Asthma in Children and Adolescents

WHAT IS ASTHMA

The word *asthma* originates from an ancient Greek word meaning panting. Essentially, asthma is an inability to breathe properly. When any person inhales, the air travels through the following structures:

- Air passes into the lungs and flows through progressively smaller airways called *bronchioles*. The lungs contain millions of these airways.
- All bronchioles lead to *alveoli*, which are microscopic sacs where oxygen and carbon dioxide are exchanged.

Asthma is a chronic condition in which these airways undergo changes when stimulated by allergens or other environmental triggers. Such changes appear to be two specific responses:

- The *hyperreactive* response (also called hyperresponsiveness).
- The *inflammatory* response.

These actions in the airway cause patients to cough, wheeze, and experience shortness of breath (dyspnea), the classic symptoms of asthma.

Hyperreactive Response

In the hyperreactive response, smooth muscles in the airways constrict and narrow excessively in response to inhaled allergens or other irritants. It should be noted that the airways in everyone's lungs respond by constricting when exposed to allergens or irritants. There are major differences, however, in the hyperreactive response that occurs in people with asthma:

- When people without asthma breathe in and out deeply, the airways relax and open in order to rid the lungs of the irritant.
- When people with asthma try to take those same deep breaths, their airways do not relax but instead narrow and the patients pant for breath. Smooth muscles in the airways of people with asthma may have a defect, perhaps a deficiency in a critical chemical that prevents the muscles from relaxing.

Inflammatory Response

The hyperreactive stage is followed by the *inflammatory* response, which generally contributes to asthma in the following way:

- The immune system responds to allergens or other environmental triggers by delivering white blood cells and other immune factors to the airways.
- These so-called inflammatory factors cause the airways to swell, to fill with fluid, and to produce a thick sticky mucus.
- This combination of events results in wheezing, breathlessness, inability to exhale properly, and a phlegm-producing cough.

Inflammation appears to be present in the lungs of all patients with asthma, even those with mild cases, and plays a key role in all forms of the disease.
WHAT CAUSES ASTHMA IN CHILDREN

Asthma occurs in about five million American children and each year about 200,000 are hospitalized. It is the most common chronic childhood illness. About half of all cases of asthma develop before the age of 10 and about 80% develop symptoms before age five.

General Causes of Asthma

The mechanisms that cause asthma are complex and vary among population groups and even individuals. For example, asthma in children is highly associated with allergies. However, only a minority of children with allergies has asthma, and not all cases of asthma can be explained by allergic response. Other factors, such as genetics or environmental conditions are likely to be involved in the development of asthma. Most likely several genes are involved that make a child susceptible to environmental triggers, not only allergens, but also possibly infections, dietary patterns, or air pollution. Physical factors, particularly having smaller lungs, affect the chances for later asthma.

Factors Contributing to the Worldwide Increase of Asthma

From 1980 to 1994, asthma increased 160% in American children younger than 4 years and has also dramatically risen worldwide. Experts are puzzling over the cause of this phenomenon. Among the causes and factors that are suspects in the dramatic rise in asthma in children are the following:

- One 2000 study suggested that Western dietary habits (which commonly include more fast foods and less fruits, vegetables, fiber, minerals, and other nutrients) may contribute to the development of childhood asthma.
- Some experts observe that children are spending more time indoors watching television, playing video games, or using the computer and are, therefore, overexposed to indoor allergens.
- The trend of making homes more energy-efficient may result in dust mites being trapped inside them.
- Survival rates are now higher in low-birth-weight babies, who may be more susceptible to asthma.
- Declining rates in nursing may be contributor. Breast milk contains important anti-inflammatory agents, such as omega-3 fatty acids, which might protect against asthma.
- Better hygiene and childhood immunizations have been associated with persistence of early immune factors that might increase the risk the risk for allergies and asthma. Important studies in 2002 and 2003, however, have found no association between vaccinations and allergic conditions or asthma. [See The Complex Role of Early Respiratory Infections, below.]

The Allergic Response

Asthma and allergies often coexist, and the allergic response plays a strong role in childhood asthma. About 70% to 85% of children with asthma have allergies, with the risk being higher from seasonal allergies (e.g., hay fever) than perennial allergies (e.g., indoor allergies). (It should noted, however, that allergies are very common, and studies report that only 1% to 20% of children with allergic rhinitis actually develop asthma.)

An asthma attack can be induced or aggravated by direct irritants to the lungs. Studies indicate that the more indoor allergens a child is allergic to, the higher the risk for severe asthma. Important irritants or allergens include the following:

- Dust mites, specifically mite feces, which are coated with enzymes that contain a powerful allergen. These are the primary allergens in the home.
- Animal dander. Cats harbor significant allergens, which can even be carried on clothing; dogs usually present fewer problems.
- Molds.
- Cockroaches. Cockroaches are major asthma triggers and may reduce lung function even in people without a history of asthma.
• Pollen. An asthma attack from an allergic response to pollen is more likely to occur during extreme air changes, such as thunderstorms. Major weather changes, such as El Nino, can affect the timing of allergy seasons. For example, in 1998, when the effects of El Nino were very strong, allergy and asthma attacks were markedly increased and maximum tree pollen counts occurred two to four weeks earlier and mold counts two to three months earlier than in 1997.

• Food allergies. About 8% to 10% of children with asthma also have food allergies; these children also appear to have a high risk for very serious reactions to such foods. In infants and toddlers, allergy to eggs appears to be a major predictor of asthma.

• Fossil Fuels. Certain chemicals may trigger allergic rhinitis. Of particular note, some experts believe that refined fossil fuels, such as diesel fuel and particularly kerosene, may be important triggers for allergic rhinitis. And, in people who already have allergies or asthma, exposure to such fossil fuels may worsen symptoms.

The Allergic Response. The allergic process, called atopy, and its connection to asthma are not completely understood. It involves various airborne allergens or other triggers that set off a cascade of events in the immune system leading to inflammation and hyperreactivity in the airways. One description is as follows:

• The conductor in an orchestra of immune factors that contribute to allergies and asthma appears to be a category of white blood cells known as helper T-cells, in particular a subgroup called TH2-cells.

• TH2-cells overproduce interleukins (ILs), immune factors that are molecular members of a family called cytokines, powerful agents of the inflammatory process.

• Interleukins 4, 9, and 13, for example, may be responsible for a first-phase asthma attack. These interleukins stimulate the production and release of antibody groups known as immunoglobulin E (IgE). (People with both asthma and allergies appear to have a genetic predisposition for overproducing IgE.)

• During an allergic attack, these IgE antibodies can bind to special cells in the immune system called mast cells, which are generally concentrated in the lungs, skin, and mucous membranes. This bond triggers the release of a number of active chemicals, importantly potent molecules known as leukotrienes. These chemicals cause airway spasms, over-produce mucus, and activate nerve endings in the airway lining.

• Another cytokine, interleukin 5, appears to contribute to a late-phase inflammatory response. This interleukin attracts white blood cells known as eosinophils. These cells accumulate and remain in the airways after the first attack. They persist for weeks and mediate the release of other damaging particles that remain in the airways.

Remodeling and Causes of Persistent Asthma

Over the course of years the repetition of the inflammatory events involved in asthma can cause irreversible structural and functional changes in the airways, a process called remodeling. The remodeled airways are persistently narrow and can cause chronic asthma. Researchers are trying to determine how this process occurs:

Interleukins. Some researchers are looking at potent immune factors, including interleukins 11 and 13. They have been linked to a number of processes possibly involved in remodeling, including, overgrowth of cells in the smooth muscles that line the airways and scarring in the airways.

Growth Factors. Compounds known as vascular endothelial growth factor (VEGF) have been observed in the airways of asthma patients. VEGF is a powerful promoter of cell growth in blood vessel linings and some researchers believe they may be major factor in remodeling.

Genetic Factors

About one-third of all persons with asthma share this condition with another member of their immediate family. Asthma may be more likely to be passed to children from the mother than from the father. Both allergies and asthma are strongly associated with hereditary factors and they share certain genetic markers, but they are not always inherited together.
Research, then, on the genetics of these conditions is confusing and difficult. Of some significant promise, researchers have identified a gene (ADAM33), which has been linked to asthma. The gene regulates one of the enzymes called metalloproteases, which are involved with the smooth muscle in the airway. A mutation of this gene, then, could play a role in airway changes that occur after inflammation.

The Complex Role of Early Infections

The role of early childhood respiratory and intestinal infections is very complex. Viral respiratory infections certainly worsen existing asthma but the most common ones are unlikely to be causes of childhood asthma. In fact, early respiratory and intestinal infections may offer some protection against asthma.

