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Asthma Triggers: What Really Matters?

CHAPTER 17

Patrick H. Win and Iftikhar Hussain

CLINICAL PEARLS

- Clinicians must take time to carefully identify potential asthma triggers at the time of initial evaluation and at each follow-up visit to minimize unnecessary morbidity from asthma.
- Just as asthma phenotypes vary among patients, so too do their specific triggers. Thus, care must be individualized and reviewed regularly as triggers can change over time. New-onset, uncontrolled asthma may be a sign of a new asthma trigger previously not identified.
- After asthma triggers are identified and confirmed with testing (if necessary), every effort should be made to avoid or eliminate these specific triggers of asthma symptoms (with the exception of exercise).
- Opportunities to minimize infectious triggers must always be taken. This should include influenza and pneumococcal vaccinations.

In the preceding chapters, authors have discussed the various important aspects of the clinical asthma assessment. As is the case with assessing level of control, severity, and inflammation, identifying triggers for asthma is an integral part of the initial evaluation of newly diagnosed asthmatic individuals. Furthermore, reviewing potential asthma triggers at each follow-up visit helps educate asthma patients. This education is a preventative first step in identifying and modifying risk factors that are responsible for poor quality of life, unnecessary morbidity, and mortality. In this, the final chapter of Section III, we will review our current concepts of asthma triggers and their role in the assessment and management of asthma. We hope to organize the classification of asthma triggers, and provide quick reference tables to simplify the initial assessment and follow-up management of asthmatics. By the end of this chapter, you will be "armed" with the information to rapidly assess, educate, and intervene upon the asthma triggers that really matter.

What is an asthma trigger? Asthma triggers are any condition or stimuli that cause inflammation or hyperresponsiveness of the airways that result in the symptoms of asthma: wheezing, shortness of breath, chest tightness, and/or coughing. Given the heterogeneity of asthma phenotypes, it is important to understand that triggers will vary among patients. So focusing on the relevant triggers for each patient is of utmost importance. While some asthmatic individuals are atopic, others are not. Accordingly, while allergen avoidance may vastly help the so-called "extrinsic" asthmatic individual by preventing morbidity and exacerbations, exposure to aeroallergens may not be detrimental to the nonatopic, "intrinsic" asthmatic individual (Box 17-1). Furthermore, even within the group of atopic asthmatic individuals, some will be sensitized to seasonal allergens (trees, grasses, or weeds), while others will be triggered by perennial allergens (cat, dog, or dust mites). Given we have little, precious time at every patient encounter, it is imperative that we have a systematic approach to assessing and intervening upon asthma triggers targeted to the individual patient (Box 17-2). Accordingly, asthma triggers can be conveniently placed into groups by etiology: allergens, irritants, medications, weather changes, infections, emotions, gastroesophageal reflux, foods, and exercise (Table 17-1).

In genetically predisposed individuals, allergen exposure may lead to sensitization resulting in the formation of allergen-specific immunoglobulin E (IgE) by B lymphocytes. This process of allergen sensitization is uncommon within the first year of life, as formation of IgE to specific aeroallergens does not commonly occur before the age of 2 to 3. In these individuals, the combination of allergen sensitization to common aeroallergens (Table 17-2) and reexposure to these allergens can trigger symptoms of asthma. Subsequent allergen exposure through the respiratory tract results in T_H2-type lymphocyte recruitment, mast cell activation through IgE, and

BOX 17-1 Definitions

Aeroallergen: Any airborne substance that can result in an IgE-mediated allergic response. Typically these include tree, grass, and weed pollen; mold spores; and perennial allergens like cat and dog dander, dust mite, and cockroach.

Asthma trigger: Any condition or stimuli that cause inflammation or hyperresponsiveness of the airways that results in wheezing, shortness of breath, chest tightness, and/or coughing.

Atopy: The genetic predisposition to develop any of the classic allergic diseases (atopic dermatitis, allergic rhinitis, and asthma). Atopy involves the capacity to produce specific-IgE in response to common environmental allergens such as house-dust mites, foods, and tree and grass pollen.

Irritant: Any substance, chemical, or physical factor that triggers asthma symptoms by nonspecific mechanisms resulting in increased bronchial hyperreactivity. Examples include smoke and cold air.

Samter's Triad: A medical condition consisting of asthma, aspirin sensitivity, and nasal polyposis. This triad is typically identified in patients in their 20s and 30s and may not include other atopic diseases. It is also commonly known as aspirin-sensitive asthma, aspirin triad, and aspirin-induced asthma and rhinitis (AIAR).

