA IN PREGNANCY

Reliable data regarding the prevalence of asthma among pregnant women and women of childbearing age are limited, although research indicates that it is the most common chronic medical condition to be reported during pregnancy. Estimates show that approximately 8% of pregnant individuals in the United States are affected by asthma symptoms. Furthermore, asthma during pregnancy may cause complications such as high blood pressure and pre-eclampsia, preterm delivery, and low infant birth weight. For women who have experienced asthma symptoms prior to becoming pregnant, it is estimated that one-third of these women will each experience a decrease, increase, or no change in their experience of the condition. It is unclear which, if any, of the physiologic changes associated with pregnancy may cause changes in the symptomatology of asthma [9; 13; 46].

The NAEPP has established practice recommendations for the management and treatment of asthma in pregnant patients and is supported by the American Congress of Obstetricians and Gynecologists [9]. The goal for pregnant patients with asthma should be to maintain control of asthma, as it is for all patients, and to maintain normal fetal and maternal health throughout gestation. Severe asthma attacks or persistent asthma may cause fetal hypoxia. Therefore, treatment of maternal asthma should be aggressive and complete. Assessment, including PEF and FEV_1 measurements and patient history, should continue throughout the pregnancy.

If a woman is found to have persistent asthma or if she has a severe asthma attack, additional fetal monitoring, through ultrasound and antenatal fetal testing, may be indicated. According to the NAEPP, all patients should be instructed to be attentive to fetal activity [9; 46].

As with asthma experienced outside of pregnancy, trigger avoidance and patient education are among the most important aspects of controlling the condition. Patient education can increase adherence to the management plan and may be used to stress the importance of controlling asthma symptoms for the benefit of the fetus. In previously untested women, allergy tests may be useful to determine if any controllable allergies are present. Immunotherapy is not generally recommended in pregnant individuals, but omalizumab therapy may be considered if standard treatments are not sufficient to control severe asthma, as the benefits to the patient and fetus may outweigh the risks [9; 35; 46].

Pharmacologic treatments for asthma are generally considered more beneficial than the possible harmful side effects and are therefore recommended for the management of asthma during pregnancy. Antileukotrienes may be considered for patients whose pre-pregnancy response to the drug was favorable. However, the drug should be considered an alternative, not a preferred, treatment option for control of mild persistent asthma in pregnant patients. The goal of pharmacologic treatment should be to gain and maintain control of asthma symptoms. After control is obtained and asthma symptoms stabilize for several months, less intensive treatment should be initiated. In some patients with severe or persistent asthma, the risk of a possibly harmful asthma episode may outweigh the benefits of lessening the intensity of asthma therapy. If this is the case, the step down to less intensive treatment may be deferred until after giving birth. The greatest amount of efficacy and safety data support the use of albuterol as the $beta_2$ agonist for use during pregnancy. Albuterol is a selective beta agonist and has a good safety record for both pregnant and nonpregnant patients. The recommended inhaled corticosteroid for long-term management is budesonide, as more research has been conducted regarding the effects of this medication on pregnant individuals. No data regarding the unsafe or safe properties of other corticosteroids in pregnant patients have been published [9; 35; 46].

PSYCHOSOCIAL MANAGEMENT

Asthma does not just affect the lungs. It is a condition that touches all aspects of life. As such, treatment of the patient with asthma should include treatment of the whole person. Because so much of the success of treatment depends on the individual's adherence to the prescribed management plan, patients and caregivers may be stressed by the added responsibility. By managing these and any other stresses, patients may experience increased quality of life and, by extension, may be more compliant to treatment plans.

Successful adaptation to this chronic, cyclical, sometimes unpredictable condition demands attention to emotional, mental, and social issues as well as to the physical pulmonary problems. The biopsychosocial approach to treating asthma appears to be one of the most successful; healthcare practitioners have found that clearing away psychological and social obstacles positively affects treatment compliance and improves the patient's experience of asthma. Additionally, as discussed, ADHD and other learning and behavioral disorders commonly co-occur with asthma. Most would agree that managing and treating asthma emotionally and mentally, as well as physically, leads to a happier, healthier lifestyle. Referring a patient with asthma to a counselor or psychologist may help alleviate some of the stresses of managing the illness. Connection with others with asthma, through support groups or community involvement, may also be helpful.

PATIENT EDUCATION

As stressed throughout this course, patient education and communication are imperative to the treatment and management of asthma symptoms. It is important that healthcare providers are able to discuss the different aspects of asthma symptoms as well as treatment and management to ensure that patients are able to understand and follow the established plan. In addition to the treatment plan and common symptoms associated with asthma episodes, patient education should outline the importance of compliance, trigger avoidance, and the continuous monitoring of their condition.