**Early Respiratory Infections as Causes of Asthma.** Studies have found little evidence to suggest that most respiratory infections are important causes of asthma in children, except in certain cases. An important exception is the respiratory syncytial virus (RSV), which has been implicated in the development of asthma. RSV is the major viral cause of infant pneumonia. (Other respiratory infections may play an important role in many instances of adult-onset asthma.)

**Common Respiratory Infections Worsen Asthma.** It should be noted that even if the most common respiratory viruses, especially those that cause colds and flus, do not cause asthma in children, they can worsen asthma in children who have it. Rhinovirus, or the common cold virus, for example, has been reported to be the most common infectious agent associated with asthma attacks. In one study, it was associated with 61% of asthma exacerbations in children. Some research suggests that colds promote inflammation in patients with existing asthma and increase the intensity of airway responsiveness for weeks.

**The Hygiene Theory: Early Infections as Protection Against Asthma.** An increasingly important theory blames the dramatic increase in asthma on the reductions in childhood infections that have occurred with modern hygiene and antibiotic use. The basic theory rests on the idea that infections stimulate production of specific immune factors called TH1 cells. As these cells build up, they replace other immune factors called TH2 cells, which react to allergens—a less serious threat to the body. Without infections to stimulate the production of the TH1 infection fighters, then the TH2 allergen fighters are not replaced and they persist at high levels, making the growing child more susceptible to allergies and asthma.

A number of different studies support this theory:

- Some studies suggest that being part of a large family or attending day care increases the risk for early respiratory infections but reduces the risk of childhood asthma. The occasional cold, then, may be protective.

- In a 2002 study, researchers measured levels of bacterial byproducts called endotoxins in the mattress dust of 812 children. Those with the highest levels had an 80% lower rates in allergies and asthma.

- A 2001 Swedish study further found a strong association between allergy development and the absence of certain beneficial bacteria (called probiotics) carried in the infant’s intestines. Infants who were born in more hygienic environments tended to lack these bacteria. Antibiotic over-use and modern hygiene may specifically be reducing these helpful organisms. (Probiotics can be obtained in active yogurt cultures and in supplements, which are being studied for protection.)

The standard vaccinations against serious childhood infections, according to important studies in 2002 and 2003, pose no risk for asthma. One of the studies even reported some lower risk for asthma and allergies in the second and third years after vaccinations. Infections killed thousands of children every year before immunization became widespread. Asthma, although serious, is rarely fatal in children. No one should stop giving their children vaccinations against childhood killers.

Other Contributing Medical Conditions

**GERD.** At least half of asthmatic patients also have gastroesophageal reflux disease (GERD), the cause of heartburn. It is not entirely clear which condition causes the other or whether they are both due to common factors.

Some theories for the causal connection between GERD and asthma are as follows:
Acid leaking from the lower esophagus in GERD stimulates the vagus nerves, which run through the gastrointestinal tract. These stimulated nerves in turn trigger the nearby airways in the lung to constrict, which causes asthma symptoms.

Acid back-up that reaches the mouth may be inhaled into the airways (aspirated). Here, the acid triggers a reaction in the airways that cause asthma symptoms.

GERD is sometimes hard to detect and might be suspected as a contributor in the following asthmatic patients:

- Those who do not respond to asthma treatments.
- Those whose asthma attacks follow episodes of heartburn.
- Those whose attacks are worse after eating or exercise.
- Those whose coughs follow episodes of acid reflux. (One study found that GERD was associated with about half of the episodes of coughs and wheezes in asthmatic patients.)

Treating GERD symptoms with anti-acid agents resolves asthma in some (but not all) patients who share both conditions. [See Well-Connected, Report #85, Heartburn and Gastroesophageal Reflux Disease.]

Sinusitis. Almost half of children and adults with allergic asthma have sinus abnormalities, and in various studies, between 17% and 30% of asthmatic patients develop true sinusitis. The presence of sinusitis, however, does not appear to increase the severity of asthma.

Parental Migraines and Childhood Asthma. Some studies have reported a link between childhood asthma and parental migraines, with one small 2000 study suggesting that children are about five times more likely to develop asthma if their parents have a history of migraines.

Exercise-Induced Asthma

Exercise-induced asthma (EIA) is a limited form of asthma in which exercise triggers coughing, wheezing, or shortness of breath. [See Box Exercise-Induced Asthma (EIA).]

NSAIDs and Acetaminophen

About 10% of asthmatic adults and some fewer children have aspirin-induced asthma (AIA). With this condition, asthma gets worse when patients take aspirin. Aspirin is one of the drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs). Although aspirin is used to reduce inflammation in other disorders, it appears to have the opposite effect in many asthma cases. It is not wholly known why this occurs. AIA often develops after a viral infection. It is a particularly severe asthmatic condition and is associated with up to 25% of asthma-related hospitalizations. In about 5% of cases, aspirin is responsible for a syndrome that involves multiple attacks of asthma, sinusitis, and nasal congestion. Such patients also often have polyps (small benign growths) in the nasal passages.

Patients with aspirin-induced asthma (AIA) should avoid aspirin and most likely NSAIDs, including ibuprofen (Advil) and naproxen (Aleve).

Acetaminophen (e.g., Tylenol) has been the traditional alternative for relief of minor pain for patients who are aspirin-sensitive. Unfortunately, recent evidence has muddied these recommendations. In fact, some asthmatic episodes have been linked to high consumption of acetaminophen among adults. And a study of children with asthma reported that those who took ibuprofen were less likely to be hospitalized for asthma than those taking acetaminophen. This is of particular concern, since acetaminophen is the pain reliever of choice in small children.

Nocturnal Asthma

Asthma occurs primarily at night (called nocturnal asthma) in as many as 75% of asthma patients. Attacks often occur between 2 and 4 A.M. Factors that might play role in nocturnal asthma may include one or more of the following:
- Chemical and temperature changes in the body during the night that increase inflammation and narrowing of the airways.
- Delayed allergic responses from exposure to allergens during the day.
- The wearing off of inhaled medications toward the early morning.
- An increase in acid reflux (back up of stomach acid) that causes airways to narrow.
- Postnasal drip that occurs during sleep.
- Conditions relating to sleep, such as sleep apnea or sleeping on one's back, which may worsen any asthma attack that occurs at night.

Some experts believe that nocturnal asthma may actually be a unique form of asthma with its own specific biologic mechanisms that occur only at night and which reduce natural steroid hormones (which block inflammation).

**Exercise-Induced Asthma (EIA)**

Exercise-induced asthma (EIA) is a limited form of asthma in which exercise triggers coughing, wheezing, or shortness of breath. This condition generally occurs in children and young adults, most often during intense exercise in cold dry air. Symptoms are generally most intense about 10 minutes after exercising and then gradually resolve.

EIA is triggered *only* by exercise and is distinct from ordinary allergic asthma in that it does not produce a long duration of airway activity, as allergic asthma does. (It should be noted that some people have both forms of asthma.) People who only have EIA do not appear to require long-term maintenance therapy. A study of military recruits with EIA also reported that the condition does not hinder a person's overall physical performance.

**Medications**

Cromolyn, a mild anti-inflammatory agent, or short-acting beta2 agonists have been the treatments of choice for preventing EIA. Newer approaches for people who work out regularly include pretreatment with long-acting beta2 agonists, such as salmeterol (Serevent) or the regular use of inhaled corticosteroids.

**Hints for Reducing EIA**

EIA occurs *only* after exercise and is more likely to occur with regular paced activities in cold, dry air. The following are some suggestions for reducing its impact:

- Warm-up and cool-down periods are important.
- Patients with EIA might do better with activities that involve short bursts of exercise (tennis, football) than with exercises involving long-duration regular pacing (cycling, soccer, and distance running).
- Breathing through a scarf or through the nose helps warm up the airways.
- Some interesting evidence suggests that restricting dietary salt might help reduce EIA.
HOW SERIOUS IS ASTHMA IN CHILDREN

Asthma is the third major cause of hospitalization in children under age 15. The condition can be very serious in children, particularly those younger than five, because their airways are very narrow.

Degree of Severity

The severity of asthma is graded using the following categories: mild intermittent and mild, moderate, and severe persistent. [See Table Classification of Asthma Severity and Preferred Maintenance Treatments under What Are the General Guidelines for Treating Asthma?] A patient in any of these categories, even mild intermittent, can still experience a severe and even life-threatening attack. In fact, according to one report, 30% of asthma deaths occur in patients with mild asthma.