BOX 17-2 Assessment

1. Review the patient's history of asthma and past episodes of exacerbation, with care taken to identify potential asthma triggers
2. Confirm potential allergic triggers
   a. Epicutaneous skin testing
   b. Intradermal skin testing
   c. Radioallergosorbent testing (in vitro)
3. Review patient's environment
4. Review patient's exposures
5. Review comorbid conditions
6. Review medications

Table 17-1
COMMON ASTHMA TRIGGERS

Allergens (seasonal and perennial aeroallergens)
Nonallergic irritants (smoke, strong odors from chemicals, air pollutants, occupational exposures [Chapter 42])
Medications (beta-blockers, nonsteroidal anti-inflammatory drugs)
Weather changes (changes in temperature and humidity)
Infections (sinusitis or viral infections)
Emotions (laughing, crying)
Reflux
Food (food allergy and food additives)
Exercise

Table 17-2
AEROALLERGENS THAT TRIGGER ASTHMA

Seasonal
Pollens
1. Trees (ash, birch, maple, oak, walnut, others)
2. Grasses (timothy, Kentucky blue grass, Bermuda, others)
3. Weeds (ragweed, pigweed, cocklebur, lamb's quarters, others)
Perennial
House-dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*)
Animal (cat, dog, guinea pig, horse, hamster, mouse, others)
Cockroach (*Blattella germanica*, *Periplaneta americana*, *Blattella orientalis*)
Seasonal and Perennial
Molds (Alternaria, Aspergillus, Cladosporium, others)

eosinophil influx. The ensuing inflammation from this milieu of cells and cellular mediators is thought to be responsible for not only acute asthma exacerbations, but also chronic inflammation. Allergen sensitivity is commonly diagnosed by a combination of history and positive epicutaneous skin (Fig. 17-1) and/or intradermal testing (Fig. 17-2), and in some cases, in vitro testing such as allergen-specific radioallergosorbent testing or newer technologies. After the diagnosis is made, health care providers should strive to identify the allergic triggers of asthma, treat comorbid underlying disease (e.g., rhinitis) with appropriate medications, and implement environmental controls to eliminate or minimize exposure to these factors.

Seasonal allergens from trees, grasses, and weeds are predominantly derived from air/wind-borne pollen. Even though whole pollen grains are quite large, plants can extrude allergen-containing particles that are less than 10μm in size through the pores in their outer covering. This relatively small size likely facilitates entry into the lower airways, and results in the aforementioned allergic cascade with subsequent inflammation. The presence and time of release of these airborne allergens vary according to location and climate. Generally speaking, tree pollen is released first, in the springtime; grasses come later in the spring and early summer; and weed pollen arrives in late summer and early fall lasting until the first frost. Accordingly, pollen-allergic patients can have significant asthma exacerbations during their specific pollen season or seasons. Exposure to seasonal pollens is classically

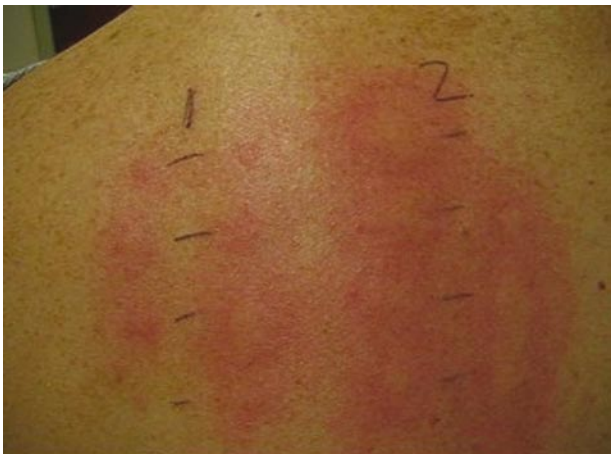

Figure 17-1 Epicutaneous skin testing (using an 8-headed multitest device) in a middle-aged asthmatic individual revealed sensitivities to multiple trees (labeled "1") and grasses (labeled "2"). Notice the negative saline control in the right-upper corner of panel 2 and the negative reaction to red maple in the left-lower position of panel 1. (*Courtesy of Patrick H. Win, MD.*)

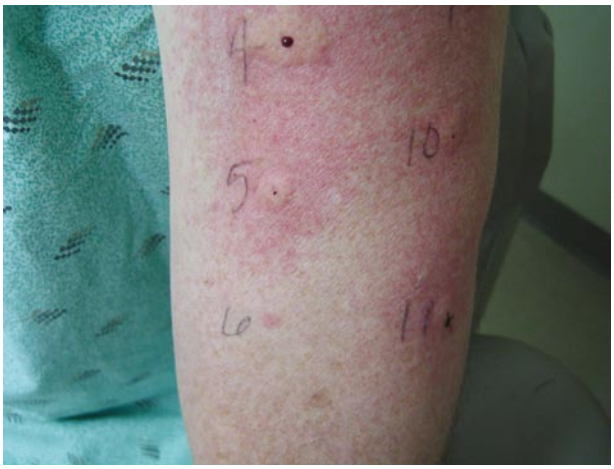

Figure 17-2 Intradermal skin testing (using a 25G 5/8 needle) to weeds on a young asthmatic male who reported itchy, watery eyes, nasal congestion, and worsening shortness of breath and wheeze in the fall. After epicutaneous skin testing revealed only minimal sensitivities to trees and grasses, intradermal skin testing (more sensitive) revealed strong cutaneous reactions to multiple weeds. With the patient's history of worsening symptoms in the fall, this testing provided a better explanation for his worsening seasonal symptoms. Although the patient displayed multiple positive intradermal tests, he was clearly not allergic to lamb's quarters (labeled "6"). (*Courtesy of Patrick H. Win, MD.*)

considered an outdoor exposure, with peak outdoor pollen concentrations occurring in the morning. Unfortunately, during the grass pollen season, pollen can be found indoors at high levels in bedding, furniture, and carpeting. This is facilitated by leaving home windows open and using window and attic fans to cool the inside environment.

