

St Anthony's Hospital

Allergic Disease

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What is allergy and what is intolerance or hypersensitivity?

In a strict sense the term Allergy simply describes altered reactivity. However, for doctors, allergy describes a particular pattern of immune reactivity. This involves the cross-linking of adjacent IgE allergy antibodies on the surface of highly reactive mast cells by the pollen, food or other allergen to which the individual is sensitive. This leads to the explosive release of several types of highly active molecules that cause itching, dilation of capillaries, mucous secretion and contraction of smooth muscle. The resulting symptoms depend on the where this reaction occurs. In the nose there is sneezing, blockage and dripping. In the lungs there is coughing, tightness, wheezing and shortness of breath while in the skin there is redness, itching and scaling.

The term intolerance is more vague and implies reactivity to a compound not involving IgE antibodies or mast cells. In some cases there is deficiency of a particular enzyme as in lactase deficiency causing lactose intolerance. In others the reaction may be due to specific substances in the food for example tyramine in cheese and wine that can cause headaches. Hypersensitivity describes an exaggeration of a normal response to a degree that causes symptoms. In many cases the immune and biochemical pathways have been defined and involve T cells in particular but not IgE.

Is Allergy increasing?

There is now very good evidence that allergic diseases of all sorts are on the increase. The reason for this increase is unclear and several theories have been proposed. These include improvements in hygiene and sanitation, better vaccination and the earlier and more liberal use of antibiotics. Together these changes have reduced the exposure of the infant's developing immune system to a sufficient number and variety of bacteria. This exposure is now considered very important in moulding the immune system in such a way that it accepts rather than attacks the harmless proteins found in pollens, animal dander and house dust mite.

Other theories that aim to explain the increase in allergic disease include the early exposure to very immunogenic foods such as nuts and soya, the increased stress of modern life and increased exposure to both indoor and outdoor pollution. In the case of peanut allergy, some have blamed the early use of emollient creams and ointments containing arachis oil in infants with eczema. Regardless of the cause of this increase, it is clear we can expect to see more and more people with asthma, eczema and hayfever as well as certain types of food allergy. The latter in particular is likely to increase the incidence of anaphylaxis and the need for more of our patients to be armed with an injectable adrenaline.

What are the different types of allergic disease?

The pattern of allergic disease varies with age. In infancy, eczema is the most common problem along with some sort of milk or egg allergy. These problems get less with age and many children are entirely symptom free by 3 to 4 years of age. However, as the frequency of eczema gets less, so the frequency of asthma increases. This continues to varying degrees throughout life. By 5 to 8 years of age there is then an increase in the frequency of hayfever. This may improve by the late teens in some people while in others it may get worse. In adult life, those with significant eczema, asthma and hayfever continue to suffer symptoms. However, others may develop one of several problems without an obvious allergic basis such as irritable bowel syndrome and chronic fatigue syndrome. These are likely to be due to interactions between several factors such as an unusual microbial infection, persistent stress, a subtle alteration in immune function and alterations in the perception of sensory signals.

How serious is food allergy?

Allergy to foods is most common in infancy and childhood. This lessens as the immune system learns to recognize and tolerate the harmless proteins that are present in commonly consumed foods such as milk, eggs and soya. The vast majority of infants with an allergy to these proteins causing either vomiting, diarrhoea, colic, skin rashes and skin swelling have outgrown their sensitivity by 3 years of age. In many others the severity of the symptoms lessens with age. In contrast, an allergy to nuts and fish tends to be more persistent and to be more frequently associated with significant skin, mouth, lung and cardiovascular reactions.

For all types of food allergies the quantity of food required to produce a specific reaction varies very considerably. In some highly sensitive people even the transfer of minute quantities of the allergenic food protein to their skin by someone who has handled or eaten this food may cause a local reaction. Others may suffer only mild and localized symptoms after eating 10 or 20 grams of the food. For most people with a food allergy the pattern of their allergic symptoms

tends to be established fairly quickly and remains constant for a given quantity of the food eaten. This contrasts with the popular belief that the severity of the allergic reaction gets progressively worse with each encounter.