Risk Factors for Life-Threatening Asthma

Asthma is rarely fatal in children, with only 176 asthma deaths reported in 1999 in children under age 15. (About 444 fatalities occurred in people between ages 15 and 34.) But even these low numbers are unacceptable, since asthma deaths are largely preventable.

Factors associated with an increased risk of death from asthma in children include the following:

- Previous life-threatening episodes of asthma.
- Lack of adequate and ongoing health care. (Most likely the reason for the higher fatalities rates in minority children.)
- Significant behavioral problems.
- Underestimating the severity of an acute attack poses the greatest threat. Unfortunately, one study of children found that nearly 40% of them were unaware of asthmatic symptoms when they occurred.

African-American children have more than six times the death rate of Caucasian-Americans in the age groups of four and under and 15 to 24 years. Hispanic children also have a higher risk. A 2002 study suggested that these children tend to be given inferior treatments compared to Caucasian children.

Symptoms of a Life-Threatening Attack

The following signs and symptoms may indicate a life-threatening situation:

- As the chest labors to bring enough air into the lungs, breathing often becomes shallow.
- Lacking sufficient oxygen, the skin becomes bluish.
- The flesh around the ribs of the chest appears to be sucked in.
- The patient may begin to lose consciousness.

Asthma often progresses very slowly to a serious condition or may develop to a fatal or near-fatal attack within a few minutes. It is very difficult to predict when an attack will become very serious. It should be noted that early symptoms or lack thereof do not always reflect the ultimate severity of an attack. In fact, some studies suggest that people at high risk for fatal or near-fatal asthma attacks are those with poor awareness of their own reduced ability to breathe and who are therefore slow in seeking help. Monitoring peak flow rates is, therefore, an important management component, since it provides a more accurate assessment of lung function than symptoms alone.

Long-Term Outlook

In a 2003 study, researchers followed people with asthma for longer than 30 years. About a third of children had outgrown their asthma in adulthood. In general, the more severe the childhood asthma, the greater the likelihood that it would persist. For example, only 23% of children who experienced wheezy bronchitis (wheezing during respiratory infections) suffered from frequent or persistent asthma in adulthood.
There is now some evidence that severe asthma can cause long-lasting damage and possibly permanent scarring in some patients. The risk for such injury is highest, however, when asthma strikes children in the first three to five years. Lung damage can also occur rapidly in asthmatic adults. There does not appear to be any significant risk for long-term lung damage for children who develop mild to moderate persistent asthma at age five to 12. Children adapt well to living with asthma, however, and even with severe asthma they can function as well as healthy children in virtually all areas of life.

**Psychologic Factors**

Studies are mixed over the effects of emotional disorders on the severity of asthma. In fact, one indicated that parents of asthmatic children may suffer greater psychological stress than their children. A 2000 study, in fact, reported that having mild to moderate asthma does not significantly affect the psychological well being of most children aged 5 to 12. Teenagers and preteens have particular difficulty coping with what they perceive as the social stigma of asthma. Often they will deny their condition and refuse to comply with their drug regimen. Parents and older children should not hesitate to seek help from support groups, physicians, friends, or family members. Supporting programs in camp and school may help children to better manage their asthma and may even reduce hospitalization.

**Effect on School and Work**

Although there have been few studies on the effects of asthma on schooling, a 2000 study reported that nocturnal (nighttime) asthma affected school attendance and performance in children and work attendance in their parents.
WHAT CHILDREN GET ASTHMA

At this time, asthma affects about 5.3 million American children between the ages of 5 and 14, and some experts believe that about half of American children may be undiagnosed. Asthma has dramatically increased worldwide over the last few decades, in both developed and developing countries. From 1980 to 1994, asthma increased 160% in children younger than four years old and has risen dramatically in other countries as well. There is a wide variation in asthma incidence, however, ranging from over 50% among children in the Caroline Islands to virtually 0% in Papua New Guinea. The reasons for this wide variation are not yet known.

Gender

Among younger children, asthma develops twice as frequently in boys as in girls, but after puberty it may be more common in girls.

Socioeconomic Factors

*Urban Life.* Urban life is strongly associated with a higher risk. Although poverty plays a significant role, urban life, in fact, has been associated with a higher risk for asthma in any income group and among both children and adults. In some urban areas, as many as 25% of children have asthma or show signs of wheezing. In fact, it may be greatly underdiagnosed in city children. A 1999 Chicago study reported almost a third of children in inner-city kindergartens had asthma symptoms without a diagnosis of the disorder; 10% had actually been diagnosed with asthma, mainly because their symptoms were severe.

*Ethnicity.* Since 1980, asthma rates have risen the most dramatically among African-American children, and they have significantly higher rates of asthma than Caucasian children. Hispanic children are also at higher risk. Both groups of minority children are more likely to have fatal asthma than Caucasian children.

Some studies indicate that the difference in risk exists simply because African-Americans and other minority groups are more likely to live in urban areas. Poverty and lack of access to health care may also play a role. However, Caucasian children who live in cities also face a high risk for asthma, and rural African-American children do not.

Urban life and socioeconomic factors, however, may not fully explain the ethnic disparity. For example, a 2000 study found that African-American children may have significantly higher levels of IgE than Caucasian children, suggesting a genetic susceptibility. (IgE are immune factors that play a critical role in asthma.)

Issues Surrounding Birth

*Low Birth Weight.* Infants of low birth weight are at higher risk for lung problems and asthma.

*Winter Birth.* One study suggests that children born in the winter are at greater risk for asthmatic allergies to cockroaches than children born at other times of the year.

*Breast Feeding.* Most studies on breastfeeding report some protection against wheezing and asthma in the first year of life. It should be noted that breastfeeding has many other benefits for the child as well.

*Complications of Pregnancy.* According to a 2000 study, complications of pregnancy, specifically those involving the mother's uterus (such as post-birth hemorrhage, pre-term contractions, insufficient placenta, and restricted growth of the uterus), are associated with an increased risk of childhood asthma. Another 2000 study also reported that delivery procedures such as Cesarean section, the use of vacuum extraction or forceps also raised the risk of childhood asthma.

Obesity

In both adults and children, the incidence of obesity and asthma has been increasing in parallel over recent years. Studies report a strong association between the two conditions. Some experts suggest that excess weight pressing on the lungs may trigger the hyperreactive response in the airways typical of asthma. Others believe that asthma leads to obesity by inhibiting physical activity, although studies in 2000 and 2001 found no difference in activity levels between people with or without asthma. One 2000 study suggested that
many obese people may be misdiagnosed as having asthma when in fact they are simply short of breath, possibly because of the increased effort required for breathing.

In any case, there is some evidence that losing weight can relieve asthma symptoms. Weight loss in anyone who is obese and has asthma or shortness of breath reduces airway obstruction and improves lung function. [See Well-Connected Report #53 Weight Control and Diet.]

**Other Risk Factors**

*Damp Homes.* Studies from different parts of the world reported that children who live in damp homes have a much higher risk for asthma.

*Parental Migraines and Childhood Asthma.* Some studies have reported a link between childhood asthma and parental migraines, with one small 2000 study suggesting that children are about five times more likely to develop asthma if their parents have a history of migraines.

*Mental Health.* Research indicates that poor mental health of parents and children are significant predictors of more severe symptoms in childhood asthma. A 2000 study, in fact, suggested that high stress levels can predict the onset and severity of asthma in children genetically at risk for asthma.
WHAT ARE THE SYMPTOMS OF ASTHMA IN CHILDREN

In children with asthmatic symptoms, it is particularly important to first consider as a possible cause inhaled foreign objects such as peanuts, viral infections such as croup, and bacterial infections, which may be accompanied by high fever and progress rapidly. Any child who has frequent coughing or respiratory infections should be checked for asthma.

Typical Asthma Symptoms

The classic symptoms of an asthma attack are the following:

- Wheezing when breathing out is nearly always present during an attack. Usually the attack begins with wheezing and rapid breathing, and, as it becomes more severe, all breathing muscles become visibly active.
- Shortness of breath (dyspnea). Shortness of breath is a major source of distress in asthma patients, although severe dyspnea does not always reflect a serious attack or reduced lung function. In fact, some patients, particularly elderly patients, may not experience significant dyspnea but still have very poor lung function.
- Coughing. In some people the first symptom of asthma is a nonproductive cough. In fact, in a 2001 survey, 12% of asthma patients reported coughing as a significant problem. Patients surveyed tended to feel that daytime cough was even more distressing than wheezing or sleep disturbances.
- Chest tightness or pain. Initial chest tightness without any other symptoms may be an early indicator of a serious attack.
- The neck muscles may tighten, and talking may become difficult or impossible.
- Rapid heart rate.
- Sweating.
- Chest pain occurs in about three-quarters of patients. It can be very severe, although its intensity is not necessarily related to the severity of the asthma attack itself.