To minimize morbidity, asthma patients should be educated about their specific pollen sensitivities and corresponding "high-risk" seasons, as avoidance is the best way for patients to reduce risk of asthma flare. Decreasing exposure and, in turn, asthma exacerbations can be facilitated by remaining indoors, closing windows, avoiding the use of cooling fans, and using car and home air-conditioning as much as possible. This is particularly important in the early morning, the time of peak airborne pollen concentration. Early morning outdoor exercise should be strictly avoided, as the combination of peak pollen counts and cardiovascular exercise with increased oxygen demand, increased respiratory rate, and larger tidal volumes can be a dangerous combination. Recognizing that complete avoidance is not always feasible, using locally available pollen counts to help inform patients of potential high-exposure days can be quite helpful in reducing allergen exposure.

Perennial allergens that trigger asthma include domesticated animals, house-dust mites, and cockroaches. Cat and dog exposures are among the most common causes of perennial asthma triggers; however, all warm-blooded feathered or furry animals, including hamsters, rabbits, guinea pigs, and birds can produce allergen. Exposure to these allergens, in turn, may induce IgE-mediated reactions and asthma exacerbations. Pet allergens are ubiquitous in our environment as 30% to 40% of American homes have pets, and even trace amounts of cat or dog allergen can be found in virtually any home (>90%, even in homes without cats or dogs). Acute symptoms may develop in cat- or dog-sensitive asthmatic patients within minutes after entering a home where these animals reside.

Cat allergen, mainly *Fel d* 1, is a 17-kDa heterodimer comprising two disulfide-linked peptide chains. *Fel d* 1 is produced in the sebaceous glands and is typically spread via contact with cat saliva, dander, and urine. Common allergens are present in all breeds of cat (including lions, tigers, and hairless cats), but males produce more allergen than females. Cat allergen can be very small (<3 to 4 μm), and the distribution in the household air at any time is highly variable. Cat allergen is also very light and sticky, so it becomes airborne easily and can accumulate on household furniture, carpeting, and walls. These unique characteristics allow it to remain suspended in the air for long periods and to be inhaled deeply into the lungs, possibly accounting for its greater potential to trigger asthma symptoms than other aeroallergens. The level of cat allergen that is required to induce asthma symptoms is not well defined, so strict avoidance and proper cleaning after an animal has been removed from the household are key to preventing morbidity. Cat allergen levels drop slowly after animal removal, so brief trials of cat avoidance are useless. In fact, it takes approximately 5 months for cat allergen to drop to levels similar to those found in homes without cats, and 4 to 6 months after the animal has been removed for asthma patients to achieve any improvement in symptoms. Unfortunately, the clothes of cat owners constitute the vehicle of passive transport of *Fel d* 1 to cat-free environments, so recontamination to some extent is unavoidable.

In contrast to cat allergen, where the major antigenic component has been identified, dog allergen appears to be more heterogeneous, containing many varied allergens (primarily C*an f* 1 and C*an f* 2). Contrary to popular belief, it is impossible to generalize certain dog breeds as either "nonallergenic" or "hypoallergenic." In fact, all dogs have common allergens, but there may be differences in an individual's response to a particular dog breed or possibly even an individual dog of a specific breed. Despite this, even though many patients claim that "My pet has never bothered me," patients are notoriously poor at perceiving asthma symptoms when they have chronic, continuous exposure to allergens to which they have become sensitized. This is likely due to, at least in part, their emotional attachment to their animal.

The best "treatment" for all animal allergies is strict avoidance, including removal of the animal that is triggering symptoms of asthma from the home. When animal removal is not possible, confining the pet to carpet-free areas, outside the bedroom, may be beneficial. These measures, combined with the use of a HEPA (high-efficiency particulate air) or electrostatic air filter may provide additional benefit in "light" allergen removal (e.g., cat and dog allergen). Weekly or biweekly washing of pets, by a family member or individual other than the asthmatic patient, may also help to decrease allergen exposure and symptoms. Interestingly, dog, but not cat, ownership during infancy has been shown to reduce the development of allergic sensitization, and absolute number of pets, and not the type of furred pet, might also reduce future risk.

The two species of house-dust mite, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, are the most important mite allergens in North America. House-dust mites are microscopic (approximately 0.3 mm long), sightless, eight-legged acarids that feed on sloughed human skin. The most allergenic parts of the house-dust mite are its body parts and fecal matter. One ounce of house dust can contain approximately 40,000 dust mites. Thus a bed, a common site of house dust mites, may contain approximately 2 million dust mites. In contrast to pet allergy, dust mite–sensitive asthmatic patients are rarely aware of symptoms immediately, even when levels of dust mite allergen in a home are high. Studies indicate that the critical level of house-dust mites that poses a risk factor for asthma ranges from 100 to 500 mites per gram of house dust (about 2 to 10 μg of *Der p* 1), while acutely ill mite-sensitive asthmatic patients usually reside in homes with more than 500 mites per gram of house dust (>10 μg of *Der p* 1).