CONDITION MONITORING

Continuing with follow-up consultations and symptom monitoring allows for better treatment of asthma. Peak flow meters may be used by the patient to monitor FEV_1 levels and have been useful for some in determining when and if asthma is exacerbated. Peak flow and FEV_1 readings may also be useful in determining the efficacy of an established treatment plan. If possible, encourage patients to keep asthma diaries, in which they may record occurrences of symptoms and attacks. These diaries have been useful in identifying possible asthmagens and in determining the extent and severity of asthma in certain patients. It also helps patients feel more in control, as they will begin to see changes in their lung function even before they notice symptoms. Such awareness can help patients address changes earlier in the course of possible illness (using their action plan) and avoid medical intervention or hospitalization.

COMPLIANCE

The main problem seen in both the adult and pediatric asthma populations is compliance with a prescribed treatment plan and control of asthma symptoms. It is important that, as a part of patient education, adherence to the treatment plan is stressed. As noted, much of the treatment and management responsibilities associated with controlling asthma and asthma symptoms falls on the patient. The more patients understand their treatment and the value of each aspect, the more likely they will be to adhere to the established treatment plan. Healthcare providers should take into account the possible barriers to care, such as income level, education, language, and cultural beliefs. When a child is seen frequently for uncontrolled asthma, it may also be a parenting and caretaking issue.

Education of patients regarding proper administration of medications can be time consuming, and healthcare providers are often limited in the amount of time they can spend with patients or their families. Managed care has caused many hospitals, private offices, and clinics to reduce the number of staff members while increasing the patient loads to cover basic costs. However, patient education is one of the most vital steps in effectively managing and treating asthma and should not be ignored.

TRIGGER AVOIDANCE

In addition to the importance of treatment plan adherence, trigger avoidance should be covered in detail. If a patient has known asthma triggers, avoidance of these items, substances, or situations may greatly improve, or even eliminate, asthma symptoms. Information regarding these asthmagens, where they may occur, and ways to avoid triggering an attack should be incorporated into initial patient education.

Asthma symptoms begin when lungs react to a stimulus, referred to as a trigger or asthmagen. It is important for patients with asthma to discover what triggers their asthma symptoms in order to prevent episodes and more serious lung damage. Asthma symptoms may appear slowly over several years, become noticeable only in specific environments or conditions, or result from the accumulation of repeated exposure to irritants in the environment [2; 13]. While any stimulus that induces an asthma attack is considered a trigger, the most common of these agents may generally be grouped into either the allergen or irritant categories.

Allergens are specific—either pollen is an allergen for a patient or it is not, depending on the response of the patient's immune system. In many cases, allergens are a basic cause of asthma. Allergy has attained this prominent role in the study of asthma not only due to the frequency with which it produces asthmatic episodes and the number of patients with asthma affected with it, but also because the allergic reaction serves as a model for the pathophysiology of asthma. However, numerous other asthma triggers exist as well [13; 48].

Irritants are nonspecific; in fact, irritants affect every person, if sufficiently concentrated, causing bronchospasm and aggravating the airway lining. These irritants include, but are not limited to smoke, some industrial fumes, ozone, sulfur dioxide, insecticides, air freshener, perfumes, and other aerosols. At levels usually encountered, irritants do not adversely affect most individuals. Patients with asthma, however, can have dramatic responses to exposure to some or most irritants due to the chronic inflammation of their airways and their hyper-responsive system [13; 47]. For these patients, an allergy test would reveal no specific allergies.

There are many different types of triggers; some act in isolation, and others work together. The severity of an asthma attack depends upon the number of irritants, allergens, or other stimuli in the environment and the degree of lung sensitivity to these triggers [13; 47]. The following information regarding specific asthmagens and how they may be effectively avoided may be constructive to the patient education process.

Pollen

Pollen is likely the most difficult allergen to avoid. To a great degree, this is because pollen release occurs at different times of day for different plants. For example, most grasses release pollen from about 7:30 a.m. throughout the day; however, if the ground is damp, the release will be delayed until the moisture has evaporated. A few species of grass and other plants delay pollen release until afternoon hours, so pollen may be entering the air all day. All types of plants generally favor warm, sunny days for releasing pollen and avoid rainy, wet weather. Rain also washes residual pollen out of the air. So, days of rain may be a relief to pollen-sensitive individuals with asthma. However, on cloudy and/or wetter days, there is a pollen buildup, which results in a massive release of pollen on the next day of good weather. These pollen release patterns may correspond with incidences of asthma symptoms in sensitive patients [8; 47; 48].

For certain patients with asthma, it may be useful to realize that pollen settles quickly in rural areas, reaching ground level between 8:00 p.m. and 10:00 p.m. In the city, hot pavements and buildings keep upward air currents going and pollen stays aloft longer. As most pollen lands in the city between roughly midnight and 2:00 a.m., it may contribute to night-time symptom aggravation in urban patients with asthma. If a patient with asthma has a noticeable response to a specific type of pollen, staying indoors or avoiding heavily wooded areas at release times may help alleviate symptoms. A daily pollution index figure should be available from a regional office of your state's Department of Environmental Conservation [8; 47; 48]. Many local and online weather stations include pollen counts in their daily reports as well.