The end of an attack is often marked by a cough that produces a thick, stringy mucus. After an initial acute attack, inflammation persists for days to weeks, often without symptoms. (The inflammation itself must still be treated, however, because it usually causes relapse.)
WHAT TESTS MAY BE REQUIRED TO DIAGNOSE ASTHMA

The doctor will seriously consider a diagnosis of asthma if the child has a history of periodic attacks of shortness of breath, coughing, and wheezing, perhaps accompanied by tightness in the chest. The parent should describe the pattern of symptoms and possible precipitating factors, including the following:

- Whether symptoms are more frequent during the spring or fall (allergy seasons).
- Whether exercise, a respiratory infection, or exposure to cold air has ever triggered an attack.
- Any family history of asthma or allergic disorders, such as eczema, hives, or hay fever.

Ruling Out Other Diseases

A number of disorders may cause some or all of the symptoms of asthma: Panic disorder can coincide with asthma or be confused with it. Other diseases that must be considered during diagnosis are pneumonia, bronchitis, severe allergic reactions, psychosomatic illnesses, and certain rare disorders (such as tapeworm and trichomoniasis).

- Whether symptoms are more frequent during the spring or fall (allergy seasons).
- Whether exercise, a respiratory infection, or exposure to cold air has ever triggered an attack.
  
  Any family history of asthma or allergic disorders, such as eczema, hives, or hay fever.
GENERAL GUIDELINES FOR TREATING ASTHMA

General Guidelines for Treating and Managing Asthma on an On-Going Basis

Avoiding allergens, following appropriate drug treatments, and home monitoring are key elements in preventing dangerous asthma attacks and hospitalization. In addition, good communication between the physician and patients is a key factor in a successful management program. [For information on lifestyle changes for managing asthma, see What Are Lifestyle Ways to Manage Asthma And Reduce the Allergic Response?]

The Two-Pronged Approach: Treating Symptoms and Controlling the Disease

A combination of medications is important and effective for both treating and preventing asthma attacks. Parents can greatly reduce the frequency and severity of their children's asthma attacks by understanding the difference between coping with asthma attacks and controlling the disease over time. According to a few studies, most parents do not discriminate between medications that provide rapid short-term relief and long-term symptom control. Medications for asthma are categorized by their ability to (1) relieve symptoms and (2) control inflammation and reduce the chances for long-term injury.

- **Drugs Used to Open Airways for Symptom Relief.** Medications that open the airways (bronchodilators) are used promptly for any moderate or severe asthma attack. Usually, these agents are short-acting beta-adrenergic agonists (beta2-agonists). Others used in special cases include theophylline and certain anticholinergic agents. None of these agents have any effect on the disease process itself. They are only useful for treating symptoms.

- **Maintenance Drugs Used to Control Long-Term Inflammation and Prevent Long Injury.** Simply coping with asthma symptoms without also controlling the damaging inflammatory response is a common and serious error. For adults and children over five with moderate to severe persistent asthma experts now recommend inhaled corticosteroids and long-acting beta2-agonists, such as salmeterol (Serevent). Long-term control therapy is now recommended even for infants and young children who had three or more episodes of wheezing with the year that lasted more than a day and who have other risk factors for asthma. Other anti-inflammatory agents include leukotriene-antagonists and cromolyn, but they are less effective. [See Table Classification of Asthma Severity and Preferred Maintenance Treatments.]

Asthma flare-ups are much more common in children who do not comply with the prescribed treatment. In spite of the importance of this two-pronged approach, a significant number of moderate or severely asthmatic patients overuse their inhaled beta-agonists and underuse their corticosteroid medications. Studies report that less than half of children with severe asthma take a daily anti-inflammatory, and only a third use a peak flow meter to monitor their disease. The situation is far worse in inner city children with asthma, a group at high risk for severe complication.
## Classification of Asthma Severity and Preferred Maintenance Treatments

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<th>Classification</th>
<th>Symptoms</th>
<th>Lung Function</th>
<th>Preferred Maintenance Treatment</th>
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| Mild intermittent| **General Symptoms**: Occur twice a week or less.  
No symptoms and normal lung function between attacks. 
Attacks are brief (from a few hours to a few days) and may vary in intensity.  
**Nighttime Symptoms**: Occur twice a month or less. | FEV 1 or PEF is 80% or more than predicted.  
PEF variability is less than 20%. | Children five years and under: No daily medication.  
Children over five and Adults: No daily medication. If severe attacks occur, oral, injected, or intravenous corticosteroids recommended. |
| Mild Persistent  | **General Symptoms**: Occur more than twice a week, but less than once a day.  
Asthma attacks may be severe enough to affect activity.  
**Nighttime Symptoms**: More than twice a month. | FEV 1 or PEF is 80% or more than predicted,  
PEF variability is between 20% and 30%. | Children five years and under: Low-dose inhaled corticosteroids (with nebulizer, or MDI with holding chamber with or without face mask)  
Alternative: cromolyn or leukotriene-antagonist  
Children over five and Adults: Low-dose corticosteroids.  
Alternative: cromolyn, leukotriene antagonist, nedocromil, or sustained release theophylline. |
| Moderate Persistent| **General Symptoms**: Symptoms occur daily that require use of inhaled short-acting beta2-agonists.  
Symptoms twice a week or more and may last for days.  
Asthma attacks twice a week or more and may be severe enough to affect activity.  
**Nighttime Symptoms**: More than once a week. | FEV 1 or PEF is between 60% and 80% of predicted,  
PEF variability is more than 30%. | All Age Groups: Low to medium-dose inhaled corticosteroids and long-acting beta2-agonists.  
Alternative: Corticosteroids plus leukotriene antagonist or theophylline. |
| Severe Persistent | **General Symptoms**: Continual symptoms.  
Limited physical activity.  
Frequent asthma attacks.  
**Nighttime Symptoms**: Frequent. | FEV 1 or PEF is 60% or less than predicted,  
PEF variability is more than 30%. | All Age Groups: High-dose inhaled corticosteroids and long-acting beta1-agonists plus (if needed) oral corticosteroids. |

**NOTE**: An individual should be assigned to the most severe grade in which any feature occurs. The characteristics described are general and may overlap because asthma is highly variable. Many life-threatening situations have started in patients categorized with mild intermittent asthma. An individual’s classification may also change over time.

Devices Used for Administering Inhaled Drugs

Most asthma drugs are inhaled using various forms of inhalers or nebulizers. Inhaled agents must be used regularly as prescribed and the patient carefully trained in their use in order for them to be effective and safe. Studies suggest that many children fail to use the devices properly, although newer devices are easier to use than others. The basic devices are the metered-dose inhaler (MDI), breath-actuated inhalers, dry powder inhalers, and nebulizers.

MDIs have used chlorofluorocarbons (CFCs) as their propellants, which are damaging to the environment. Over time CFCs is being replaced with other propellants (e.g., hydrofluoroalkane) that are equally effective to CFCs, are environmentally safe, and do not chill the device as CFCs do. Devices that don’t use propellants at all are also now available. [See below].

Metered-Dose Inhaler. The standard device for administering any asthma medication has been the metered-dose inhaler (MDI). This device, particularly when used with a holding chamber, allows precise doses to be delivered directly to the lungs. MDI-delivered drugs must be used regularly as prescribed and the patient carefully trained in their use in order for them to be effective and safe. Some patients hold the MDI too close to their mouths, or even inside them. Others may exhale too forcefully before inhalation. The holding chamber, or spacer, allows the patient additional time to inhale the medication and so improves delivery. They vary, however, in their ability to deliver medication. For example, in one study the AiroChamber-Plus was more effective than the EasiVent in delivering an inhaled steroid. It should be noted that often MDIs continue to deliver propellant after the drug has been used up. Patients should track their medicine and throw the device away when the last dose has been administered. Nebulizers (not MDIs) are typically used in very small children, both at home and in the emergency room. However, recent studies suggest that with the use of a face mask and a spacer, the MDI is effective even for infants in the emergency room and may prove to be useable at home.

Breath-Actuated Inhalers. Breath-actuated rotary inhalers (e.g., Easi-Breathe and Autohaler) deliver the drug directly to the back of the throat as the user inhales. Their primary advantage over the MDI is their ease of use. They also do not use CFCs as propellants. In comparison studies, patients have been very successful with the breath-actuated inhalers. They are not recommended for children under eight years old.

