Asthma

Asthma, or reactive airway disease, is a chronic respiratory disease in which reversible bronchial obstruction and bronchospasm lead to dyspnea, wheezing, chest tightness, and/or cough. Inflammation of the airways is key to the pathogenesis of asthma. Inflammatory cells—including mast cells, eosinophils, T lymphocytes, plasma cells, and basophils—release histamine, various kinins, leukotrienes, prostaglandins, lipid mediators, tumor necrosis factor α (TNF-α), neuropeptides, substance P, and a host of other inflammatory mediators. Other features are smooth muscle hypertrophy, edema, basement membrane thickening, and mucous accumulation in airways.

The inflammatory process is triggered by allergens, which play a central role in approximately 60% of asthma patients. Other triggers include respiratory infections; inhaled irritants (particularly tobacco smoke and occupational exposures); gastroesophageal reflux; stress; exercise; cold temperatures; and medications such as aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and beta-blockers. Asthma is also caused by agen ts to which a person has specific sensitivity, such as aspirin and tartrazine, which is a petroleum-derived colorant (FD&C Yellow #5).[1]

The prevalence of asthma in the US is approximately 8%. Although the disease commonly begins in childhood, up to 40% of patients develop asthma as adults. Among adult patients, 10%-20% have occupational asthma. An increase in the global prevalence of asthma over the past 30 years has been attributed to climate change, allergen exposure, urbanization, and air pollution, among other factors, but the precise pathogenesis of the observed increase is not clear. Asthma is more prevalent in affluent countries, leading to the question of whether overuse of antibiotics has led to reduced bacterial antigen exposure and a shift of the immune system to a more atopic phenotype. Air pollution's direct contribution to asthma is not clear; certain components may exacerbate asthma.

Risk Factors

In children, asthma occurs more commonly in boys. Among adults, however, the disease is most prevalent in women over 40. Both mortality and morbidity are greater in African Americans, compared with whites. These differences are attributed in part to socioeconomic factors.[2]

Other risk factors include the following:

Atopy. Serum levels of IgE, the antibody most commonly associated with respiratory allergy, appears to be closely linked with airway hyperresponsiveness.

Family history. About 75% of children with 2 asthmatic parents also have asthma.

Environmental and occupational factors. These factors include tobacco smoke, animal dander, dust mites, cockroach allergens,[3] plants, pollen, mold, enzymes, chemicals, and metals.

Body Weight. Recent studies suggest that obesity might modify airway smooth muscle function, increasing the risk for developing asthma.[4] In both pediatric and adult populations, increased body weight is directly associated with the odds of incident asthma, suggesting that incidence could be reduced by weight loss.[1],[5]

Diagnosis

A characteristic history of periodic bronchospasm and variable airflow obstruction, occurring with or without stimuli that provoke an attack, is usually present. During acute attacks, symptoms such as tachypnea, chest tightness, wheezing, shortness of breath, and cough, with or without sputum production, are common. Difficulty taking deep breaths, difficulty finishing sentences, and/or lethargy indicate greater severity, and, possibly, status asthmaticus.

Physical examination often reveals use of accessory respiratory muscles, a prolonged expiratory phase with diffuse wheezing, and sometimes hyper-resonant lung fields with diminished breath sounds due to air trapping. Severe attacks may have less wheezing (due to reduced air flow), cyanosis, and signs of mental obtundation.

Peak expiratory flow rate (PEFR) can suggest a diagnosis of asthma when below-normal values respond to bronchodilators. In addition, PEFR may be used to diagnose exacerbations.

Routine pulmonary function tests during asymptomatic periods may be entirely normal. During exacerbations or in patients who have had asthma for many years, spirometry typically shows reduced forced expiratory volume in 1 second (FEV1), a reduced FEV1/ forced vital capacity (FVC) ratio, and/or reduced peak flows, and may also demonstrate increased total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC).

Blood testing may reveal eosinophilia and elevated serum IgE levels in asthma patients with atopy.

Skin testing can identify allergens that may be environmentally controlled.