Outdoor Pollution

The verdict regarding the effects of outdoor pollution on the condition of asthma remains controversial. Consider two main types of outdoor pollution: industrial smog (such as sulfur dioxide) and photochemical smog (a combination of ozone and nitrogen oxides). Physicians and scientists are cautious about implicating these and other environmental pollutants as asthma triggers. But the findings of several studies confirm a relationship between pollutants and asthma, particularly when nitrogen oxide, acid aerosols, and ozone are involved [8; 47; 48].

Air pollution plays a variety of roles in asthma and allergy. Some pollutants irritate the nose, airways, and/or skin, making them more sensitive to allergens. Specifically, ozone can increase the effects of allergens and may take 4 to 24 hours to produce its effects on the lungs and airways. Such pollutants can worsen existing asthma symptoms and may even promote development of allergies and/or asthma, particularly in children, whose airway membranes are more permeable. Other chemical pollutants may affect the immune system directly, which would tend to increase any existing tendency to allergic reactions [8; 47; 48].

In many regions, air quality is also reported. A government-backed program, AIRNow, is available online to monitor the air quality in various areas around the United States [49]. This information can be used to determine when indoor activities should be encouraged. Local air quality monitoring services may also be available.

Tobacco Smoke

One of the worst irritants in indoor air, and perhaps the most obvious, is tobacco smoke. Cigarette, cigar, or pipe smoke can trigger asthma attacks in the short term and generally worsen asthma symptoms in the long term. Passive, or second-hand, smoking may also adversely affect the immune system. Smoking should not be permitted around a patient with asthma or in rooms an individual with asthma uses. Patients who smoke should be advised to stop smoking. Patients should also be advised of the many techniques available to assist in smoking cessation, including the various nicotine replacement agents [8; 47; 48].

Smoking during pregnancy significantly increases the risk of the infant developing allergies and asthma. In addition, research also reveals that, for those who had asthma as children for whom symptoms have resolved, cigarette smoking greatly increases the chance of the asthma returning. Generally, pediatric patients with asthma who have one or more parents who smoke indoors tend to have more severe and frequent asthma symptoms. It has been found that teenagers can be just as affected by passive smoking as young children [8; 50]. Smoking has many distressing effects on patient health, and smoking cessation should be integrated into all care plans and general assessments.

Gases, Chemicals, and Foreign Contacts

In addition to tobacco smoke, other air pollutants can irritate the lungs of patients with asthma. Such pollutants can worsen existing allergic symptoms and may promote development of allergies in pediatric patients. Common household soaps, detergents, and cleaners may be very irritating for a patient with asthma; contact with strong odors and sprays should be reduced. The use of natural cleaning products can be helpful; however, even the safest products and thorough cleaning may still leave an environment with airborne pollutants. Other chemical contaminants may affect the immune system directly, which would tend to increase any existing tendency to allergic reactions [8; 47; 48].

Nitrogen Oxide

Traffic pollution, most often characterized by the presence of nitrogen oxide, has long been considered a trigger or cause of asthma symptoms; yet, some research reveals the link between traffic pollution and asthma to be, for the most part, tenuous. However, there have been several studies confirming the negative impact of exposure to freeway traffic on lung development in children and on respiratory infections, allergy, and asthma [8; 47; 48]. The exact mechanism responsible for this association is still being investigated.

Cooking with a gas stove generates a significant amount of nitrogen dioxide, the same pollutants emitted from motor-vehicle traffic. But, peak levels of nitrogen dioxide in kitchens with gas stoves are often ten times the average level on city streets, frequently exceeding standards for outdoor air set by the WHO. Other sources of nitrogen dioxide include cigarettes, gas fireplaces, and kerosene heaters. If a patient has a nitrogen oxide sensitivity, he or she should be encouraged to use electric stoves and heaters as often as possible and to always use a ventilation fan or open windows when cooking with a natural gas appliance [8; 47; 48].

Formaldehyde

Patients with asthma seem to have more frequent symptoms if exposed to high formaldehyde levels. Formaldehyde is common in both gas and liquid forms; the vapors expelled by the compound may irritate the lining of the eyes, nose, and lungs when inhaled. A formaldehyde solution is often used as a preservative in laundry detergents, air fresheners, shampoos, dish soaps, medications, cosmetics, cigarettes, and some processed foods. Additionally, it may be found in manufacturing plastics, wrinkle-free clothes, and some building materials, such as particle board, plywood, pressed board fiberboard, carpet backing, glues, and foam insulation. The frequent use of formaldehyde in the production of so many different items makes it a very commonly encountered irritant. Materials that produce formaldehyde should be eliminated from the environment of patients with asthma as much as possible. If a manufactured product contains formaldehyde, it should be noted that the emissions generally decrease as the item ages. Formaldehyde is also created by the combustion of wood and natural gas. Flues for wood burning fireplaces and stoves must be clear; if smoke can be smelled, there is formaldehyde present in the air. When a natural gas appliance is used, adequate ventilation, preferably with a powered vent, is necessary [8; 48; 51].