Dry Powder Inhalers. Dry powder inhalers (DPIs) deliver a powdered form of beta2 agonists or corticosteroids directly into the lungs. They also do not use CFCs. Such devices include Rotahaler, Spinhaler, Turbohaler, Clickhaler, Easyhaler, Diskhaler, Discus, Twisthaler, Spiros, and others. DPIs are as effective as the older devices, and generally have a better taste and are easier to manage. They may differ among themselves, however, in their ability to deliver drugs into the airways. In one study, for example, the Turbohaler was easier to use than the Diskhaler and so achieved better delivery. The Discus is another effective DPI; it has a dose counter and protects against exhalation effects. More research is needed.

Humidity or extreme temperatures can affect their performance, so they should not be stored in humid places (e.g., bathroom cabinets) or locations subject to high temperatures (e.g., glove compartments during summer months).

Dry powder may cause tooth erosion and children are advised to rinse their mouths out right after taking the drug and to brush twice a day with a fluoride toothpaste.

Other Hand-Held Inhalers. Respimat delivers a fine-mist spray that is created by forcing the liquid medication through nozzles. It does not use any propellant.

Nebulizers. A nebulizer is a machine that delivers a fine spray of medication-containing liquid. Nebulizers are often used for children younger than three years and sometimes for older children who have difficulty using the MDI. It takes five to 10 minutes to administer any medication using a nebulizer. And, because the spray is less targeted than with the inhaler, it must deliver large amounts of the drug. This increases the risk for toxicity and severe side effects. Nebulizers should not be used by children who can manage an inhaler. Their use has been associated with a higher rate of hospitalizations and longer duration of symptoms than inhalers. If children must use an albuterol nebulizer, parents should be sure that it does not contain the preservative benzalkonium, which actually narrows the airways.
Non-Medical Treatment Strategies

Asthma triggers a vicious emotional-physical cycle:

- Breathlessness and wheezing incite a fear of suffocation and death, even in very small children.
- This anxiety produces further constriction on the muscles surrounding the airways, which makes breathing even more difficult.

Caregivers must first focus on alleviating their own anxiety, which can heighten a child's own fears. The next step is to help the child relax. One method for this is as follows:

- The child sits comfortably, bending slightly forward with the eyes closed.
- The hands are placed gently over the navel.
- The child is then told to pretend the stomach is a balloon.
- The "balloon" must be "blown up" by inhalation, not exhalation. The child can tell if this working because the hands will move slightly apart.
- When the child breathes out, the "balloon" will be made flat.

This exercise both relaxes the child and discourages shallow, oxygen-poor breathing. Massaging the child in gentle circles on the chest is relaxing and may also loosen mucus.

Other recommendations include the following:

- A child may also find relief by lying stomach-down on several pillows so that the head is slightly lower than the chest while the caregiver gently pats the back between the shoulder blades.
- Giving the child warm liquids, such as soup or hot cider, is effective in loosening mucus and may also relax bronchial muscles. Cold fluids, like cold air, should be avoided.
- Overhydration, too much liquid, can be harmful, however, so these drinks should not be forced on the child.
- Warm, moist air from vaporizers can greatly ease and moderate asthma attacks.
- Daily massages and breathing and relaxation techniques to reduce stress can be very helpful.

Monitoring

Many adults self-manage their asthma using daily monitoring of peak air flow with adjustments of the medications as needed. It involves the use of a peak flow meter, which measures peak expiratory flow rate (PEFR). Studies suggest, however, that for most children with asthma, an educational program is just as effective for managing the condition as monitoring. Most children, then, do not need to monitor their peak air flow on any regular basis.
DRUGS TO TREAT SYMPTOMS OF ACUTE ASTHMA ATTACKS

Short-Acting Beta2-Agonists

Beta2-agonists do not reduce inflammation or airway responsiveness but serve as bronchodilators, relaxing and opening constricted airways during an acute asthma attack. A short-acting inhaled beta2-agonist, taken as needed, is often the only medication used by children with chronic mild asthma.

Specific short-acting beta2-agonists include the following:

- Albuterol (Proventil, Ventolin), called salbutamol outside the U.S., is the standard short-acting beta2-agonist in America. Other similar beta2-agonists are isoproterenol (Isuprel, Norisodrine, Medihaler-Iso), metaproterenol (Alupent, Metaprel), pirbuterol (Maxair), terbutaline (Brethine, Brethaire, Bricanyl), and bitolterol (Tornalate). Isoetharine (Bronkometer, Bronkosol is available in nebulizers.
- Newer beta2-agonists, including levalbuterol (Xopenex), have more specific actions than the standard agents. Xopenex is administered with a nebulizer and studies have indicated that it is as effective as albuterol with fewer side effects. (It is very expensive, however.)

Short-acting bronchodilators are generally administered through inhalation and are effective for three to six hours. They relieve the symptoms of acute attacks, but they do not control the underlying inflammation. If asthma continues to worsen with the use of these

Side Effects of Beta2-Agonists. Side effects of all beta2-agonists include the following:

- Anxiety.
- Tremor.
- Restlessness.
- Headache.
- Patients may experience fast and irregular heartbeats. A physician should be notified immediately if such side effects occur.
- These drugs should be taken with caution by children with diabetes or a history of seizures.
- Beta2-agonists have serious interactions with certain drugs and parents should tell the physician about any other medications their child is taking.

Loss of Effectiveness and Overdose. There has been some concern that both short-acting beta2-agonists become less effective when taken regularly over time, increasing the risk for overuse. Over time some patients may become tolerant to many effects of short-acting beta2-agonists. The degree to which this affects the airways is uncertain. In some studies, the duration of action has declined but the peak effect appears to be preserved, making these drugs still useful for acute attacks. Regular use of long-acting beta2-agonists may increase the chances of a reduced effect from the short-acting forms.

Other Bronchodilators

Theophylline. Theophylline (Theo-Dur, Theolair, Slo-Phyllin, Slo-bid, Constant-T, Respbid) is a mild to moderate bronchodilator that has been used to treat childhood asthma for more than 30 years. It is useful for treating nocturnal asthma and may also have anti-inflammatory qualities even in low doses.

Available in tablet, liquid, and injectable forms, some theophylline sustained-release tablets and capsules have a long duration of action and can therefore be taken once or twice a day with good results.

It does have some problems, however. Side effects include changes in behavior, mood, and memory. If theophylline is not taken exactly as prescribed, an overdose can easily occur. Toxicity causes the following symptoms: nausea, vomiting, headache, insomnia, and, in rare cases, disturbances in heart rhythm and convulsions. A physician should be contacted immediately if any of these side effects occur.

The risks for these adverse effects are small if the drug is taken exactly as prescribed but the following precautions should be noted:
• Infants tend to metabolize the drug extremely slowly and, therefore, should receive very low doses.
• By the time asthmatic children reach one year old, however, they metabolize the drug faster than adults. There is a risk, therefore, of toxic effects.
• Fever and certain antibiotics may slow down the rate at which theophylline is eliminated from the body. In such cases, the doctor may want to reduce the dosage of theophylline.

If a child is taking theophylline on an ongoing basis, the doctor should monitor the drug level at the start of therapy and at regular intervals thereafter.

Anticholinergic Agents. Inhaled ipratropium bromide (Atrovent) acts as a bronchodilator over time. Ipratropium bromide alone is only modestly beneficial for acute asthma attacks. In fact, the drug is not approved specifically for asthma. Some parents report benefit for treating wheezing in infants. It is also sometimes used in the emergency room to treat children with severe asthma to enhance the effects of intravenous beta2-agonists.
DRUGS TO PREVENT ASTHMA ATTACKS & REDUCE AIRWAY INFLAMMATION

Corticosteroids
Corticosteroids, also called glucocorticoids or steroids, are powerful anti-inflammatory drugs. Steroids are not bronchodilators (that is, they do not relax the airways) and have little effect on symptoms. Instead, they work over time to reduce inflammation and prevent permanent injury in the lungs. Many studies have now shown that the use of inhaled corticosteroids in patients with moderate to severe asthma significantly reduce the rate of rehospitalizations and deaths from asthma. Nevertheless, they are still significantly underprescribed in the patients who need them most.

**Inhaled Corticosteroids.** Inhalation of corticosteroids makes it possible to provide effective local anti-inflammatory activity in the lungs with minimal systemic effects. (Oral steroids have considerable side effects.) They are currently recommended as the primary therapy under the following circumstances:

- For any asthmatic condition more serious than occasional episodes of mild asthma. (Low-doses of inhaled steroids may even be safe and effective for some people with mild asthma, particularly those who find themselves using beta2-agonists daily.)
- When treatment with bronchodilators is not effective.