House-dust mite levels vary with humidity, temperature, season, and type of home furnishings. The most important factor influencing growth of house-dust mites is humidity. Asthmatic patients who are mite-sensitive and live in environments with suitable sites for mite growth (e.g., wall-to-wall or bedroom carpeting and upholstered or overstuffed furniture) are at greater risk in more humid climates. House-dust mites optimally reproduce in bedding and carpeting where the relative humidity in the home is higher than 50%. Accordingly, improper setting of the central air humidifier (commonly part of a home's central heating and air-conditioning unit) may worsen asthma control; while dehumidifiers set to keep humidity levels lower than 50% may be beneficial in reducing asthma symptoms from house-dust mite exposure. Although using other environmental control measures to minimize dust

mite exposure are generally endorsed by allergists as a preventative first step to reduce asthma flares, studies examining their use are conflicting and have provided much controversy. Some studies using relatively basic dust mite control measures have shown no effect on asthma symptoms or reduction in mite growth; whereas other studies that use methods of extensive cleaning and dust mite proofing (e.g., mattress and pillow covers) to minimize mite exposure have been associated with a reduction in asthmatic symptoms, medication use, and morbidity. Furthermore, some studies have shown that patients exposed to lower levels of house-dust mites not only have decreased asthma symptoms and medication use, but also have improvement in nonspecific bronchial hyperresponsiveness. Having said this, the Cochrane Library meta-analysis on house-dust mite control measures for asthma, including 49 trials that examined the use of physical, chemical, and combination methods to reduce house-dust mite exposure, showed no benefit/effect on frequently reported outcomes (AM peak flow, asthma symptom scores, and medication use). The reviewers mention that many of the trials included in this analysis were of poor quality, making their conclusions difficult to interpret. If environmental control measures are suggested, the bedroom is the most important room to target, as most of our day in the home (approximately 8 to 10 hours during the night for sleep) is spent there. Other areas of the home, such as the living or family room that contains overstuffed furniture or carpeting, must be considered as potential sites of significant house-dust mite exposure. Proposed environmental controls to be considered include replacing wall-to-wall carpeting with hardwood or vinyl flooring, encasing bedding in dust-mite impermeable material, frequent dusting (with mask or by an unaffected individual), replacing upholstered/overstuffed furniture with leather furniture, replacing fabric curtains with blinds, washing bedding weekly in hot water (60°C or 130°F), washing and high-heat drying or freezing of stuffed toys, reducing humidity to less than 50%, frequent vacuuming (with HEPA filter and double-thickness bags) by an individual not sensitive to dust mites (or with mask), and using acaricides and/or tannic acid to mitigate house-dust mite infestation.

Cockroach has also been identified as a major allergen capable of triggering asthma exacerbations. The ability of cockroach allergen to stimulate the formation of specific IgE antibodies has been demonstrated by end point skin test titration and radioallergosorbent testing. Furthermore, a causal relationship between bronchospasm and sensitivity to cockroach allergen has been proved in bronchial provocation studies. Positive skin tests to cockroach allergen are reportedly present in 20% to 53% of allergic patients and as high as 49% to 61% of asthmatic patients. Although there are about 50 species of cockroaches that live in the United States, only 3 have been shown to induce allergen-specific IgE: the American, German, and Asian/Oriental cockroaches. Cockroach allergen usually is found in kitchen cabinets and kitchen floor dust, as they usually hide out in cabinets and behind refrigerators. A study in urban asthmatic patients has shown that cockroach sensitivity may be as important a risk factor for inner-city asthmatic individuals as house-dust mite allergy. Because elimination of cockroach infestation requires aggressive, repeated extermination efforts with irritant chemicals (deltamethrin powder or cypermethrin), it is best performed by professional exterminators. Cockroach baits and gels (fipronil and hydramethylnon) can be purchased at local superstores. These are generally safer and relatively nontoxic to mammals (pets and children), but may not be as effective in cases of severe infestation. Other partially effective measures include restricting havens by caulking and sealing cracks in plaster work and flooring, controlling dampness, reducing the availability of food, and restricting access to the dwelling (sealing sources of entry around doors).

Molds and fungi are aeroallergens that can trigger significant asthma symptoms in both a seasonal and perennial fashion. Unlike pollens, molds have ill-defined seasonal peaks and nadirs for airborne mold spore levels. Only in the northernmost areas of the United States are there consistent seasonal increases in mold counts. In this region, mold counts increase starting in May or June and decrease by October or November, having peaked in July or August. In the South, airborne molds are present throughout the winter, with a peak in summer or early fall. Clinically, molds are divided into two groups: outdoor and indoor.

The two most common outdoor molds are *Alternaria* and *Cladosporium*. Other common outdoor molds include *Fusarium*, *Spondylocladium*, and *Helminthosporium*. These outdoor or field molds grow in soil, on plants, and in decaying vegetation such as cut grass or raked leaves. Mold levels are affected by temperature, wind, rainfall, and humidity. Rain or high humidity levels will lower mold spore counts temporarily, but afterwards, counts rise rapidly. Generally, a late summer–autumn peak is seen for common fungal spores.