Aerosol and Scented Sprays

Cleaning products, furniture polish, and even deodorant were never intended to enter the nasal airways, but substances sprayed from aerosols do just that and can trigger asthma attacks. Patients with asthma should be advised to avoid the use of aerosols as much as possible. Additionally, air fresheners and perfumes with strong odors can trigger asthma attacks in sensitive individuals. Avoidance of strong fragrances may help alleviate symptoms [8; 47].

Sulfur Dioxide

The FDA estimates that 1 out of every 100 people is sulfite-sensitive and that 5% of those who have asthma are at risk of experiencing an adverse reaction to the substance. Patients with asthma should be aware of instructions and ingredients listed on all usable or edible products. It is important not only to be knowledgeable as to what is in the product but also as to what gases may be given off when used. One such example is sulfur and sulfur dioxide gas. "Sulfuric," "sulfate," or "sulfite" in a list of ingredients should serve as a warning for a patient with asthma; the product may give off sulfur dioxide gas [8; 52].

In 1986, the federal government established guidelines for sulfites, and a partial ban on sulfites was enacted for restaurant and market fresh salad bars. Regulations also require labels to indicate if sulfites have been added to prepared products. Many medications and processed foods, including some wines, juices, and shellfish, contain sulfites. Due to the fact that inhaled asthma medications may include sulfur-based preservatives, care should be taken when prescribing or administering medications to patients with sulfite sensitivity [8; 9; 52].

Chlorine

For a patient with asthma, bleach and other chlorine-based cleaning products, such as toilet cleaner and scouring powder, should be used sparingly and with plenty of ventilation. These products release chlorine gas, which, in large amounts, can irritate air passages. Bleach and toilet cleaner should not be mixed with any other products, as chemical reactions may exacerbate the amount of chlorine gas expelled. Patients should be instructed to be careful when using any manufactured good containing hypochlorite, chloramines, ammonia, acids, morpholine, or chemicals used for swimming pool water, as all of these agents have the ability to trigger asthma attacks [8; 47; 48].

Paint

The possible harmful effects of paint for people with asthma are mainly due to the presence of solvents; these solvents can act as irritants to nasal air passages. Areas where paint is being used should be well ventilated. Solvent-free, odorless paints are also available and may be useful for patients who are unable to avoid paint fumes as part of their occupation or daily lives [8; 47; 48].

Isocyanate

One of the most powerful asthmagens is isocyanate. "Instant foam" kits sold for do-it-yourself insulation can provoke asthma in those who were previously not asthmatic. This is due to two different substances that are mixed to create the polyurethane foam, one of which is unreacted isocyanate. The combination of these substances results in the release of isocyanate at potentially harmful levels[[8; 48]. The most common incidences of isocyanate asthma occur in patients who have high exposures in their occupation. The National Institute for Occupational Safety and Health has published an alert regarding the risks to U.S. workers exposed to diisocyanate [54]. Although IgE antibodies against isocyanate may be detected by a RAST, this test is positive in only a minority of cases of isocyanate asthma.

Occupational Asthmagens

Any job may present a worker with some environmental hazards. For a patient with asthma, this risk is heightened as a result of the many harmful agents that may be released into the environment and inhaled into the lungs. Some of the most potent irritants are hard metal dusts, such as silica, asbestos, and talc, used in mining and refineries. Fumes from fluorocarbon propellants and oxide of such metals as copper, zinc, manganese, and iron are also on a long list of agents that provoke lung diseases and disorders, including asthma. Other work-related agents that can cause asthma include animal proteins, enzymes, wheat flour, and certain reactive chemicals [8; 55].

Since the healthcare industry has required personnel to wear protective gloves, more healthcare professionals have discovered that latex allergies trigger airway sensitivity. Healthcare providers who have known sensitivities should also be aware of contact with irritants such as disinfectants, formaldehyde, sulfathiazole, chloramine, and psyllium [8; 55].

Office workers in insulated office buildings with central air conditioning systems may never find the source of their symptoms; fewer than 40% of those who feel sick on the job ever discover exactly which pollutant to avoid. Common office triggers include paper dust, perfumes or colognes, industrial cleaners, and mold. Additional and ongoing research continues to provide information about irritants and occupational asthma [8; 55].

Viruses

Many consider upper respiratory tract infection or rhinoviruses to be the most important (and for many patients, the most significant) asthma trigger other than allergy. Viral infections such as these, also referred to as "the common cold," are known to cause complications for many (30% to 40%) patients with asthma. For those without asthma, these infections are usually single nuisances characterized by spontaneously resolving symptoms typically lasting about 7 to 10 days. Symptoms include nasal congestion and drip, postnasal drainage, sore throat, edematous glands, and at times, fatigue. In some instances, the lower respiratory tract may also be involved, and individuals without asthma can develop bronchitis with cough; these symptoms can be confused with allergic reactions in atopic patients. There are more than 200 viruses capable of causing what is generally recognized as a cold. It may be worth noting that colds, especially versions produced by RSV, are often the event that precipitates the onset of asthma in children and adults. In fact, these infections not only often precipitate acute events, but they seem to alter the immune system response to initiate the development of allergy or asthma [8; 47; 56].