What is anaphylaxis?

Anaphylaxis describes a severe and generalized allergic reaction that may threaten a person's life if it causes a collapse of the blood pressure, constriction of the throat or severe asthma. Most cases of anaphylaxis are preceded by widespread itching of the skin with either hives or flushing and swelling of the mouth, tongue or face. In some people nausea and vomiting or rarely, diarrhoea, may also occur.

Among the more common causes of anaphylaxis are allergy to nuts, fish, milk, eggs, insect venom and antibiotics. From early childhood onwards there is a gradual increase in the frequency of nut and later on fish allergy. While nut allergy tends to be a lifelong problem in the vast majority of children, a small proportion of children may develop a tolerance to fish after many years. Bee and wasp venom allergy is evident particularly from late childhood onwards. However, children suffering a severe reaction on being stung frequently lose their sensitivity with age. Injection therapy is required only with major life threatening reactions and avoiding bee and wasps is difficult. For adults, however, anaphylaxis occurring after a bee or wasp sting often requires either the carrying of an injectable adrenaline desensitization therapy.

Anyone suffering a significant episode of anaphylaxis needs full evaluation by a specialist. This requires assessment of the risk of a future reaction and the whether they need to carry an oral anti-histamine and an injectable adrenaline e.g. epipen. People requiring an epipen need full instruction on how and when this should be used. There is now good evidence that many people issued with an epipen for an anaphylactic reaction have little knowledge about how or when this device should be used nor indeed what action to take afterwards. Thus a full and careful assessment is important for the anaphylactic person's long term safety and management.

How is allergy diagnosed?

Allergy is confirmed only when compatible symptoms and signs can be paired up with an appropriate allergen using scientifically validated testing methods. In the first instance, therefore, a careful history of the person's skin, nose or lung symptoms is required. The presence of itching within the nose, mouth or skin caused by the release of histamine certainly suggests an allergic cause. A seasonal variation of symptoms suggests an allergy to either tree or grass pollen or occasionally to fungal spores. Symptoms that occur exclusively

indoors suggest a sensitivity to house dust mite, animal dander or even a mould. Checking to see if symptoms occur only at home, school or work and if they are absent when a person is away on holiday also provides valuable clues.

The time of onset of symptoms after allergen exposure is also very important. Thus symptoms that occur within one hour of eating and with small quantities of food may be due to an allergy while those that occur several hours later suggest a non-allergic cause. When allergic inflammation is established the affected area can become easily irritated by non-allergic factors. Thus people with non-allergic rhinitis may start sneezing or have a runny nose with changes in temperature or smelling strong perfumes, deodorants or paints. These physical factors can also exacerbate asthma when this is not under optimal control. In those with eczema, the skin may become very itchy and inflamed with harsh soaps or shampoos.

For any severe acute reaction it is extremely important to know the quantity of allergen that produced the reaction, the rate of progression of anaphylactic symptoms and the response, or otherwise, to any emergency treatment. As anaphylaxis is a very frightening experience it can sometimes be difficult to work out if faintness or difficulty breathing is due to the allergic reaction or hyperventilation arising from apprehension. However, the presence of noisy breathing whether due to constriction of the throat or wheezing from acute asthma is always a cause for concern.

Once allergy is suspected as a cause for a person's symptoms, identification of the causative agents may be undertaken using either blood or skin tests. Skin prick testing is an extremely safe procedure. It produces minimal discomfort that is less than with a blood test but does require that the person avoids all anti-histamines for at least seven days. For the vast majority of allergens it is as sensitive and specific as blood tests and for some it is more sensitive and specific. In contrast to blood-based allergy tests the results of skin testing are available within the space of an outpatient consultation. However, blood tests are required when anti-histamines cannot be stopped, when severe eczema leaves little normal skin for testing or if there is any concern that skin testing may cause a significant systemic reaction.

