A CLOSER LOOK AT ASTHMA, PART II

by Bill Wojciechowski, MS, RRT

Asthma was defined as a chronic inflammatory disease of the tracheobronchial tree. It is characterized by airway hyperresponsiveness to a variety of antigens or stimuli that cause bronchoconstriction, chest tightness, wheezing, increased mucus production and air flow limitation, all of which are reversible either spontaneously or through pharmacologic intervention. The literature is filled with numerous definitions of asthma.

Regardless of the phenotype of asthma a person has, these pathophysiologic developments generally occur during all asthma exacerbations. At the same time, however, some asthma phenotypes (allergic and non-allergic) are controlled somewhat pharmacologically different. The more well-known asthma phenotypes include allergic asthma, non-allergic asthma, nocturnal asthma and aspirin sensitivity asthma.

Allergic (extrinsic) asthma

Allergic asthma, also called extrinsic asthma, is the most common form of asthma. It is responsible for up to 90 percent of all childhood asthma and about 50 percent of all asthma in adults. Interestingly, allergic asthma in children often abates when these patients reach their teen to late teen years, but it commonly re-emerges later in adult life.

An allergy is a hypersensitive, or exaggerated, reaction by the body's immune system in response to an encounter with a substance that the immune system perceives as a foreign or harmful substance. These substances are called allergens. When a person who is predisposed to allergies initially comes in contact with an allergen, antibodies called immunoglobulin E (IgE) are generated by the immune system. These IgE antibodies attach to mast cells by way of surface receptors.

Mast cells are residents of tissues throughout the body, and reside in connective tissue. Ordinarily, they do not circulate in the blood. They are located predominantly in proximity to blood vessels along surfaces that interface the external environment such as the nose, lungs and gastrointestinal system.

Each IgE molecule is specific for one type of allergen only. This IgE-allergen specificity explains why one person is allergic only to dust mites, while another person tolerates dust mites but is allergic to animal dander. Why one person has a predilection for a certain allergen and another person has a proclivity for another is not understood. That disparity encompasses genetics because these traits are often common among some family members. Persons who have inherited the tendency to develop IgE antibodies to certain allergens are said to have atopy.

Allergic asthma has innumerable triggers. They include house dust mites, animal dander, various pollens and cockroach droppings. After a number of contacts with a particular allergen, a person predisposed to allergies will become sensitive to that allergen. Eventually, when enough IgE molecules are positioned on the surface of mast cells, an encounter with the responsible allergen will cause antigen-antibody reactions to occur along the mast cell surface. During that time, the mast cell membrane degranulates, and preformed mediators of inflammation are unleashed. These mediators include leukotrienes, prostaglandins, platelet activating factor, histamine and cytokines, to name a few.

Two hypersensitivity reactions are typically involved with allergic asthma: immediate and delayed. Immediate hypersensitivity reactions are mediated by IgE. An immediate hypersensitivity reaction generally occurs within five to 15 minutes after exposure to the offending antigen. Sometimes the reaction will develop in less time, hence the term immediate. The delayed response tends to occur about four to six hours following exposure to the allergen. This delayed response accounts for a quick return to the emergency department when a person with this type of asthma is discharged early or without oral corticosteroids.

The primary cellular components responsible for the immediate hypersensitivity reactions are the mast cells or basophils. On the other hand, cytokines from mast cells appear to play a role in the persistence of long-term effects influencing the delayed hypersensitivity response.

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Depending on the severity of a person's asthma, a patient who has allergic asthma tends to receive an inhaled corticosteroid and a long-acting bronchodilator. They also have a short-acting beta-2 agonist available for quick relief when necessary.

Omalizumab, a monoclonal antibody, also may be used for severe IgE mediated asthma. Omalizumab binds with IgE molecules in circulation, preventing the IgE molecules from binding with receptors on the mast cell surface. The dose varies with the patient's weight and IgE level and is administered subcutaneously.

Non-allergic (intrinsic) asthma

Approximately 30 percent of all asthma involves non-allergic asthma. As the name implies, non-allergic asthma is not caused by allergies. It usually develops after the age of 40 and is not typically associated with allergies. Women are more frequently involved. The condition tends to be difficult to treat, and symptoms are often chronic and year-round.

The triggers of non-allergic asthma include tobacco smoke, wood smoke, chalk dust, perfumes, household cleaners, stress, viral infections and gastroesophageal reflux. The immune system is not involved with intrinsic asthma.

As with allergic asthma, essential to managing intrinsic asthma is learning to recognize one's triggers. These patients generally maintain asthma control with daily use of a combination of inhaled corticosteroid and long-acting beta-2 agonist, and having a short-acting beta-2 agonist available for quick relief.

Nocturnal asthma

Nocturnal asthma is characterized by chest tightness, shortness of breath, cough and wheezing at night that interrupts the patient's sleep. Statistics reveal that most deaths related to asthma take place at night. Nocturnal asthma attacks can cause significant problems sleeping, resulting in sleep deprivation, daytime sleepiness, fatigue and irritability. These problems often affect the patient's quality of life overall and make controlling daytime asthma symptoms more difficult.

Studies have demonstrated that alveolar tissue eosinophils increase in patients with nocturnal asthma, and that they exhibit a decrease in nighttime pulmonary function. Exactly why asthma symptoms worsen at night for these patients is unknown. However, studies have also shown that lung volumes decrease, and these asthma patients have increased airway resistance at the same time. Some of these may involve increased exposure to allergens at night, cooling of the airways, the reclining position or hormone secretions that follow a circadian pattern.

Some causes of this asthma phenotype include assuming the reclining position, exposure to allergens in the bed or pillows, increased pulmonary secretions, decline in body temperature inducing bronchospasm, gastroesophageal reflux, and having the air conditioner operating at night. Additionally, nocturnal asthma patients experience reduced responsiveness to steroids.

Aspirin sensitivity asthma

Aspirin sensitivity was described in 1922 by Samter. In fact, patients demonstrating aspirin sensitivity, nasal polyps and asthma have Samter's triad (the aspirin triad). Symptoms generally include rhinorrhea or nasal congestion, airway inflammation, coryza, and wheals.

Aspirin sensitivity is not IgE dependent. The cause of this asthma phenotype is an overproduction of leukotriene C4. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the cyclooxygenase pathway but lead to an overproduction of leukotriene C4. The abundance of leukotrienes will produce inflammation, which in turn causes bronchospasm and airflow limitation.

These patients seem to respond favorably to inhaled corticosteroids and leukotriene receptor antagonists. In terms of controlling this form of asthma, importance is placed on the avoidance of NSAIDs. Cyclooxygenase-2 (COX-2) inhibitors show promise for these patients.

"A Closer Look at Asthma, Part III" will look at some of the "Guidelines for the Diagnosis and Management of Asthma" (EPR-3) components of asthma control and asthma severity.

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