Asthma episodes that are the result of viruses may be severe and sudden in onset; lower respiratory tract symptoms of coughing, wheezing, and shortness of breath can occur within 24 hours after the onset of upper respiratory tract viral symptoms, such as nasal congestion. Occasionally, wheezing may occur without any premonitory upper respiratory tract warning, so the patient with asthma should be alert to the earliest onset of chest symptoms as well as the premonitory upper respiratory tract symptoms that usually precede them. It is known that early treatment, especially with oral corticosteroids, may prevent the often serious asthmatic consequences of a viral infection. It is imperative, therefore, that patients are able to recognize early warning signals. Vaccination for typical respiratory viruses, such as influenza, measles, varicella (chicken pox), and pertussis, should be considered as a preventive measure, especially in children. The CDC Advisory Committee on Immunization Practices and GINA recommend that people with asthma receive either the Moderna or Pfizer-BioNTech COVID-19 vaccine series [8; 57].

Weather

Some patients with asthma will indicate that they are able to predict weather because they notice their symptoms worsen or disappear with fluctuating barometric pressures and sudden, extreme temperature shifts. Symptoms such as chest tightening and excess mucus production may warn of high humidity, thunderstorms, snowstorms, or freezing temperatures [8; 47; 48].

Cold air, which usually does not limit airflow with other lung diseases, is a major trigger for many individuals with asthma. Bronchial muscles constrict in cool, dry air, and muscles may not relax until temperatures rise. Even ingesting cold foods or drinks can cause muscle constriction. Exercise during cold weather increases the risk of bronchial constriction by forcing inhalation of cold air [8; 47; 48].

Diet

An anti-asthma diet is generally neither an avoidance diet nor a diagnostic diet, but rather a health-promoting diet, designed to protect against asthma and asthma symptoms. However, if specific food allergies or triggers are identified, they should be avoided as much as possible. Patients with asthma with food sensitivities and/or those who care for them should be made aware of potentially allergenic-specific food ingredients (***Appendix***).

Because overweight and obesity have been linked to an increased risk for asthma, some patients may benefit from weight loss and limiting their calorie intake to lose weight. Dieting patients with asthma should be taught that some packaged goods, including some recommended by several diet plans, contain sugar substitutes, food coloring, and preservatives, all of which have been associated with exacerbation of asthma symptoms in sensitive individuals [8; 19; 47].

Before any dietary treatment, investigation, or recommendation is initiated, a physician or healthcare provider should be aware of assessed risks; referral to a dietician or nutritionist may also be necessary.

Physiologic Triggers

Hormone Changes

The relationship between hormonal changes and asthma is unclear. However, there are types of asthma that are triggered by changes in hormone levels. The number of girls who develop asthma at puberty, when large amounts of estrogen are produced, is growing. A higher incidence of asthma among women, as compared to men, continues through reproductive years [8; 18].

Many women have reported that their asthma worsens when they menstruate. Indeed, research suggests that the decreased levels of progesterone and estrogen during menstruation alter the body's water and salt balance and may negatively affect bronchial muscles and smooth muscles. A few studies concur that premenstrual hormone changes stimulate airway constriction [8; 47; 18].

Contraceptive pills and hormone replacement therapy (HRT) during menopause are being studied as possible asthma stimulants. A Harvard research team surveyed 23,035 women in the Nurses' Health Study and revealed that asthma was twice as prevalent among women who took hormones for 10 years or more, during and after menopause, compared to those women who did not take HRT [58]. However, more research is necessary to discover how and when hormonal changes during the menstrual cycle or menopause affect lungs and asthma symptoms.

Stress

There was once a theory that asthma was the body's way of communicating emotions. The current understanding of asthma is that emotions and mental disorders do not cause asthma in otherwise healthy patients. However, there is evidence that strong emotions may arouse symptoms in individuals with asthma; extreme bouts of laughter or fear can cause bronchial lumens to narrow abruptly. Also, any activity that stresses the respiratory system, including crying or shouting, can stimulate nerves to constrict bronchial lumens. If asthma seems worse during particularly stressful times, specific activities and medications may be used to reduce asthma symptoms [8; 9; 47]. Referral to a counselor, psychologist, or support group may be helpful for patients whose stress is prompting asthma symptoms.

Exercise

Exercise is a proven asthmagen in some individuals. Exercise-induced asthma (EIA) refers to airway changes following activity, which distinguish it from chronic asthma. In patients with chronic asthma, symptoms surface any time, in response to one or more triggers. With EIA, the trigger is more obvious, as symptoms appear when the patient is engaged in exercise and can persist for several hours after activity ends. It is estimated that between 80% and 90% of patients with chronic asthma experience symptoms from exercise at some time [8; 9; 59].