Skin testing involves putting small drops of special highly purified and concentrated allergen onto the skin of the forearm and then gently pricking the skin through this allergen droplet with a special lancet. There is no bleeding and an extremely small quantity of allergen enters the upper part of the skin to react with the allergen specific IgE antibodies on the surface of the many allergy cells found here. Controls ensure that entirely negative results are not caused by

residual anti-histamines in the person's body and that simply pricking the skin does not cause a positive reaction.

Blood tests for measuring allergen specific IgE antibodies use a variety of different methods on several types of automated analysers and caution is required in the interpretation.

Scientifically unvalidated methods of allergy testing include electrodermal testing, applied kinesiology, the pulse test and blood based cytotoxic tests. These are totally unreliable and are not recognized for allergy testing by either the European or American academies for Allergy and Clinical Immunology.

How are Allergic conditions treated?

Wherever possible, allergen avoidance should be practised. This includes simple measures such as staying indoors and closing the windows when the pollen count is high for people with hayfever. For those with house dust mite allergy, the use of special allergen excluding mattress, pillow and duvet covers may be helpful especially when combined with the regular use of a high filtration vacuum cleaners and the hot washing of all bed linen to over 60C. Clearly any foods that cause or exacerbate allergic symptoms should be avoided. However, it is frequently impossible to practise allergen avoidance to a degree that prevents all allergic symptoms. In this case drug therapy and occasionally desensitization therapy is required.

As histamine is released in virtually all allergic conditions and causes itching, redness and swelling, anti-histamines are an important part of allergy management. Many of the new anti-histamines cause virtually no drowsiness and are effective within one hour of consumption. Many are formulated for once daily dosage and can be safely combined with other anti-allergy treatments. In addition to anti-histamines, steroids are the other main stay of allergy treatment. These start to work many hours after application by dampening the activation of the allergy immune cells and by reducing inflammation. For asthma and hayfever the steroids are inhaled into the lungs and nose respectively and for eczema they are applied topically to the skin. Other treatments include drugs that stabilize the allergy mast cells and those that dry up nasal secretions. More recently drugs have been introduced that act against some of the other important chemicals that cause allergic inflammation. Using combinations of these drugs will allow a reduction in the amount of each drug used and is more effective than either drug used alone.

Desensitization therapy is best reserved for those patients with severe allergic symptoms which are unresponsive or only partially responsive to full allergen

avoidance measures and maximum drug treatment. It is most effective for patients with hayfever and less so for asthma. The therapy is of virtually no value for eczema or food allergy. In practical terms, sensitivity needs to be confined to a single or at most two allergens. These need to be conclusively identified by history and skin or blood tests. The treatment is undertaken with full resuscitation facilities at hand and involves the subcutaneous injection of increasing doses of the allergen(s) causing a person's symptoms. This incremental phase normally takes about 12 to 15 weeks. Rush schedules can be used but may have a higher rate of adverse effects. After successful completion of the incremental phase, maintenance monthly injections are continued for a period of 3 to 5 years. Using this regime roughly one third of patients will gain considerable benefit, a further one third some benefit and the final third little or no benefit. A new shorter pre-seasonal desensitization therapy has recently become available but its efficacy has not been fully established although it does look promising. Importantly, there is now evidence that early attention to the allergic nasal disease with desensitization therapy may reduce the progression to allergic lung disease. New therapies for the future.

With the central role of the IgE antibody in allergic conditions, one promising approach is the use of genetically engineered antibodies that bind and neutralize all IgE molecules regardless of their allergen specificity. This will allow treatment of allergic problems where there are multiple allergens involved and make desensitization therapy safer. The therapy is presently given by subcutaneous injections which, if the therapy proves safe, may be given by patients themselves. At present desensitization therapy is almost entirely injection based. However, trials looking at oral desensitization have shown a high safety profile as well significant effectiveness. It is hoped that this may allow patients to self-administer the special allergy drops at home without fear of a reaction. This approach may also allow children to receive this valuable therapy without a needle being in sight.

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