Trends in allergy treatment
Improving quality of life for patients
By Nancy Ott, MD

Stop me if you've heard these before:

Allergies are nothing to sneeze at.
Shouldn't your feet run, not your nose?
Eczema is the itch that rashes.

Now for the real punch line: As many as 50 million people in the United States suffer from various types of allergies; and allergic conditions such as rhinitis, eczema, and asthma are on the upswing, along with a profusion of pollen spores due to global warming.

Why is this? Speculation on the causes has honed in on a variety of factors—too-clean homes with fewer children and less animal exposure; not enough natural infectious disease; less rural living; and too much cement in cities (not enough soil saprophyte exposure), among others—that have resulted in reduced exposure to endotoxins.

The origin of the so-called "hygiene hypothesis" is attributed to David Strachen's 1989 British Journal of Medicine article, "Hay fever, hygiene and household size." His epidemiologic study looking at a cohort of children in 1958 and again in 1981 found that the younger children (who are exposed to more germs by older siblings) in large families had less atopy. Shortly thereafter, research in Austria showed that fewer allergies occurred in babies who spent time in barns or lived in homes attached to barns. In Finland, von Hertzen and Haahtela (2006) found that more cement and city living correlated with an increase in allergies. They speculated that missing out on playtime in the dirt with saprophytic mycobacteria, lactoba-cilli, and some intestinal parasites reduces the ability of a baby's early T-regulator cells to become tolerant to allergens.

In addition, the carbon dioxide-enriched city air associated with global warming has caused pollen production to increase (Wayne 2002). Paul R. Epstein, MD, MPH, associate director of the Center for Health and the Global Environment at Harvard Medical School, has suggested that pollen seasons are also increasing by one day per year. Molds also become more productive with increased CO2. Further compounding the problem, the number of board-certified allergy, asthma, and immunology providers in the U.S. is decreasing. The good news is that a number of treatments, reviewed below, continue to help control these chronic illnesses.

Asthma

An estimated 20.3 million Americans have asthma, and 6.3 million of them are under the age of 18. Research has shown that although treating early childhood asthma won't change the natural history of the disease, it can help control it (Bisgaard 2006, Guilbert 2006). The Childhood Asthma Management Program, a five-year, eight-center study funded by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health, also showed that inhaled corticosteroids (ICS) controlled the disease and that children with asthma treated with ICS will attain expected adult height, although their growth progressed a little more slowly than their peers' growth (2002). Over half of infants and preschool children with asthma will outgrow this condition (Taussig 2003).

More severe wheezing, combined with a history of eczema or family history of atopy, increases the risk of persistent asthma (Taussig 2003, Phalen 2002). Asthma that begins in adulthood often is associated with occupational triggers (allergic and nonallergic) or sinusitis, polyps, and aspirin sensitivity, the so-called triad complex not associated with allergies.

Inhaled corticosteroids (ICS) control asthma and help prevent hospitalizations. Long-acting beta-agonists (LABAs) combined with ICS for moderate to severe asthma have proven very helpful for asthma control and in keeping patients out of the hospital. Because LABAs alone can be harmful (as for any prolonged extensive use of a beta-agonist as monotherapy), a black-box warning now appears on the label. Concerns have been raised regarding polymorphisms in the beta receptor that were thought to increase the risk of worsening asthma with the use of LABAs, particularly in African Americans. However, Bleeker (2006) showed that this polymorphism alone is not the cause of worsening asthma with LABA use in any ethnic group.

New NHBLI asthma guidelines to be made public this fall will place new emphasis on impairment and risk in asthma management. Persistent asthma will still be labeled as mild, moderate, and severe. Intermit-tent asthma will not be referred to as "mild," as flare-ups may be severe and dangerous. Deaths from asthma have declined from 5,000 per year to 3,800 in the U.S. but are seen equally across all categories of severity. Allergy shots (subcutaneous immuno-therapy, or SCIT) can be used to treat controlled allergic asthma and to prevent asthma in allergic rhinitis. Moderate or severe uncontrolled allergic asthma can now be treated with injections monthly or bimonthly of monoclonal antibody to the IgE molecule, omalizumab (anti-IgE).

Allergic rhinoconjunctivitis and nonallergic rhinitis

Patients rate allergic rhinoconjunctivitis (ARC) and nonallergic rhinitis (NAR) as even more detrimental to quality of life than asthma. Secondary complications of

rhinitis include sinusitis and otitis media, which are less likely to occur if the rhinitis is controlled.