It is very important to realize that any burst of exercise or sustained exercise can trigger asthma flare-ups; reactions can be immediate or delayed, in some cases occurring several hours later. The exact cause of EIA is unknown. One theory focuses on the loss of warmth and moisture from the airways during exercise. After the activity concludes, patients with asthma warm their airways four times faster than those without asthma; some researchers believe that this warming is a sign of edematous airways. Exercise-related airflow problems result in coughing, wheezing, and shortness of breath. The earliest symptoms, such as wheezing, may not be apparent at first because exercise stimulates the increased production of epinephrine, which can mask the symptoms associated with the onset of an attack. Patients with EIA usually begin to have difficulties about 10 minutes into strenuous activity or within 5 to 20 minutes of ending the activity [8; 9; 59].

Another theory suggests that the major cause of EIA is hyperventilation. In fact, the bronchial constriction that occurs during exercise in those with EIA may also be induced by hyperventilation, even in the absence of vigorous physical activity [59].

Some exercises are more likely than others to cause asthma. Team sports that require short bursts of energy (e.g., baseball, football) are less likely to cause symptoms than sports such as soccer or long-distance running that require ongoing activity. Cold weather activities (e.g., cross-country skiing, ice hockey) also tend to make symptoms worse. Swimmers are exposed to warm, moist air, which does not tend to trigger asthma symptoms. Walking, leisure biking, and hiking also are good activities for individuals with EIA [8; 9; 59].

Generally, patients with EIA would be categorized as having mild intermittent asthma and their treatment plans would reflect this categorization. Practitioners should discourage any patients known to experience EIA from engaging in high-risk activities without access to fast-acting medications. This is not to say patients with asthma should not be active. On the contrary, the majority of individuals with asthma

benefit greatly from daily exercise, as better physical conditioning generally results in decreased asthma symptoms. The trick is to map out a routine and group of exercises that work best for the patient.

Medications

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

It is important to realize, as mentioned before, that at least some patients with asthma are particularly sensitive to NSAIDs, which are used to treat pain and inflammation. Several of these medications, such as aspirin, naproxen, ibuprofen, and ketoprofen, are available over the counter. NSAIDs available by prescription only include [35; 60]:

- Diclofenac sodium
- Indomethacin
- Meclofenamate
- Naproxen
- Piroxicam
- Sulindac
- Tolmetin

Known NSAID sensitivity should be noted in a patient's record, as prescribing any of these medications may be extremely hazardous. Other medications, such as paracetamol, may be prescribed instead.

Beta Blockers

The beta-adrenergic system includes the neurologic system, which relaxes the smooth muscle of the bronchial tree and stimulates the heart. Blockage of this system can calm the heart but may also constrict the muscles of the bronchi. This bronchoconstrictive tendency can occur in an exaggerated form in patients with asthma. Beta blockers are used in treating a number of conditions, including hypertension, cardiac arrhythmias, glaucoma (as ophthalmic drops), and migraines. Medications within this category include propranolol, labetalol, atenolol, and timolol [35; 60].

Patients with asthma should be educated regarding the risks of beta blockers and instructed on the appropriate steps to take if they begin to experience asthma symptoms after taking these agents.

Common Household Triggers

Pets

The number of household pets is on the rise; surveys indicate that there are 62 million dog-owning households in the United States and 37 million cat-owning households [61]. These domestic animals, as well as mice, guinea pigs, and even horses and sheep, give off saliva, fur, and dander as they live their normal lives—rubbing against or licking their owners or other individuals. Exposure to any of these elements may trigger asthma symptoms in sensitive individuals.

Certain breeds of dogs and most cats shed clumps of fur throughout the year; saliva holds and spreads dander and fur throughout a house. Further, animals that explore outdoors bring pollen and mold spores indoors on their fur, another potential problem for those with asthma[8; 47].

For very sensitive patients, even the slightest exposure to dander can result in airway constriction. The situation can become dangerous for a child with allergies who keeps rodents in a bedroom or sleeps with a dog or cat. In fact, those with asthma may react whether or not the animal is in the room because dander and/or other allergens may remain in the air for long periods of time [8; 47].

Cat dander is one of the smallest allergens; most of the particles are less than 2.5 microns and the smallest may be only 0.5 micron. A sensitive individual would require a very good dust mask or high efficiency particulate air (HEPA) filter to eliminate these particles in a contaminated indoor area. It should be noted that, in many cases, dander can linger in house dust for approximately six months after a pet has been removed from the environment [8; 47; 48]].