Medicines, such as beta-blockers, NSAIDs, and aspirin, may reveal an underlying asthma diagnosis if symptoms are triggered after ingestion.

Treatment

With optimal asthma management, patients should not have symptoms, exercise limitations, exacerbations, or any need for oral steroids or albuterol. Overall, medications and side effects should be minimal.

Types of Asthma

Mild intermittent asthma (< 2 days/week; < 2 nights/month) is treated on an as-needed basis with inhaled short-acting beta-2-selective agonists, such as albuterol. Beta-adrenergic medications are bronchodilators and can be used before exercise or when symptoms occur; these are sometimes called “rescue medications”.[6] Alternatives for exercise-induced asthma are cromolyn and nedocromil (mast cell stabilizers) taken just before exercise.

Mild persistent asthma (> 2 days/week; > 2 nights/month) usually requires daily low-dose inhaled corticosteroids, along with a short-acting beta-agonist for breakthrough symptoms. Inhaled corticosteroids decrease the risk of exacerbations and reduce the need for rescue medication. Common steroid preparations include budesonide, fluticasone, triamcinolone, beclomethasone, and flunisolide.

Moderate persistent asthma (daily or > 1 night/week) calls for an increased dose of inhaled corticosteroid and/or the addition of a long-acting beta-agonist or leukotriene antagonist. Examples of leukotriene antagonists are zileuton, montelukast, pranlukast, and zafirlukast. Sustained-release theophylline and cromolyn are alternatives. Failure to control symptoms with the use of 2 of the above medications suggests the patient may have severe asthma or perhaps another diagnosis.

Severe asthma (continual, frequent attacks) requires high-dose inhaled corticosteroids or oral corticosteroids, along with other controller medicines.

Adverse effects of inhaled steroids include dysphonia and oral candidiasis (thrush). For this reason, it is advisable to use a spacer with each dose.

The 2007 National Asthma Education and Prevention Program guidelines recommend annual administration of influenza vaccine. The pneumococcal vaccine is also recommended in patients with severe asthma and those who require chronic oral glucocorticoid therapy.[7]

Other Considerations

Leukotriene antagonists are no substitute for inhaled corticosteroids,[8] but in patients who make an excess of leukotrienes, leukotriene antagonists may complement the above therapies. Patients with exercise-induced bronchoconstriction, nasal polyposis, and aspirin sensitivity (triad asthma) tend to respond well to leukotriene antagonists.

Long-acting beta-agonists, such as salmeterol and formoterol, are not to be used as monotherapy,[9] as they have no significant anti-inflammatory effects. Indeed, they cause prolonged bronchodilation, which may mask a progressive inflammatory process that could eventually lead to a severe attack.

A recent study showed a small increase in risk of death among patients, particularly for African Americans, using salmeterol in addition to typical asthma drugs.[10]

Cromolyn and theophylline are rarely considered as first-line agents. However, in combination with inhaled corticosteroids, they may be beneficial.

Omalizumab is a new monoclonal antibody directed to human IgE for use in asthma patients with a positive skin test or in-vitro reactivity to a perennial aeroallergen. For atopic patients with refractory asthma or those for whom inhaled and/or oral steroids cause major side effects, anti-IgE therapy may reduce steroid requirements and side effects and provide improved control.

Emergency Treatment

Immediate bronchodilation with inhaled albuterol is the mainstay of emergency treatment. In the emergency room, the delivery method for albuterol is most often continuous nebulization (approximately 10 mg/hr), or 2.5 mg every 20 minutes for 3 doses. However, data show that using a metered-dose inhaler (with a spacer) for 4-6 successive inhalations is approximately equal to 1 nebulizer. The metered-dose method has the advantages of reducing the total amount of albuterol administered and shortening the length of stay in the emergency department, without increasing hospital admissions.[11]

Systemic corticosteroids, such as prednisone, prednisolone, and methylprednisolone, should be started concurrently in a patient who does not adequately respond to albuterol therapy. Their effect is often delayed up to 6 hours. Inhaled ipratropium bromide (an anticholinergic agent) is indicated if a person has moderate to severe airway obstruction that is unresponsive to beta agonists alone.