Similar to the aforementioned avoidance measures for pollen-sensitive asthmatic individuals, asthma symptoms from exposure to mold spores may be minimized by staying indoors as much as possible (especially during peak spore concentrations) and keeping home and automobile windows closed. The importance of minimizing mold exposure in mold-sensitive asthmatic individuals cannot be overemphasized. It is clear, from the observation of "New Orleans asthma" and other recently described cases of mold-induced asthma, that inhalation of large quantities of mold spores can produce severe, life-threatening asthma exacerbations in mold-sensitive patients. Although it is unclear what etiological factors are responsible for these cases of severe mold-sensitive asthma flares, it is hypothesized that because mold spores are smaller than pollen, they are more likely to enter and inflame the lower airways.

The two most important indoor molds are *Aspergillus* and *Penicillium* (also known as mildew). The amount of indoor mold in any dwelling depends on several important factors: age and composition of the structure, type of heating and cooling system, and use of humidifiers. Dark and humid (often poorly ventilated) basements are ideal sites for mold growth. The next most common sites of mold growth are the bathroom and the kitchen. In tropical and subtropical climates, fungi may grow on the walls of the house as a result of water seepage and humidity. To avoid this, the walls can be tiled or cleaned as necessary. Home heating, cooling, and humidification systems are also potential sources of fungal growth, although air-conditioning generally reduces indoor humidity and hence discourages mold growth. Most fungal spores in an

indoor environment are nonviable spores that will be found in house-dust reservoirs such as carpeting, bedding, and furniture. Implementing the same precautions used to reduce levels of dust mites is the best way to eliminate mold spores from the home. Levels of viable indoor mold spores can be reduced by removing or cleaning mold-laden objects. Levels may also be reduced by use of dehumidifiers (set humidity level < 50%) in the basement and air-conditioners in the bedroom or family room. Air-conditioners and dehumidifiers reduce humidity and filter large fungal spores, lowering the mold and yeast count indoors, although their benefit in reducing asthma symptoms is controversial. Home humidifiers should be used with caution and cleaned frequently because of the potential for mold and *Actinomyces* growth. Bathrooms and kitchens should be well ventilated. Electronic air filters also lower the level of mold spores within a dwelling. When the major source of molds within a home is a wet or damp cellar, the basement should be kept free of carpeting, immediately dried out after a rainstorm, and, whenever possible, protected with a drain tile and sump pump.

Nonallergenic indoor triggers (Table 17-3) of asthmatic symptoms are a heterogeneous group of irritants that affect bronchial hyperreactivity in a non-IgE–dependent fashion. As with all other asthma triggers, each should be identified and meticulously eliminated or avoided. Active and passive tobacco cigarette smoke, consisting of very small, light particles that remain airborne for long periods, is a high-risk trigger for all asthmatic individuals. Studies have demonstrated that children may be at increased risk of developing asthma and allergic sensitization when exposed to passive smoke. Other studies in children show worsening asthma symptom severity, higher medication requirements, more frequent emergency department visits, and increased airway responsiveness when exposed to passive maternal tobacco smoke. Active cigarette smoking not only has direct, deleterious effects on the lung parenchyma, it also reduces the efficacy of inhaled and systemic corticosteroids. Thus, smoking cessation must be a primary objective for the patient, friends, and family members of asthmatic patients. Other forms of smoke, such as that of wood-burning stoves, also have negative effects on the lower respiratory tract. Additional airborne irritants, fumes, and strong odors (e.g., chalk dust, talcum powder, paint fumes, insecticides, household cleaning sprays, polishes, cooking oil fumes, perfumes, and cosmetics) may initiate or exacerbate asthmatic symptoms in some patients. Other indoor pollutants include carbon monoxide, formaldehyde, nitric oxide, nitrogen oxides, and bacterial endotoxin. In all of these cases, adequate ventilation plays a pivotal role in successful prevention of asthma symptoms, as air stagnation has been shown to be a surrogate marker for the accumulation of indoor pollutants. Other important preventative avoidance measures include household cleaning and proper maintenance of gas appliances.

Table 17-3
NONALLERGIC IRRITANTS THAT TRIGGER ASTHMA

Indoor
Smoke (tobacco, wood-burning stove)
Strong odors (perfumes and cosmetics)
Particulates (chalk dust, talcum powder)
Fumes (household cleaning products, insecticides, paints, chemicals, cooking)
Outdoor
Smoke (wood/tree, refuse and chemical fires)
Exhaust (diesel fumes)
Other (ozone, chemicals)