Other, less common pets may produce allergens through shedding of fur or dander. For example, horses are known to produce very powerful allergens. In the case of small mammals, such as mice or guinea pigs, urine is usually the main cause of allergic and asthmatic reactions. Proteins in the urine become airborne and are carried throughout the environment. Allergic reactions to reptiles and amphibians are extremely rare; however, cases of reactions have been documented [62]. With pet insects and snakes, lizards, and other reptiles, the allergens are found in tiny skin particles that float in the air. In addition, live grasshoppers and other insects used to feed reptiles may cause allergic reactions. Because reptiles and amphibians are known to carry Salmonella, which can cause life-threatening infection in young children, the CDC recommends against keeping them in homes with children younger than 5 years of age [8; 47; 48].

Dust Mites, Cockroaches, and Rodents

Allergy research reveals that dust mites play an important role in the development of asthma symptoms. The dust mite allergen provokes immune cells, and after an allergy to dust mites has developed, other allergies become more likely.

It should also be noted that researchers have demonstrated that 18% of children in urban areas in the United States have an allergic reaction to mice, and this can surely contribute to asthma. Cockroaches are another significant cause of asthma symptoms in urban environments. Meticulous cleaning to combat cockroach allergen is advisable, as even slightly reducing exposure can be of great benefit to individuals with asthma. One study of children with asthma who were allergic to cockroaches concluded that the levels of the allergen in the homes were directly related to the severity of the asthma symptoms; children exposed to the highest levels of cockroach allergen were more likely to be hospitalized for asthma, miss more school due to asthma, and have sleepless, wheezy nights [8; 47; 63].

As noted, the NAEPP updated guidelines include recommendations for the assessment of environmental factors during any stage of asthma management, to provide applicable patient education and manage comorbidities. For example, [9; 10]:

- In individuals with sensitization (or symptoms) related to exposure to pests: Conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention
- In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens: Conditionally recommend a multicomponent allergen-specific mitigation strategy
- In individuals with sensitization (or symptoms) related to exposure to dust mites: Conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention

Mold

Except in very dry climates, mold spores are the predominant particulate in the air. In the United Kingdom, a relatively damp country where molds flourish, the record count is more than 160,000 spores/m^3, compared to a record pollen count of only 2,800 grains/m^3. The size of most mold spores is between 2 and 10 microns, but a few species have spores that are smaller than 2 microns[8; 47; 64].

Molds and fungi reproduce through the release of spores. Often, healthcare providers will refer to mold allergies singularly, because molds are the most common offenders, but layer fungi, including mushrooms and toadstools, also produce allergenic spores. There are different species of mold in different environments, and these species can grow in a very wide range of situations, including indoors. A sensitive individual may have cross-reactions between some molds, meaning that a sensitive individual will react to a variety of mold species [8; 47; 64].

One mold allergy in particular has a risk of severe reaction. During the spore-producing season, healthcare professionals should consider increasing the dose of preventive inhaler medications for individuals with asthma who also have allergy to the mold *Alternaria*. Research shows that severe, near-fatal asthma attacks often occur during the *Alternaria* spore season among those allergic to this mold. These individuals may also be referred to a local pollen/spore monitoring service. *Alternaria* spore release usually occurs in the summer or fall, although timing varies from one part of the world to another. *Alternaria* may colonize outdoors, in soil, seeds, or plants, or indoors, in window frames, carpets, or textiles [8; 47; 64].

Mold-sensitive individuals with asthma should be advised to avoid the following places as much as possible; if avoidance is not possible, the use of HEPA facemasks is recommended when patients are in these environments [8; 47; 64]:

- Fields of cereal crops in late summer, due to molds that may be present on the leaves. Symptoms are most exacerbated at harvest time, when the harvesting process results in the dispersal of spores.
- Forests and old orchards
- Gardens with compost piles or piles of dead leaves
- Greenhouses
- Springs, waterfalls, or any damp, shady places

Healthcare professionals should note that mold-sensitive individuals, just as those with pollen allergy or sensitivity, often experience more frequent or intense asthma symptoms during certain times of the year. Increased symptoms during late summer and autumn, when molds flourish outdoors, or following the first frost, which prompts spore release by fungi living in the soil, may indicate a mold allergy. Patients with asthma should be advised to avoid disturbing compost piles, damp straw or hay, piles of grass clippings, or heaps of fallen leaves, all of which are likely to be full of molds. These same patients should not collect fallen leaves or fruit, remove dead leaves or flowers from plants, or water gardens because mold spores are released when water hits dry soil [8; 47; 64].

Indoor molds and the indoor conditions that promote mold growth can be difficult to endure for mold-sensitive patients. Sensitive patients should be advised to avoid the following places, wear a mask while in these areas, or correct the problem areas at their source [8; 47; 64]:

- Buildings that are damp or display mold infestation
- Houses with central evaporative cooling systems (i.e., "swamp coolers")
- Buildings built in damp environments, near lakes, rivers, or the ocean
- Rooms with humidifiers
- Bathrooms and shower rooms, unless the rooms are well ventilated
- Buildings with dry rot, although not all mold-sensitive individuals react to the spores of these timber-rotting fungi
- Buildings where central heating has recently been installed
- Buildings with many indoor plants
- Cellars and basements
- Sun rooms, unless well-maintained
- Antique shops and vacation homes
- Farms or mills
- Portable school classrooms

Nocturnal Asthma

Asthma symptoms can be influenced by the time of the day. Often, asthma worsens at night, especially between 2:00 a.m. and 4:00 a.m., or in the early morning prior to or upon awakening. Many patients with asthma awaken with a choking cough, wheezing, breathlessness, or chest tightness; symptoms may last a short period or may persist for minutes or hours. For patients with persistent nocturnal asthma, symptoms disrupt sleep and may affect ability to function normally during waking hours.