Heliox can benefit patients with severe airflow obstruction and mild hypoxemia in the acute setting. In patients with severe hypoxemia, the helium concentration should be decreased to a level less than what has been shown to be effective for improving airflow obstruction (70%-80% helium) in order to deliver oxygen concentrations needed to maintain normoxia. Therefore, heliox is contraindicated in severe hypoxemia.

Magnesium sulfate, given intravenously, may be tried when a patient does not respond to bronchodilators, but further study is needed, especially in children.

Nutritional Considerations

Roles have emerged for plant-based diets, healthy weight maintenance, modification of fatty acid intake, and avoidance of of dairy products, fast food, sugar-sweetened beverages and excess sodium in the prevention and management of asthma, as described below.

Maintenance of a healthy body weight. A meta-analysis of weight and asthma in children found that being overweight increases the risk for asthma by 35%, while being obese raises the risk by 50%, when compared with

normal weight children.[12] Loss of excess weight results in improved lung function.[13]

Modifying fatty acid intake. Omega-6 fatty acids (found in animal products and in margarine and other vegetable oils) may increase risk for asthma, in part because the long-chain omega-6 fatty acid arachidonic acid is a precursor of leukotrienes with bronchoconstrictive effects. In contrast, omega-3 fatty acids have anti-inflammatory effects.[14] A high ratio of omega-6 to omega-3 fatty acid intake has been significantly associated with the risk for asthma in a pediatric population.[14]

Clinical evidence shows that a diet high in total and saturated fat increases the expression of genes involved in airway inflammation in people with asthma,[15] and diets enriched with omega-6 fatty acids hinder the incorporation of omega-3 fatty acids into plasma and tissue lipids.[16] Given the high amount of omega-6 fats present in a Western diet, the latter may help explain why a meta-analysis of fish and fish oil intake found a nearly 25% lower risk for childhood asthma with higher fish intake when compared with the lowest intakes. These findings did not, however, extend to the adult population.[17]

Studies are conflicting with regard to a benefit of omega-3 supplementation in adults with asthma, with some showing inhibition of mild airway responses to exercise and eucapnic voluntary hyperventilation and reductions in markers of airway inflammation, and others showing no improvement in test-challenged bronchial hyperreactivity, sputum eosinophil counts, or excretion of mast cell mediators in people with mild to moderate asthma.[18]

Avoidance of dairy products. Women who consumed low-fat yogurt once or more per day or low-fat milk 5.5 times or more per week during pregnancy had a 21% and 8% higher risk, respectively, for having a child diagnosed with asthma, when compared with those consuming none.[19] In the French Six Cities Study, a roughly 50% greater asthma prevalence was found in children who consumed butter 3 or more times per week, compared with those who consumed butter never or only occasionally.[20]

Avoidance of fast foods. The International Study of Asthma and Allergies in Childhood (ISAAC) study found a nearly 40% greater risk for severe asthma in children and adolescents who consumed fast food 3 or more times per week, when compared with those who ate fast food never or only occasionally.[21]

Nut consumption. Although peanuts and tree nuts can be allergenic, t he Danish National Birth Cohort study found that the intake of these during pregnancy was inversely related to a diagnosis of asthma in their offspring at 18 months of age.[22] In the E3N study of French women, the risk of frequent attacks (defined as 1 or more attacks per week) was lower in women with the highest consumption of nuts and seeds (>5.3 g/day) than in those with the lowest consumption (≤ 1.0 g/day).[23]

Avoidance of salty foods. A low-sodium diet maintained for 1 to 2 weeks decreased bronchoconstriction in response to exercise in individuals with asthma, but evidence does not yet support a benefit of a low-sodium diet on either the prevalence or severity of asthma.[24]

Fruits, vegetables, and other foods high in antioxidants. A meta-analysis found a roughly 45% lower risk for asthma in both children and adults who consume the most fruits and vegetables, compared with those who eat the least amount.[25] A study that manipulated antioxidant-containing foods found that individuals in the low fruit and vegetable intake group (3 servings/day, typical of Western diets) had more than twice the risk for asthma exacerbation when compared to those eating 7 daily servings of fruits and vegetables.[26]