Examples of inhaled corticosteroids are the following (not all are available to children):

- The most recent generation of inhaled steroids include (in order of potency) fluticasone (Flovent), budesonide (Pulmicort), triamcinolone (Azmacort and others), and flunisolide (AeroBid). In general, the newer agents, are more powerful than the older generation of inhaled agents. Budesonide (Pulmicort Respules) is available in a jet nebulizer for children from 12 months to 8 years. It is, in fact, the first such medication to be approved for children in this age group.
- The older corticosteroid inhalants are beclomethasone (Beclovent, Vanceril) and dexamethasone (Decadron Phosphate Respihaler and others). They are less powerful than the newer steroids when delivered with standard inhalers. New inhalers that use very fine sprays (e.g., QVAR, Autohaler) deliver the agents deep into the lungs may prove to be as effective as the newer, more potent steroids.
- Inhalers that combine both long-acting beta2-agonists and corticosteroids are now available.

Evidence strongly suggests that early treatment with corticosteroids is important for children with severe asthma to prevent deterioration in lung function.

Side effects of inhaled steroids are the following:

- The most common side effects are throat irritation, hoarseness, and dry mouth. These effects can be minimized or prevented by using a spacer device and rinsing the mouth after each treatment.
- Rashes, wheezing, facial swelling (edema), fungal infections (thrush) in the mouth and throat, and bruising are also possible but are not common with inhalators.
- Some children experience changes in mood, memory, and behavior. They are not are not permanent.
- Some studies have suggested a higher risk for gum inflammation.
- It is well known that oral steroids reduce bone density and research now reports that inhaled steroids--both older and newer agents--also may affect bone growth and density. Of some comfort are a number of studies reporting only a slightly less (about half an inch) effect on children's growth, which may be only temporary. It is still unknown if these drugs have any significant long-term effect on bone density. Calcium supplements appear to help prevent bone loss due to inhaled steroids.
- It is not yet known, however, whether inhaled steroids affect lung growth in very young children. Steroids administered using nebulizers are of particular concern.
There is also some concern that the more potent agents, particularly fluticasone, suppress the adrenal system to a greater degree than other steroid inhalants. This effect in turn reduces levels of natural steroids—notably cortisol, the major stress hormone. (This is a serious side effect of oral steroids.) Of note, sudden changes in consciousness may suggest hypoglycemia, which can occur with adrenal insufficiency and was reported in a few children taking high doses of fluticasone. A 2002 study also observed abnormally lower morning levels of cortisol in children taking fluticasone. Because the newer potent agents, particularly fluticasone, may produce major side effects similar to oral steroids, it is important to aim for the lowest effective dose possible. Fortunately, some studies suggest that low doses of fluticasone may achieve the same benefits as with high ones, thus reducing risks for serious side effects. Better delivery methods may also allow lower doses. For example, an encouraging 2002 study suggested that administering lower doses of beclomethasone using an Autohaler, which delivers the drug in an extra-fine spray, were as effective as higher doses delivered with an MDI. At this time experts caution against corticosteroids for infants and toddlers with mild asthma and urge close monitoring especially for children under five with severe asthma who are receiving high doses.

Oral Corticosteroids. Oral agents are usually the last drugs to be added to an asthma treatment program and the first to be removed. Common oral corticosteroids include prednisone/prednisolone, dexamethasone, methylprednisolone, and hydrocortisone. They reduce inflammation very effectively, but children generally take them only for five days after hospitalization for an acute attack. Compliance among children can be low, however, since these agents have a bitter taste and can cause vomiting. Taking oral dexamethasone for two days may be as effective and more tolerable than the standard a five-day regimen of prednisone/prednisolone. Prolonged use of oral steroids has widespread and sometimes serious side effects, and so they are not generally give to children for longer than a few days.

Long-Acting Beta2-Agonists and Corticosteroid Combinations

Long-acting beta2-agonists, including salmeterol (Serevent) and formoterol (Foradil) plus inhaled corticosteroids are now the preferred preventive treatment for adults and children with moderate to severe asthma. Long-acting beta2-agonists are used for preventing an asthma attack (not for treating symptoms). The effects of one dose of a long-acting beta2-agonist last for about 12 hours, so they are particularly effective during the night. These agents also may be used for prevention of exercise-induced asthma in people and to protect against aspirin-induced asthma.

In comparison studies, salmeterol and formoterol appear to be equally beneficial. Formoterol has a much faster action, however, and may achieve better control of nighttime asthma. Formoterol, in fact, works almost as fast as the short-acting albuterol and is sometimes used to treat asthma symptoms. Salmeterol should never be used for treatment of acute episodes [See Specific Warning on Salmeterol, below.] For this purpose, short-acting bronchodilators should be used. (Formoterol has a faster action and may, in some cases, be used for treating symptoms, but patients should check with their physician.)

Long-acting forms are not used alone on any regular on basis, since they may reduce the effectiveness of the short-acting beta2-agonists (the mainstays for treating acute attacks). In patients with moderate to severe asthma, the long-acting beta2 agonists are best used in combination with anti-inflammatory drugs. In fact, unlike short-acting forms, these beta2-agonists may even have anti-inflammatory properties. A single inhaler (Advair Diskus) that combines both long-acting beta2-agonists and corticosteroids is now available for children over age 12. This inhaler appears to be safe and possibly more effective that either agent used alone for patients who do not respond well to other treatments.

Studies indicate that these are safe for children and may, in fact, be particularly effective for them. In one year-long study of children with mild to moderate asthma, salmeterol was not as effective as the corticosteroid beclomethasone, but it did reduce asthma symptoms without retarding growth.

Side Effects. Side effects of long-acting beta2-agonists are similar to the short-acting agents. [See Short-Acting Beta2 Agonists under What Are the Specific Drugs Used to Treat Symptoms of Acute Asthma Attacks?]

Specific Warning on Salmeterol. A 2003 study using salmeterol (Serevent) was stopped after observations of a trend toward a higher incidence of serious and even fatal asthma episodes in patients who used the drug. For some time, experts have warned that salmeterol requires up to 20 minutes to achieve
effectiveness and there is a danger of overdose if a patient is not aware of this delay and takes additional doses to achieve faster relief. Serevent, then, should never be used for stopping an attack. (Overdose has been fatal in rare cases.) The risk for serious asthma episodes with salmeterol appears to be highest in African-American and elderly patients with severe asthma.

Leukotriene-Antagonists

Leukotriene-antagonists (also called anti-leukotrienes) are oral medications that block leukotrienes, powerful immune system factors that, in excess, produce a battery of damaging chemicals that can cause inflammation and spasms in the airways of people with asthma. As with other anti-inflammatory agents, leukotrienes are used for prevention and not for treating acute asthma attacks.

The leukotriene-antagonists include zafirlukast (Accolate), montelukast (Singulair), zileuton (Ziflo), and pranlukast (Ultair, Onon). These agents are proving to be effective for long-term prevention of asthma, including exercise-induced asthma and aspirin (or NSAID)-induced asthma. Unfortunately, most studies to date are still reporting better success with inhaled corticosteroids than with the leukotriene-antagonists. Their anti-inflammatory actions are different from those of steroids, however, and combinations of the two agents are being tried. A 2002 analysis of 13 studies, however, reported only modest benefits when anti-leukotrienes were added to corticosteroids. The combination did improve asthma control in some of the studies, but they did no reduce corticosteroid use. (In all but one of these studies the subjects were adults. It is not clear if these results are applicable to children.)

Nevertheless, studies suggest that montelukast, which comes in a chewable tablet, may be particularly useful for managing asthma in small children (ages two to five) with asthma, since they have trouble with inhaled steroids. As suggested by another 2000 study on the effects of zafirlukast, they may also reduce the severity of cat allergies, regardless of whether or not asthma is also present.

Side Effects and Complications. Gastrointestinal distress is the most common side effect of leukotriene-antagonists. Very few other side effects have been reported. In general, these agents appear to be safe and well tolerated.

Of some concern are reports of Churg-Strauss syndrome in a few people taking zafirlukast or montelukast. Churg-Strauss syndrome is very rare, but it causes blood vessel inflammation in the lungs and can be life threatening. Oral steroids quickly resolve the problem. In fact, usually the syndrome has occurred in patients who were tapering off steroids and changing over to the leukotrienes-antagonists. Some experts believe that, in such cases, the steroids may simply have masked the presence of the disorder, which then developed when the steroid drugs were withdrawn. Symptoms include severe sinusitis, flu-like symptoms, rash, and numbness in the hands and feet.

