

Primary Immunodeficiency Diseases and Allergies



Chapter 27

Allergic diseases and symptoms occur because of an active immune system that reacts to things that are usually harmless, such as pollens, pet dander or foods. For that reason, it can be puzzling that people with immune deficiencies would have allergies. In fact, taken as a whole, people with immune deficiencies probably have a far greater disease burden of allergy than the general population, although perhaps not in the same patterns. It is generally true that people with immunodeficiencies do not have problems with allergies as often as those who are immunocompetent. However, specific changes to the immune system in some immune deficiency diseases may increase the risk of the developing allergies.

Definition of Primary Immunodeficiency Diseases and Allergies

Allergies manifest in a number of very specific ways, including nasal and eye symptoms, allergic asthma, eczema, hives and anaphylaxis. It is common for a person to have more than one allergic disease. The immune system in people with allergies reacts in a specific way to allergens. Allergens are those things that trigger allergic symptoms. Common allergens include materials and particles in the air and environment such as dust mites, molds, pet dander, tree pollen, grasses and weeds, foods, drugs and stinging insect venoms.

Generally, an allergic reaction occurs when a person develops “allergic” antibodies, called IgE, which are specific for an allergen. The IgE antibodies bind tightly to allergic cells, called mast cells or basophils, in the skin, airways, gastrointestinal tract and around blood vessels. The allergic cells get activated when the bound IgE recognizes an allergen, and these cells then release histamine, a chemical that can cause hives, runny nose, sneezing and itching. Depending

upon where in the body the reaction between the IgE and the allergen happens, different symptoms can occur.

Hay Fever

Hay fever, or allergic rhinitis, causes itchy, stuffy, and runny noses and sneezing when the affected person breathes in certain allergens. Watery, red and itchy eyes (allergic conjunctivitis) can also occur. The timing and severity of symptoms depends upon exposure to the allergens to which the person reacts; for example, symptoms are prominent in the spring for patients with tree pollen allergy but occur in the fall for patients with ragweed allergy. When the stuffiness gets very bad, it can lead to rhinosinusitis where fluid and pressure accumulates in the sinuses, leading to discomfort and risk of infection. This is particularly a problem in people with immune deficiencies, as it can be difficult to determine whether sinus problems are due to infection, allergy or, as is often the case, a combination of the two.

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Managing hay fever can include:

- Avoidance of allergens when possible, such as dust mites, mold or pet dander.
- Oral ‘non-sedating’ antihistamines, such as Zyrtec (cetirizine), Allegra (fexafenidine) or Claritin (loratidine); Benadryl (diphenhydramine) or Atarax (hydroxyzine) are anti-histamines that are sometimes used, but these usually cause drowsiness, so should be used with caution.
- Nasal steroids for more severe symptoms, particularly with nasal congestion.
- Allergy shots (immunotherapy).

Allergic Asthma

Allergic asthma is a chronic allergic condition of the lungs. In people with allergic asthma, breathing difficulties such as wheezing, chest tightness and coughing can be triggered after inhaling something to which they are allergic, like tree pollen or mold. Changes in temperature, smoke, strong smells and other non-allergens can trigger symptoms as well. Asthma is usually diagnosed based on symptoms and by using pulmonary function tests where a computer measures airway function. Asthma is a chronic disorder that requires ongoing management. Treatment of asthma includes therapy, such as albuterol, to dilate constricted airways for immediate relief of symptoms. For many patients, depending on the severity and frequency of symptoms, daily inhaled steroids and other medications are also used to prevent symptoms and control the disease.

Of special relevance to people with known or suspected immune deficiencies, asthma attacks, especially those, which occur when the affected person has a fever, can often be confused with pneumonia. It is important to differentiate between an asthma attack and pneumonia as the treatment for the two problems is very different.

Food Allergies

Food allergies result from the development of specific immune responses to foods. Symptoms of food allergy usually occur within minutes to a few hours of eating a food to which a person is allergic. Symptoms of food allergy can include hives (which look like mosquito bites), flushing and itching of the skin, vomiting, diarrhea or abdominal cramping. In severe cases, difficulty breathing, a feeling of throat closure. Significant decrease in blood pressure and unconsciousness can occur. Food allergies are treated by carefully avoiding the offending foods. In cases of an anaphylactic reaction, an injection of epinephrine is used.

Food Intolerances

Food intolerances do not involve the immune system, and they are not usually life threatening. An example of food intolerance is lactose intolerance in which the lack of an enzyme to break down milk sugars results in abdominal cramping and diarrhea, when dairy products are consumed. Celiac disease, in which affected people experience gastrointestinal symptoms after eating gluten-containing products, like wheat, is an immune disease directed at wheat and not a “true” food allergy.