Nonallergic outdoor irritants (see Table 17-3) that trigger asthma are also exceedingly common and important to identify and eliminate. Studies have implicated several outdoor pollutants as potential triggers of asthma symptoms. Air pollutants such as ozone, nitrogen oxides, acidic aerosols, and particulate matter can lead to asthma symptoms and frank exacerbations. Other important outdoor asthma triggers include exposure to vehicle traffic (especially diesel exhaust), which might exacerbate preexisting allergic conditions by enhancing airway responses to allergen, a potential compounding effect. On occasion, weather and atmospheric conditions create brief periods of intense air pollution in a defined geographic area. At these and other times and in areas of high outdoor pollution, patients with asthma should avoid unnecessary outdoor physical activity (especially exercise) and try to stay indoors in a clean environment. As with pollen and aeroallergens, air-conditioning and filters may be helpful in preventing unnecessary morbidity. When working outdoors in polluted areas is unavoidable, taking a preventative, short-acting inhaled bronchodilator beforehand may prevent acute asthma symptoms. If prolonged outdoor polluted conditions are likely to persist, it is a good idea to tell patients to leave the polluted area before mild symptoms spiral into an acute asthma flare.

Hundreds of substances have been identified as occupational irritants or allergens that can trigger asthma symptoms. One can access a fairly comprehensive list of potential occupational asthma triggers at http://asmanet.com. An overview of these triggers and occupational asthma is covered in Chapter 42. Levels of exposure above which sensitization occurs have been proposed for many chemicals, so primary prevention is possible with proper precautionary measures. However, once a patient has been sensitized, the level of exposure necessary to induce symptoms may be very low, and resulting exacerbations may become progressively severe on reexposure. Attempts to reduce occupational exposure have been successful, especially in the industrial setting, where potent sensitizers have been replaced by less allergenic or sensitizing substances. For example, primary prevention of latex allergy has been very successful. This has been accomplished by producing powder-free, lower allergen-content gloves. In cases where prevention is not possible, the early identification of occupational sensitizers and the removal of affected patients from these environments are critical to the successful management of occupational asthma.

Numerous medications (Table 17-4) have been implicated in triggering asthma symptoms. The most common offenders include nonsteroidal anti-inflammatory drugs (NSAIDs) and β-blockers. Approximately 5% to 10% of adult asthmatic patients will have an acute worsening of asthma symptoms after ingesting NSAIDs. Samters Triad or "the aspirin triad" can be identified in some adult asthmatic patients. The response to aspirin or other NSAIDs typically begins within

Table 17-4
MEDICATIONS AND AGENTS THAT TRIGGER ASTHMA

ACE-inhibitors	Nebulized medications (beclomethasone, pentamidine, propellants)
Aldesleukin (IL-2)	Nonsteroidal anti-inflammatory drugs
Amiodarone	Nitrofurantoin
Beta-agonists (paradoxical)	Propafenone
Beta-blockers (systemic and ocular)	Protamine
Dipyridamole	Radio-contrast media
Ergots	Vinblastine (+ mitomycin)
Hydrocortisone	
Illicit drugs (cocaine and heroin)	

an hour of aspirin ingestion and may be associated with profound rhinorrhea, lacrimation, and, potentially, severe bronchospasm. Patients sensitive to aspirin usually are reactive to all other NSAIDs (e.g., ibuprofen, naproxen), and variations in the frequency and severity of adverse responses appear to depend on the potency of each drug within this class of compounds to inhibit the activity of the COX-1 enzyme. Sensitivity to NSAIDs is not IgE-mediated and involves the modulation of eicosanoid production. NSAIDs likely act by reducing the formation of prostaglandins that help maintain normal airway function while increasing the formation of asthma-provoking eicosanoids, including hydroxyeicosatetraenoic acids and cysteinyl leukotrienes. Thus, if aspirin-sensitive asthmatic individuals require treatment with an NSAID, the use of a selective COX-2 inhibitor is a viable treatment option, especially when combined with an inhibitor of leukotriene synthesis or leukotriene receptor antagonist. In addition, there is evidence that mast cell activation occurs, and its mediators can be detected in nasal secretions during an episode of aspirin-induced asthma. This syndrome should be of concern in any asthmatic patient with nasal polyposis, chronic sinusitis, and eosinophilia, although nasal polyposis and sinusitis may precede the onset of recognized NSAID-sensitivity by years. β-Blockers administered either orally or via eye drops (for hypertension or glaucoma, respectively) may exacerbate asthma symptoms via bronchospasm. As a general rule, these medications should be not be used by asthmatic individuals, as other classes of drugs may be used to successfully treat these underlying comorbidities. If β-blockers are used, close medical supervision is essential to prevent unnecessary morbidity. As is the case with all of the aforementioned asthma triggers, avoidance is the treatment of choice.

Weather and atmospheric changes also commonly trigger asthma symptoms. Classically, cold dry air can induce bronchoconstriction in asthmatic individuals. Atmospheric conditions that typically trigger asthma symptoms include changes in temperature and humidity, barometric pressure, or gusts of wind. Perhaps of greater importance than these changes are the effects these atmospheric changes have on seasonal and perennial allergens. For example, pollen and mold counts have seasonal patterns and release of these allergens is highly dependent upon "proper" environmental conditions to allow successful release and plant pollination/procreation. As aforementioned, it is well recognized that exposure to molds or pollens during a particular season can induce asthmatic attacks in sensitized (allergic) individuals, so any atmospheric change (seasonal change or sudden gust of wind) that increases exposure to these allergens is potentially detrimental to allergen-sensitized asthmatic individuals. Furthermore, with seasonal changes (particularly the fall and winter) also comes an increased exposure to viruses like rhinovirus and influenza that commonly precipitate asthma attacks.