Other concerns are indications of liver injury in patients taking zileuton and zafirlukast when taken at higher than standard doses. No adverse effects on the liver have been reported to date with montelukast.
EXPERIMENTAL & OTHER TREATMENTS USED FOR ASTHMA

Monoclonal Antibodies

Monoclonal antibodies (MAbs) are genetically developed agents that are designed to target and attack very specific factors. The following are under investigation. Omalizumab (Xolair) is currently the best studied MAb for asthma. It prevents the antibody immunoglobulin E (IgE) from triggering the inflammatory events that lead to asthmatic attacks. Studies are reporting lower use of corticosteroids, fewer hospitalizations, and significant symptom improvements. The agent is showing promise in all age groups. Because IgE may play a greater role in causing childhood asthma, however, omalizumab be even more helpful for children than adults. It is currently awaiting FDA approval.

Alternative Treatments

Alternative therapies are being widely used by children, adolescents, and adults with asthma. In one study, nearly half of asthma or allergy sufferers resorted to alternative treatments. To date, however, evidence does not support any value from most alternative therapies, including high-dose vitamins, urine injections, homeopathic remedies, and most herbal remedies.

Relaxation and Stress-Reduction Techniques. Patients report benefits from many stress reduction and physical techniques, such as acupuncture, hypnosis, breathing relaxation techniques, the Alexander technique, massage therapy, and meditation practices. There have been very few well-conducted studies supporting their use, however.

Breathing Exercises. Some studies have suggested that breathing exercises or training may be helpful. A number of different methods are available. One example is the Buteyko breathing method, an experimental approach designed to increase levels of carbon dioxide in the body. To do this, patients are trained to reduce their volume of breath and to avoid hyperventilation (over-breathing). Some studies are reporting that patients use this method reduce their use of medications and improve their quality of life. The system originated in Australia and is not yet widely available in the U.S.

Probiotics. Probiotics are beneficial bacteria that may help protect against allergies and asthma. Antibiotic over-use and modern hygiene may specifically be reducing these helpful organisms. Probiotics can be obtained in active yogurt cultures and in supplements, which are being studied for protection.

Herbal Remedies. Herbal remedies have been used with apparent success in Eastern nations, but few have been studied rigorously in the United States. Butterbur (also known as Petasites hybridus, butter dock, bladderock, bog rhubarb, and exwort), a traditional herbal remedy, is used for seasonal allergies and asthma. In a 2002 study, it was as effective and less sedating than a commonly prescribed antihistamine for treating seasonal allergies over a two week period. More research is needed. Even when natural remedies appear to be effective in trials, there are no standards or regulations in the U.S. to guarantee their quality, effectiveness, or safety. Of great concern are their growing use and the possibilities of serious drug interactions. Patients who try alternative treatments must be sure to inform their physician.

Warnings on Alternative and So-Called Natural Remedies

Alternative or natural remedies are not regulated and their quality is not publicly controlled. In addition, any substance that can affect the body's chemistry can, like any drug, produce side effects that may be harmful. Even if studies report positive benefits from herbal remedies, the compounds used in such studies are, in most cases, not what are being marketed to the public. There have been a number of reported cases of serious and even lethal side effects from herbal products. In addition, some so-called natural remedies were found to contain standard prescription medication.

The following are special concerns for people with asthma and allergic rhinitis:

- Grapeseed extract is sometimes touted as a natural antihistamine. A 2002 study, however, reported no benefits from it.
- A 2002 study found no benefits with homeopathy immunotherapy for asthmatic patients allergic to dust mites.
• Some allergic patients have reported worse symptoms after drinking herbal teas, which may contain leaves or pollens that the patient is sensitive to. In fact herbal remedies themselves can trigger an allergic reaction. For example, echinacea is of special concern. This herbal remedy actually boosts the immune system. People with nasal congestion may mistakenly take it because it is often used to treat colds. In the case of allergies, however, echinacea may worsen symptoms or even trigger them in people who haven't experienced them. People with autoimmune diseases or who have plant allergies should particularly avoid it.

• Aller Relief Chinese herbal cold and allergy contains trace amounts of aristolochic acid, a chemical that is toxic to the kidneys and a carcinogen. Products containing aristolochic acid have been associated with several reports of kidney failure in Europe. Of specific concern are studies suggesting that up to 30% of herbal patent remedies imported from China having been laced with potent pharmaceuticals such as phenacetin and steroids. Most reported problems occurred in herbal remedies imported from Asia, with one study reporting a significant percentage of such remedies containing toxic metals.

• Aromatherapy is now often used for relaxation. Some exotic plant extracts in these formulas have been associated with a wide range of skin allergies.

The following website is building a database of natural remedy brands that it tests and rates. Not all are available (www.ConsumerLab.com). The Food and Drug Administration has a program called MEDWATCH for people to report adverse reactions to untested substances, such as herbal remedies and vitamins (call 800-332-1088).
WAYS TO MANAGE ASTHMA & REDUCE THE ALLERGIC RESPONSE

The more allergies a child has, the more severe the asthma. Making lifestyle changes to reduce allergy attacks and other triggers is extremely important.

Indoor Protection

House dust is a reservoir for pollen and dust mites. Some experts believe that reducing household allergens and pollutants in the home could reduce asthma in children by 40%. In addition, a 2002 study suggested that this approach might reduce the risk for asthma and allergies before it develops in small children.

Controlling Pets. People with asthma who already have pets and are not allergic to them probably have a low risk for developing such allergies later on. In fact, when children are exposed to more than one dog or cat during their first year, they have a much lower risk for allergies and asthma.

For children who have an existing allergy to pets, however, the pets should be given away or kept outside. If this isn't possible, they should at least be confined to carpet-free areas outside the bedroom. Cats harbor significant allergens, which can even be carried on clothing; dogs usually present fewer problems. Washing animals once a week can reduce allergens. Dry shampoos, such as Allerpet, are now available for both cats and dogs that remove allergens from skin and fur and are easier to administer than wet shampoos.

Preventing Exposure to Cigarette and Cooking Smoke. Parents who smoke are strongly urged to make strenuous efforts to quit. Studies are finding that exposure to second-hand smoke in the home increases the risk for asthma and asthma-related emergency room visits in children. And, just smoky cooking can worsen asthma.

Parental smoking has been shown to increase the airway responsiveness of infants as early as the first two to 10 weeks of life. This extends even to the fetus of pregnant women who smoke. Such mothers tend to have babies born at a low birth weight, which affects lung function and increases babies' risks for asthma.

Sadly, the more heavily parents smoke, the less likely they are to seek treatment for their asthmatic children, according to a 2000 study. The authors of this study speculate that either the parents may have reduced awareness of their children's symptoms, or else they may not want to be told to quit smoking by their children's doctors. [For help in quitting, see the Well-Connected Report # 41, Smoking.]

Controlling for Dust. A 2002 study reported that simply using a spray furniture polish is very effective for reducing both dust and allergens. Air cleaners, filters for air conditioners, and vacuum cleaners with HEPA filters can help remove particles and small allergens found indoors. Neither vacuuming nor the use of anti-mite carpet shampoo, however, is effective in removing mites in house dust. In fact, vacuuming stirs up both mites and cat allergens. Carpets and rugs should be avoided, if possible.

Bedding and Curtains. Using semipermeable coverings to fully encase mattresses and pillows is the most proven effective step in reducing dust mite levels. (Vinyl mattress covers limit airflow and may also exacerbate, or even cause, asthma in children. Synthetic pillows may pose a significantly higher risk for severe asthma attacks in children than feather or no pillows, although well-conducted studies are needed to confirm this.) Curtains should be replaced with shades or blinds and bedding washed using the highest temperature setting.

One 1999 study found that children sleeping in bottom bunk beds are significantly more likely to develop asthma than siblings occupying the upper bunks. Families with asthmatic or allergic children should avoid bunk beds or be sure that children with asthma sleep in the top bunk. Even with standard beds, it may be useful to have them sleep as high off the floor as possible.

Reducing Humidity in the House. Although warm, moist air from vaporizers can greatly ease and moderate asthma attacks, living in a damp house is counter productive. Dust mites thrive in humidity and damp houses increase the risk for mold. On-going humidifiers, then, can be counterproductive. If they are used, humidity levels should not exceed 40% and they should be cleaned daily with a vinegar solution.