Nocturnal asthma not only leads to sleep loss but also usually indicates uncontrolled asthma [8; 13; 65]. There are many possible causes of nocturnal asthma.

In sensitive individuals, increased amounts of dust mites and other allergens, such as fungal spores, embedded in bedding may trigger allergic asthma. This would, of course, only affect those patients with specific sensitivities. Levels of the hormones epinephrine and cortisol, which play an important role in keeping bronchial airways open, reach their lowest point between midnight and 6:00 a.m. Additionally, histamine levels, which may worsen asthma symptoms, peak at night. Reduced adrenal gland function at night may also be responsible for the decreased amounts of epinephrine and corticosteroids in the blood [8; 13; 65].

The cold night air may lower bronchial airway temperatures, inducing lumen constriction and triggering asthma symptoms. Furthermore, about half of individuals with asthma notice that their symptoms intensify 4 to 12 hours after the first reaction, suggesting that a nocturnal attack may result from a trigger encountered earlier in the day. Lastly, a reclining sleep position may increase the likelihood of gastric reflux symptoms, which may exacerbate or mimic an asthma episode [8; 13; 65].

CONCLUSION

Asthma is one of the most common respiratory conditions affecting children, adolescents, and adults, and the number of individuals affected continues to grow each year. Diagnosis may be complex, especially in certain populations, but it is a vital key to providing the effective treatment and management of the disorder. Affected individuals' signs and symptoms vary in severity, and treatment plans should be determined accordingly. Healthcare professionals should keep current with the latest treatments and medications as well as the latest studies and theories for asthma treatment and exacerbation prevention in order to provide the best patient-centered care.

RESOURCES

AIRNow
https://airnow.gov

American Lung Association
https://www.lung.org

Asthma and Allergy Foundation of America
https://www.aafa.org

Centers for Disease Control and Prevention
https://www.cdc.gov/asthma

National Heart Lung and Blood Institute
Asthma Action Plan Template
https://www.nhlbi.nih.gov/resources/asthma-action-plan-2020

National Institute of Allergy and Infectious Diseases
https://www.niaid.nih.gov/diseases-conditions/asthma

APPENDIX

COMMON FOOD SENSITIVITIES FOR PATIENTS WITH ALLERGY AND/OR ASTHMA

The following items could, even unexpectedly, contain problem food ingredients for individuals with food-allergies. Though it is not an exhaustive list, the most commonly encountered sensitivities are addressed [8; 9].

- Corn: May appear in an ingredient list as cornmeal, cornstarch, dextrose, or polenta
- Eggs: Known to cause anaphylactic shock in sensitive patients
- Fish and shellfish: Fish meal is used in some Asian sauces and other foods as a usual flavoring or condiment
- Milk: Also appears as casein, caseinate, lactalbumin, and whey

- Tree nuts: Be very cautious about nut oils. Also, almond essence may be produced chemically, in which case it is safe, but it may also be manufactured from true almonds. It may also be listed as frangipane, marzipan, or praline.
- Peanuts: Are highly allergenic and may have cross-reaction with soy and/or lupin (a novel food ingredient), but reactions with other legumes are rare. Cross-reactions with tree nuts are quite common. If a patient is highly allergic to peanuts or any nuts, they should be instructed to carefully read labels on all prepared foods and on sweets, including jelly beans, ice cream, and milkshakes. Also, caregivers should be advised to be wary of homemade playdough and some animal foods, such as mixes for birds or gerbils or the pellets used at petting farms, if a child reacts to skin-contact with peanuts.
- Sesame: May also appear as furikake, gomashio, halva, hummus or houmus, or tahini
- Soy: Is present in such foods as miso, soy protein, soy protein isolate, soy sauce, textured vegetable protein, tofu, and vegetable protein
- Wheat: Often listed as bran, flour, graham flour, hard flour, strong flour, or whole-wheat flour. There are non-wheat brans and flours, but the word "bran" or "flour" without any qualification usually means wheat.
- Yeast: Leavening for many products
- Latex: Certain individuals with latex allergy may react to very small traces of it in food, particularly packaged food or restaurant food that has been prepared by workers wearing latex gloves. There are also reports of certain individuals with latex allergy reacting, usually very mildly, to cold-seal adhesives in food wrappers, such as those used for ice cream. The reaction only occurs if the wrapper actually touches the lips or mouth.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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