Eczema

Eczema, or atopic dermatitis, is chronic skin inflammation that is sometimes made worse by exposure to foods or environmental allergens, particularly in children. The main problem with eczema is usually a breakdown of the skin barrier and activation of the immune system in the skin, leading to inflammation with severe itchiness. The skin barrier functions to keep water in the skin and to keep other things (such as bacteria and allergens) out. Loss of this barrier leads to skin dryness and increased risk of infection. Interactions between genetic susceptibility and environmental exposures early in life are likely to play a major role in the development of eczema. Several immune deficiencies are associated with the

(Definition of Primary Immunodeficiency Diseases and Allergies continued)

development of eczema, including Wiskott-Aldrich Syndrome, the autosomal dominant hyper-IgE syndrome and IPEX, but the underlying genetic causes are quite different.

Treating eczema requires ensuring that the skin barrier stays intact by frequently bathing to soak the skin, applying emollients to lock in moisture and lock out unwanted exposures, and adding topical steroids or

other drugs that can calm down the immune response (inflammation) in the skin. In some patients with primary immunodeficiency, skin bacteria can worsen the symptoms, and so oral and topical antibiotics are often used. In addition, many patients also respond well to bleach baths (or swimming in chlorinated pools) as another way of killing the bad skin bacteria.

Drug Allergies and Intolerances

Drug allergies and intolerances are more common in people with immune deficiencies largely because they are exposed to more drugs. In general, the more types of drugs and exposures to drugs people have had, the greater the chances to develop drug allergies or intolerances. Having reactions to drugs does not necessarily mean that the person is an “allergic” person, but of course, much care must be taken to avoid serious reactions.

As with food allergies, many reactions to drugs are not true “allergies” caused by IgE; however, these reactions still can be severe and must be taken very seriously. A

thorough evaluation of previous reactions is critical to ensuring that the use of potentially dangerous medications is avoided, while not restricting medications unnecessarily. In some patients with allergic reactions to drugs, particularly antibiotics, allergists can temporarily “desensitize” patients so that they can receive these medications in life-threatening situations.

Diagnosis of Primary Immunodeficiency Diseases and Allergies

Diagnosing allergies can be tricky, especially in the context of an immune deficiency. The most common tests used are skin prick testing and a blood test for IgE specific for allergens (sometimes referred to as a RAST test, Cap RAST or ImmunoCap). Skin prick testing involves taking a drop of allergen and poking the surface of the skin. Positive reactions lead to what looks like a hive. Blood tests can be sent to see if the person has IgE that reacts to specific allergens. The validity of the results varies depending on which allergen is being tested (food allergens tend to be the most accurate). However, especially in settings when the IgE is high, and when people have immune deficiencies, it is sometimes difficult to interpret these results. Allergy testing in patients with primary immunodeficiency should never be interpreted without the help of someone who regularly cares for patients with primary immunodeficiency diseases and allergies.

Some primary immunodeficiencies are more commonly associated with allergic issues. These include Hyper-IgE syndromes (HIES) and IPEX.

Omenn's Syndrome is caused by the same genetic mutations that lead to Severe Combined Immune Deficiency (SCID). However, for reasons we do not fully understand, a few T- and B-cells "leak out" as it were and lead to swelling of the lymph nodes, spleen and liver, and lead to a head to toe rash that looks like terrible eczema. Patients have very high IgE levels and many eosinophils. However, they do not really have allergies to specific foods or anything else because the T-and B-cells they make are unable make a specific response.

Hyper IgE Syndromes (HIES) are a series of immune deficiencies, which are characterized by extraordinarily high levels of IgE. These patients are prone to serious infections. The most wellknown and best-characterized HIES are the autosomal dominant hyper-IgE syndrome (AD-HIES), which is due to STAT3 mutations, and autosomal recessive HIES cause by DOCK8 deficiency. Not everyone with a high level of IgE has a HIES. Many people with bad eczema or allergies can have high IgE (thousands to tens of thousands), and no other symptoms at all. People with AD-HIES have a specific set of symptoms that includes Staph abscesses, pneumonias, fungal infections of the skin, easily broken bones, very flexible joints and retained childhood teeth. People with DOCK8 deficiency not only have bacterial infections but also have severe viral infections, especially of the skin, very bad eczema, allergies to foods and an increased risk of a number of cancers. *(See chapter titled "Hyper IgE Syndrome.")*

IPEX is a syndrome of immunodeficiency, endocrine, gastrointestinal and skin disease, which has an X-linked pattern of inheritance. Boys with IPEX have severe eczema, high levels of IgE and allergies.