Exterminating Pests (Cockroaches and Mice). Cockroaches should be eliminated by professional exterminators. (One study reported that ridding a home of cockroaches and cleaning the house using...
standard housecleaning techniques failed to eliminate the cockroach allergens themselves.) Mice should be eliminated, and attempts should be made to remove all dust, which might contain mouse urine and dander.

*Disposable Diapers.* Of concern was a 1999 study that reported lung irritation in mice exposed to chemical emissions from several brands of disposable diapers. Researchers in this study recommend that children with asthma or other respiratory diseases should use cloth diapers and avoid disposable diapers until more research has been conducted.

**Outdoor Protection**

*Avoiding Outdoor Allergens.* The following are some recommendations for avoiding allergens outside:

- Camping and hiking trips should not be scheduled during times of high pollen count (in the Northern states, May and June for grass pollen and mid-August to October for ragweed).
- Patients should avoid strenuous activity when ozone levels are highest, which usually occur in early afternoon, particularly on hot hazy summer days. Levels are lowest in early morning and at dusk.
- Asthma attacks are often higher during thunderstorms. Some evidence points to a build-up of ozone that accompanies such storms. Other evidence suggests that the changing airflow patterns bring a sudden downdraft of air containing concentrations of pollens, small particles and allergens.
- Patients who are allergic to mold should avoid barns, hay, raking leaves, and mowing grass.
- Exposure to automobile fumes may worsen asthma. Fungi in car air conditioners can also be a problem.

*Reducing Exposure to Air Pollution.* A number of studies have linked air pollution to asthma. Children breathe faster than adults, taking in more pollutants, and therefore appear to be particularly susceptible to soot and other small particles in the air. A 2001 study found an association between higher rates of asthma and other health problems in children who were exposed to high levels of specific pollutants (particularly sulfur dioxide and nitrogen dioxide). Diesel fuel exhaust has also been associated with worsened asthma in children.

Some experts point out that asthma rates in North America have increased over recent years while the prevalence of many common air pollutants have declined. So pollution is unlikely to be a primary cause of asthma. Regardless of whether pollution is an important cause of asthma, evidence strongly suggests that it can worsen existing asthma.

The effects of specific pollutants are unclear and conflicting. For example, some research indicates that nitrogen dioxide increases hospitalization in childhood asthma by precipitating upper respiratory infections. There are conflicting reports on the effects of ozone, however. Some studies indicate that high levels do not increase the risk for hospitalization from asthma attacks, although other studies indicate that such findings may apply to children.

**Medications for Treating Seasonal Allergies**

Patients with chronic allergic rhinitis may require daily medications. Patients with severe seasonal allergies may be advised to start medications a few weeks before the pollen season, and to continue it until the season is over. Effective medications include the following:

- Anti-inflammatory Agents. Nasal corticosteroids are now considered to be the most effective measure for preventing allergy attacks. Comparison studies are reporting that nasal steroid sprays are more effective than the second generation antihistamines loratidine (Claritin) and cetirizine (Zyrtec). One study also indicated that nasal steroid treatment was more effective than allergy shots. Leukotriene-antagonists and nasal cromolyn may be beneficial in specific cases of allergies.
- Antihistamines. A 2002 study reported that infants with allergies who were given the antihistamine cetirizine (Zyrtec) were much less likely to develop asthma later on. This encouraging research warrants more work.
- Allergen immunotherapy ("Allergy Shots"). Immunotherapy, commonly called allergy shots, is proving to reduce asthma symptoms and the use of asthma medications in patients with known allergies. It is not yet
known if this approach is more effective or safer than other therapies. Although injections are the standard method of delivery, immunotherapy is also being delivered as tablets under the tongue (sublingual). They are safe but less effective than the shots. Immunotherapy poses some risk for severe allergic reactions, particularly in people who are allergic to multiple allergens.

[For detailed information see Well-Connected Report #77 Allergic Rhinitis (Hay Fever and Rose Fever) and Chronic Nasal Congestion.]

**Dietary Factors**

*Weight Loss.* Children who are both asthmatic and overweight may reduce asthma symptoms simply with weight loss.

*Fruits, Vegetables, and Whole Grains.* Healthy foods are important for lung function. Specific foods that may be important for healthy lungs are those that contain antioxidants (best obtained from fresh, deep green and yellow-orange fruits and vegetables), selenium (fish, red meat, grains, eggs, chicken, liver, garlic), plant chemicals called flavonoids (apples, onions), and magnesium (green leafy vegetables, nuts, whole grains, milk, and meats).

*Fish Oil.* Omega-3 fatty acids, found in cold water oily fish and in supplements (preferably DHA-EPA, which are the important compounds in fish oil) have anti-inflammatory effects. Some evidence suggests they may be helpful for people with asthma, although it is weak.

*Caffeine.* Caffeine has properties that are similar to theophylline, an agent used to treat asthma. A major analysis of studies reported that caffeine improved lung function for up to four hours after consumption. Although tea and coffee are the major sources of caffeine some sodas contain it and perhaps could tried when children have an asthma attack during the day. (People who are going to have their lung function tested should avoid drinking coffee, tea, or other caffeinated beverages for at least four hours beforehand.)

*Food Allergies.* Although 67% of asthmatics believe their symptoms are aggravated by food allergies, studies indicate that this belief may be true in only 5% of cases. If young children show signs of or test positive for food allergies, however, parents should be extra cautious in preventing exposure to any asthma trigger. Some physicians now counsel all children with asthma to avoid nuts entirely, and, of course, children who experience reactions to any foods should avoid them. Chemicals that may pose some risk for an allergic reaction are monosodium glutamate, or MSG (found in some canned soups, cheese, and certain vegetables), and sulfites (preservatives in foods, such as frozen potatoes and tuna). Contrary to what many believe, dairy products do not appear to exacerbate asthma symptoms in people who are not already allergic to them.

**Exercise**

Asthmatic children should be encouraged to swim and play sports, such as baseball, that will present less difficulty for them. Intense activities lasting less than two minutes, such as sprinting or competitive swimming, are less problematic than longer exercises.

It should be noted that asthma is no reason to avoid exercise. Historically, about 10% of US athletes who participated in the Olympics have been asthmatic. Some studies are indicating that long-term exercise may even help control asthma and reduce hospitalization.

Young people who enjoy running should probably choose an indoor track to avoid pollutants. Swimming is excellent for people with asthma. Yoga practice, which uses both stretching, breathing, and meditation techniques may have particular benefits. One study reported that two thirds of patients who practiced yoga regularly were able to reduce or stop taking their asthma medications.

Patients should consult their physicians before embarking on any exercise program. Exercise-induced asthma is a limited that has specific recommendations. [See Box Exercise-Induced Asthma (EIA).]

**Preventing and Treating Respiratory Infections**

People with asthma should try to minimize their risk for respiratory tract infections. Washing hands is a very simple but effective preventive measure.
There has been some question concerning influenza vaccinations because of some reports that vaccines may worsen asthma. Recent and major studies have been reporting, however, that the vaccination is safe for adults and children. It is also very important for patients to reduce their risk for respiratory diseases. Still, 90% of asthma patients remain unvaccinated.

Asthma patients should ask their physicians about the flu vaccine and also whether they should receive the vaccination against pneumococcal pneumonia.

**Reducing Stress and Negative Moods**

People with asthma have no higher rate of anxiety or depression than the general population. However, such emotions interact with the effects of asthma and its treatments in important ways:

- Negative emotions can discourage compliance with medication and the ability to cope.
- Poor control of asthma symptoms, in turn, increases the risk for negative emotions.
- Stress and depression have been associated with more severe symptoms and even an increased risk of fatal asthma attacks.

Some evidence suggests that stress reduction techniques, a positive attitude and relaxation techniques may be very helpful in the long-term management of asthma. [See the Well-Connected Report # 31 Stress.]
WHERE ELSE CAN CHILDREN WITH ASTHMA GET HELP

Allergy and Asthma Network, Mothers of Asthmatics (www.aanma.org). Call (800-878-4403).
The American Lung Association (www.lungusa.org). Call (800-LUNG-USA)
American College of Allergy, Asthma & Immunology (www.allergy.mcg.edu). Call (847-427-1200).
American Academy of Allergy, Asthma, and Immunology (www.aaaai.org). Call (800-822-2762).
National Jewish Center for Immunology and Respiratory Medicine (www.njc.org). Call (800-222-LUNG).
National Allergy Supply (www.natlallergy.com). (Call 800-522-1448).
Allergy Control Products (www.allergycontrol.com). Call (800-422-DUST).