Respiratory viral and bacterial infections (Table 17-5) are a major cause of morbidity and mortality in people with asthma. Respiratory viruses trigger acute exacerbation of asthma in children and adults. These infections frequently result in outpatient visits and hospitalizations. Additionally, these infections make asthmatic individuals more sensitive to other asthma triggers. Typical respiratory tract infections that cause airway inflammation and trigger asthma include the "common cold" and flu, bronchitis, ear infections, sinusitis, and pneumonia. Asthma attacks that occur in conjunction with an upper or lower respiratory tract infection may be more severe than exacerbations that occur without concomitant infection.

The most common respiratory viruses are the rhinovirus ("common cold" virus), respiratory syncytial virus (RSV), and certain influenza viruses. These viruses are present in most patients hospitalized with life-threatening asthma exacerbations and acute non–life-threatening asthma flares. Asthmatic individuals are not more susceptible to upper respiratory tract rhinovirus infections than healthy, nonasthmatic individuals, but they do suffer more severe consequences of lower respiratory tract infections. Recent epidemiologic studies suggest that viruses provoke asthma attacks by additive or synergistic interactions with allergens or irritants like air pollutants. An impaired antiviral immunity to rhinovirus may

Table 17-5
COMMON INFECTIONS THAT TRIGGER ASTHMA

Viruses (bold is most common respiratory clinical presentation)
Rhinovirus (1–100+ serotypes; causes "**common cold**," bronchitis and bronchiolitis)
Coronavirus (2299E and OC43 serotypes; causes "**common cold**")
Influenza (A, B, and C serotypes; causes "common cold," **pneumonia** and bronchitis)
Parainfluenza (1, 2, 3, and 4 serotypes; causes "common cold," **laryngotracheobronchitis**, and bronchiolitis)
Respiratory syncytial virus (A and B serotypes; causes "common cold," pneumonia, bronchitis, and **bronchiolitis**)
Adenovirus (1–4 serotypes; causes "common cold," **pneumonia**, bronchitis and bronchiolitis)
Metapneumovirus (**bronchiolitis**)
Bacteria
Streptococcus pneumoniae (sinusitis and pneumonia)
Haemophilus influenzae and *parainfluenzae* (sinusitis and pneumonia)
Moraxella catarrhalis (sinusitis and pneumonia)
Staphylococcus aureus (pneumonia)
Klebsiella pneumoniae (pneumonia)
Atypical *(Chlamydia pneumoniae* and *Mycoplasma pneumoniae* causing pneumonia)

lead to impaired viral clearance and, in turn, prolonged symptoms. Viral respiratory tract infections exacerbate asthma by recruiting T_H2-type cells into the lungs. Currently, we have no specific antiviral strategies for preventing the exacerbation of asthma by respiratory viral infection; however, clinical trials of potential antiviral agents are ongoing. Indirect prevention strategies focus on reducing overall airway inflammation to reduce the severity of the host response to respiratory viral infections.

Although many bacterial infections are known to cause asthma exacerbations in susceptible individuals, recent attention has been focused on lower respiratory tract infections with atypical bacteria. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are thought to be common triggers of asthma. Whether these bacteria are the inciting agents for the onset of disease or acute exacerbations has yet to be definitively determined; however, there are also data supporting the notion that infection with atypical bacteria may be a contributing factor to difficult-to-treat asthma.

Strenuous physical exercise can also trigger asthma attacks. Exercise can cause asthma symptoms to flare, especially when asthma is not well controlled. Mouth breathing; exercising in cold, dry air; or prolonged, strenuous activities such as medium- to long-distance running can increase the likelihood of exercise-induced bronchospasm—an obstruction of transient airflow that usually occurs 5 to 15 minutes after the onset of physical exertion. Although exercise can trigger asthma in certain people, it is one trigger that should not be avoided. Exercise strengthens the cardiovascular system and may lessen the sensitivity to asthma triggers. To minimize the effects of this trigger, asthmatic individuals should start any new exercise regime slowly, gradually building strength and endurance, and warm up gradually at the beginning of each exercise session. Avoiding exercise outdoors in extremely cold weather or during peak pollen seasons is also a prudent measure.

Asthma and gastroesophageal reflux disease (GERD) are common medical conditions that often coexist. Studies have shown conflicting results on whether lower esophageal acidification can act as a trigger for asthma. In fact, asthma might precipitate GERD symptoms; thus, a temporal association between the two does not establish that GERD triggers asthma. Randomized trials investigating different treatment modalities for GERD in asthma have been conducted to determine whether treatment of GERD improves asthma symptoms and outcomes. A meta-analysis of randomized controlled trials concluded that therapy for GERD, including acid-suppressive treatment with a proton-pump or histamine-2 receptor antagonists, does not consistently improve lung function, asthma symptoms, nocturnal asthma, or lessen the use of asthma medications. Littner and colleagues showed that in adult patients with moderate-to-severe persistent asthma and symptoms of acid reflux, treatment with 30 mg of lansoprazole twice daily for 24 weeks did not improve asthma symptoms, pulmonary function, or reduce albuterol use. However, this dose significantly reduced asthma exacerbations and improved quality of life, particularly in those patients receiving more than one asthma-controller medication. With all of this being considered, untreated GERD symptoms may affect airway reactivity in patients with asthma. Thus, treating patients for symptoms of GERD with concomitant asthma has become standard practice and should be considered.