Avoidance of allergenic foods, beverages, and preservatives. Food allergies often precede the development of asthma, and in the National Cooperative Inner City asthma study, 45% of children showed IgE sensitization to at least 1 of the 6 most common food allergens.[27] Food-induced bronchospasm occurs with the intake of certain foods in 2%-24% of persons with asthma. Foods implicated most often as a cause include peanuts, milk, eggs, tree nuts, soy, wheat, legumes, beans, and turkey.[28] Most studies report a 3%-10% prevalence of sulfite sensitivity among asthmatic subjects,[29] and double-blind, controlled studies have demonstrated that sulfite-containing beverages and foods can cause potentially life-threatening asthmatic reactions in as many as 5% of the asthmatic population.[30] , [31] Most sulfite-sensitive persons with asthma are steroid-dependent. Avoidance is the most beneficial approach to sulfite sensitivity.[32] Further evidence that food allergy is a risk factor for life-threatening asthma is demonstrated by

a substantially higher rate of food allergy in children requiring intubation for asthma compared with controls.[32]

Allergy testing should be considered in patients who appear to experience exacerbation of asthma in relation to certain foods or food groups. Alternatively, patients can attempt to determine if a food triggers asthma by eliminating all common potentially allergenic foods and then reintroducing them one at a time. Patients should keep careful records of food intake and any change in symptom frequency to confirm that a given food is provoking an exacerbation of asthma.

Vegetarian and vegan diets. In a study of 27,766 Seventh-day Adventists, vegetarian women reported a lower incidence of asthma, compared with women on nonvegetarian diets.[33] The theoretical basis for the value of vegan diets is the absence of potential triggers, particularly dairy products and eggs, as well as a relative lack of arachidonic acid.

A review of dietary patterns in asthma also found that 7 out of 10 studies noted a protective effect of a Mediterranean diet on the incidence of child asthma. Higher adherence to such a diet conferred a roughly 15% lower risk when compared to low adherence.[34] Additional clinical trials are required to investigate the role of plant-based diets in asthma incidence and management.

Avoidance of sugar-sweetened beverages. In the 2009 Youth Risk Behavior Survey, the odds of having asthma were 28% greater among students who drank regular soda 2 times per day, and 64% greater in those who drank regular soda 3 or more times per day. Previous research studies found that asthma symptoms were worsened by regular soda consumption.[35] The Behavioral Risk Factor Surveillance System found that non-obese adults who consumed 2 or more servings per day of sugar-sweetened beverages had a roughly 65% greater risk for asthma, compared to non-consumers.[36] The risk for asthma in children ages 2-9 was also significantly higher when they consumed either apple juice or high fructose corn syrup-sweetened beverages 5 or more times per week, compared to consuming only 1 per month or less.[37]

Alcohol. Alcohol consumption has a U-shaped association with the development of new onset asthma in adults.[38]

Vitamin D status. A meta-analysis found that vitamin D deficiency was more common among persons with asthma than control subjects and was associated with decreased lung function in asthmatic children.[39] Reviews of the possible benefit of vitamin D supplementation, however, have come to varied conclusions, with one concluding that the evidence was of poor quality[40] and another concluding that vitamin D-supplemented children had a roughly 25% lower risk for asthma exacerbations when compared with groups without supplemental vitamin D.[41]

Preventive measures. Measures recommended to decrease the risk for developing asthma include breastfeeding for the first 4-6 months of life and avoiding the following foods until children reach the specified ages: dairy products until at least 1 year old; eggs until at least 2 years old; nuts and fish until at least 3 years old.[42]

Orders

Smoking cessation.

Avoidance of allergic triggers identified in the patient history.

Vegetarian diet, nondairy, may be tried on a prospective basis.

Weight loss.

What to Tell the Family

Asthma can generally be well managed with diet and medications. Family members can help by encouraging a diet high in fruits, vegetables, and whole grains, and by minimizing fats and oils. Adopting such a diet themselves may help protect family members from later health problems, as well as make it easier for the patient to adhere to the dietary changes.

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