Control medications work well if patients use them consistently. Topical corticosteroids in microgram doses are still the most efficacious controller and preventer. Nonsedating antihistamines can help symptoms of sneezing and rhinorrhea but do not control nasal mucosal swelling. Allergy shots are still a viable option to reduce symptoms for ARC but not NAR. Allergy serums are now standardized for many common aeroallergens, resulting in better symptom control. Finally, ad-junct nasal lavage with saline solution also can reduce symptoms by washing away chemical mediators. Omalizumab controls ARC but is too costly to be used for ARC alone.

Research is now being done on oral immunotherapy (OIT), which is being given in Europe for some pollen allergies. How-ever, symptom control sometimes is not reached until up to two years after beginning OIT, whereas conventional SCIT relieves symptoms within six to 12 months.

Hives and angioedema

Hives and angioedema continue to be the bane of allergists. An estimated 20 percent of Americans have hives at some point in their lives, and the itch of urticaria can be severe and debilitating. Allergies to drugs, foods, and insect stings do not account for most cases, although a thorough history is of utmost importance to rule these out. Antibodies against the mast cell receptor for IgE account for 30 percent of nonallergic hives. Thyroid autoantibodies can also be elevated despite no evidence of thyroid disease. This is another indication that these hives are likely to be an autoimmune phenomenon.

If a trigger can't be identified (as is often the case), the mainstay treatment is itch control. Histamine type-1 receptor blockers are the most common treatment for itch control. Augmentation with a histamine type-2 blocker such as ranitidine may help in up to 30 percent of cases. Although histamine-type 2 receptors are mainly in the stomach, some are in skin. Oral (not topical) corticosteroids are still used for severe or persistent breakouts.

Atopic dermatitis

Atopic dermatitis (eczema) affects 10 percent to 20 percent of children and 1 percent to 3 percent of adults. In infants and young children, the condition can be debilitating for the child as well as the parents. Neither child nor parent sleeps well because of the intense itching and the child's distress.

Thirty percent of children under the age of 2 years will have a food trigger. The list is short, however, and 90 percent of food triggers are milk, egg, soy, wheat,

peanut, tree nuts, fish, or shellfish. CAP RASTs (which are not really Radio-AllergoSorbent Tests, but a fluorescent enzyme immuno-assays using a CAP method, a trademark of Pharmacia Diagnostics), laboratory blood tests used to detect IgE antibodies to specific allergens, can be both helpful and harmful. Too many RASTs may overestimate the food allergies, since 80 percent of children with eczema have a high total serum IgE level that increases the chance of a false positive CAP RAST. The negative predictive value is over 90 percent, however.

Although most infants and toddlers will outgrow food allergies related to milk, soy, egg, and wheat, research has shown that it is a different story for allergies related to peanuts, tree nuts, fish, and crustacean seafood. These foods can cause an allergy anytime in life and are less likely to resolve. Fur-thermore, the severity of such allergies can increase over time, even if the initial reaction was mild. More information, for patients and health care pro-viders alike, can be found on the Food Allergy & Anaphylaxis Network Web site (www.foodallergy.org).

Immunodeficiency
Recurrent severe infections (more than two confirmed bacterial sinopulmonary infections) in a patient deserve a closer look to determine whether or not an immunodeficiency is present. Many immunodeficiencies are caused by a specific gene defect of antibody production or function. Screening tests include immunoglobulin levels and specific antibody-response testing for B-cell function, the most common cell to have a defect.

T-cell numbers and delayed-type hypersensitivity testing can screen for T-cell defects. [A more thorough discussion of the complex topic of immunodeficiencies and other allergy/immunology issues may be found in the Practice Parameters at aaaai.org or acaai.org.]

Less common immunodeficiencies can be assessed by complement levels and phagocytic cell function. If an immunodeficiency that causes life-threatening infections is present, the treatment is gamma globulin to prevent the infections.

Vivaglobulin immunoglobulin replacement therapy recently was FDA-approved for subcutaneous infusion, making life more manageable for patients by allowing home infusions.

Proper treatment: nothing to sneeze at
Many discoveries have yielded important knowledge about the immune cells that cause allergic reactions. Our growing understanding of T-cell, mast-cell, and eosinophil function; trafficking; receptors; cytokines; and apoptosis (cell death) may lead to the development of new allergy medications.

Used correctly, the current treatments can control disease. Allergic conditions can be costly if not treated correctly or in a timely fashion. Proper care is of the utmost importance to prevent ongoing disease and make quality of life better for the patient. For allergists, the mantra is, "Never trust a mast cell."

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