Exposure to food allergens and additives (see Fig. 17-3) can cause a variety of symptoms. It is widely believed that allergic reactions to foods are common asthma triggers, but definitive evidence to support this concept is lacking. Despite this lack of data, some asthmatic individuals report worsening asthma symptoms after ingesting specific foods and food additives. Food additives that have been implicated include salicylates, food preservatives, monosodium glutamate, and some food-coloring agents. Sodium metabisulfite, a preservative in many beverages (including beer and wine) and foods, is thought to release sufficient sulfur dioxide to provoke bronchoconstriction. For some people, eating a particular food (common culprits include milk, eggs, peanuts, tree nuts, soy, wheat, fish, and shellfish) can trigger asthma symptoms. This constellation of food sensitivity and worsening asthma symptoms tends to correlate with a more severe course of disease. Patients with food allergies and underlying asthma experience more severe reactions to food allergens than do patients without asthma, because their reactions are more likely to involve life-threatening respiratory symptoms.

Allergic reactions that involve respiratory symptoms are almost always more severe than reactions that do not involve the

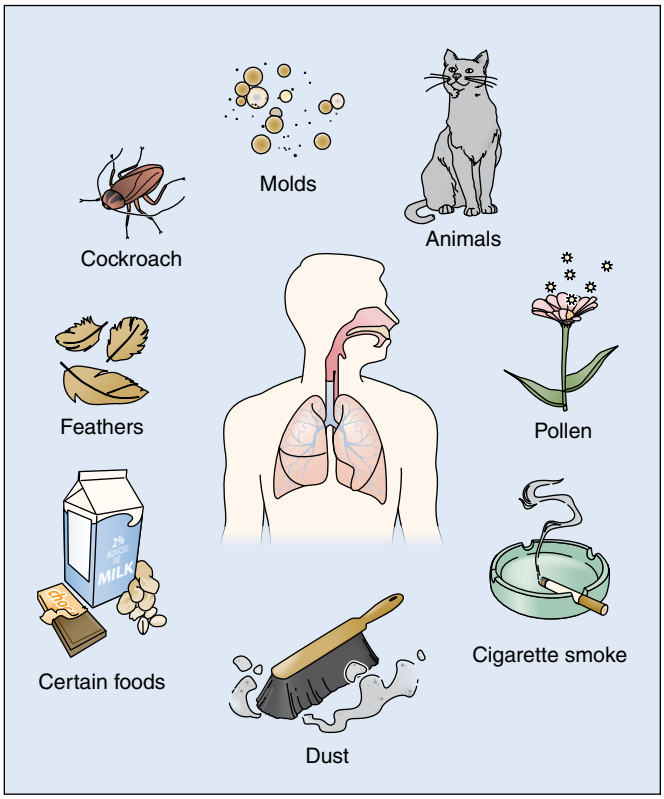

Figure 17-3 Common triggers of asthma include allergens, irritants, gastroesophageal reflux disease, medications, weather changes, viral and bacterial infections, emotion stressors, foods and food additives, and physical exercise.

respiratory tract. Particularly susceptible food-sensitive asthmatic individuals have been reported to react to merely inhalation without ingestion; however, isolated symptoms of rhinitis or asthma without concomitant cutaneous or gastrointestinal symptoms are rare. Nevertheless, if any type of food triggers an asthma attack, the best treatment is strict avoidance.

Although asthma is not a psychological condition, emotional or nervous stress can trigger asthma symptoms. Stress alone cannot provoke asthma; however, if accompanied by anxiety, stress can cause fatigue, potentiating coughing, shortness of breath, and wheezing. A strong feeling or emotional behavior, such as laughing or crying, may trigger asthma symptoms because of the accompanying change in breathing patterns. As with any other chronic health condition, proper rest, nutrition, and exercise are important to overall well-being and can help in managing asthma.

Effective control of asthma depends on identification and alleviation of exacerbating factors. Triggers of asthma frequently include ongoing exposure to allergens and irritants, medications, weather and atmospheric changes, upper and lower respiratory tract infections, uncontrolled gastroesophageal reflux disease, foods and food additives, and emotional stress and anxiety (Fig. 17-3). It is of paramount importance to recognize contributing factors early, and eliminate exposure to prevent unnecessary morbidity and mortality. A key theme to this chapter has been avoidance, which in many cases is quite difficult; but by following a systematic method for identifying and removing potential triggers from the asthmatic individual's environment, the goal of optimum asthma control can be accomplished with a combined, concerted effort on the part of the physician and patient.

SUGGESTED READING

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