The end of the peanut allergy epidemic?

Mohammad Abdullah

Allergy to peanuts is one of the most common food allergies in the world and there is no cure. Medical student Mohammad Abdullah explains why some individuals develop peanut allergy and describes some exciting recent research that gives hope for new preventative treatments

An allergy is an abnormal response by the body's immune system to substances that are harmless to most people. Substances that trigger allergic reactions are called allergens. A food allergy results when an allergic reaction occurs as a consequence of eating certain allergenic food products. This reaction is usually directed against one or more proteins present in the food. In the case of peanuts, there are at least eight proteins that are known to start allergic reactions — i.e. to act as allergens.

Key words

- Allergy
- Allergen
- Antibody
- Type I hypersensitivity reaction
- Immune response

This type of harmful immune response is known as **hypersensitivity** reaction. There are different types of hypersensitivity reactions. Those, like peanut allergy, that involve immunoglobulin E (IgE) antibodies are called type I hypersensitivity reactions. Some individuals are more susceptible to this type of reaction than others. These individuals are said to be **atopic** — they have the genetic tendency to develop IgE allergic diseases.

The first time an atopic individual is exposed to an allergen, their immune cells are stimulated to produce IgE antibodies which bind to receptors on the surface of other immune system cells — **mast cells**. This process is called sensitisation. If the individual is then re-exposed to this same allergen, the allergen binds to the IgE, causing cross-linking of their receptors. This stimulates the mast cells to release molecules, including **histamine**, which cause the allergic reaction (see Box 1).

Allergic reactions can lead to mild symptoms such as itching, swelling and rash. But they can also be dangerous — causing difficulty in breathing and death in some cases. This is called **anaphylaxis**. Symptoms usually occur within minutes of coming into contact with an allergen and so must be treated quickly (see Table 1). The severity of the symptoms depends on the quantity of peanuts eaten and the individual's genetic makeup.

How common is peanut allergy?

The number of people in the UK and USA affected by peanut allergy has doubled in the last 10 years. In the UK, it affects about 1–2% of the population.

Table 1 Symptoms of hypersensitivity and their management

Severity of symptoms	Treatment
Allergic symptoms (itchiness, rash, runny nose)	Take an antihistamine tablet. If symptoms get worse, get medical help.
Anaphylaxis symptoms (difficulty breathing, generalised swelling)	Call an ambulance. If you have an adrenaline (epinephrine) injection pen (Epipen) use it.

Globally, the rates are even higher, affecting 3–4% of adults and 1 in 20 children worldwide. The reasons for this increase are complex, because peanut allergy results from both environmental factors (i.e. exposure to different allergens) and genetic factors (i.e. whether an individual is atopic).

Peanut allergy is more common in Western countries than elsewhere. The hygiene hypothesis was proposed to explain this. The hygiene hypothesis is based on the fact that in Western and developed countries, children grow up in cleaner environments than their counterparts in

An Epipen injects a measured dose of adrenaline in an allergy emergency

Terms explained

Anaphylaxis An abnormal reaction by the body to a particular antigen. Histamine is released, which causes local effects such as rash, itchiness and a runny nose. Occasionally, the symptoms are more widespread and potentially lethal — this is called anaphylactic shock. This may produce narrowing of the bronchioles in the lung, heart failure and death unless treated.

Atopic A tendency to develop certain allergic hypersensitivity reactions.

B cell A lymphocyte that, when it comes into contact with the appropriate antigen, proliferates to produce antibody-secreting cells and memory cells.

Histamine A substance produced as part of the immune response. Histamine is a local chemical mediator and only affects cells in the immediate vicinity. It dilates blood vessels and increases the permeability of capillaries to white blood cells and to proteins.

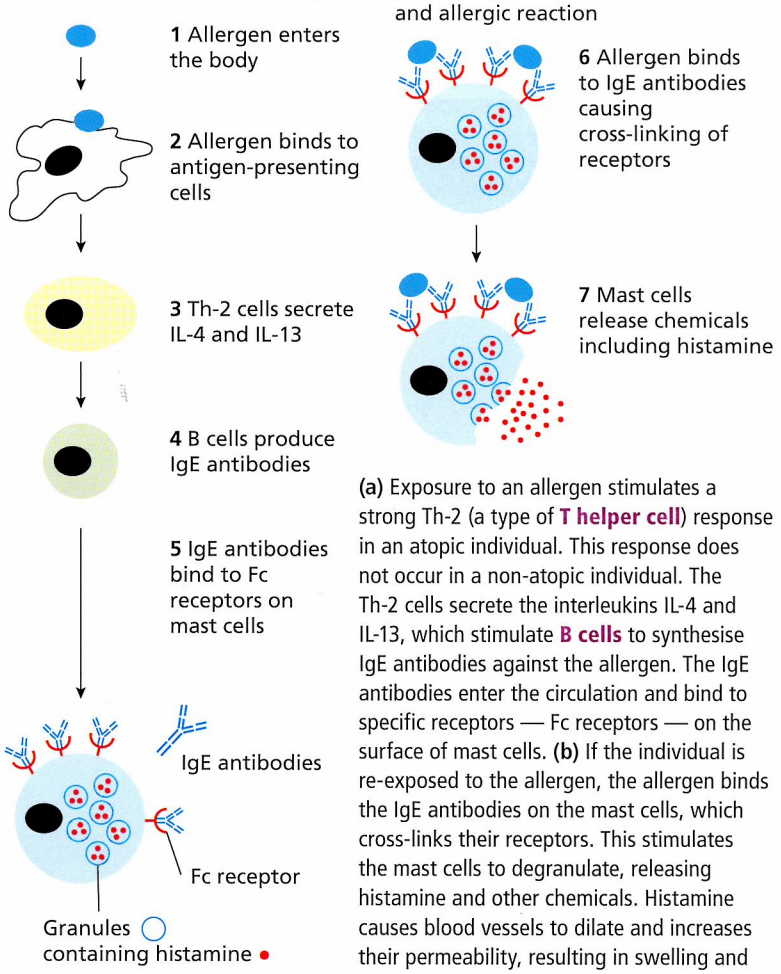
Hypersensitivity An abnormal reaction to a particular antigen.

Mast cell A cell that is part of the immune system. Mast cells release histamine and other substances that produce the responses characteristic of inflammation and allergy.

Protective immunity The way in which lymphocytes and some of the antibodies they produce enable the body to fight infection.

T helper cell A type of lymphocyte that does not secrete antibodies. T helper cells synthesise substances that activate or enhance the effects of other cells in the immune system.

Box 1 Type I hypersensitivity reaction



(a) Exposure to an allergen stimulates a strong Th-2 (a type of **T helper cell**) response in an atopic individual. This response does not occur in a non-atopic individual. The Th-2 cells secrete the interleukins IL-4 and IL-13, which stimulate **B cells** to synthesise IgE antibodies against the allergen. The IgE antibodies enter the circulation and bind to specific receptors — Fc receptors — on the surface of mast cells. **(b)** If the individual is re-exposed to the allergen, the allergen binds the IgE antibodies on the mast cells, which cross-links their receptors. This stimulates the mast cells to degranulate, releasing histamine and other chemicals. Histamine causes blood vessels to dilate and increases their permeability, resulting in swelling and redness.

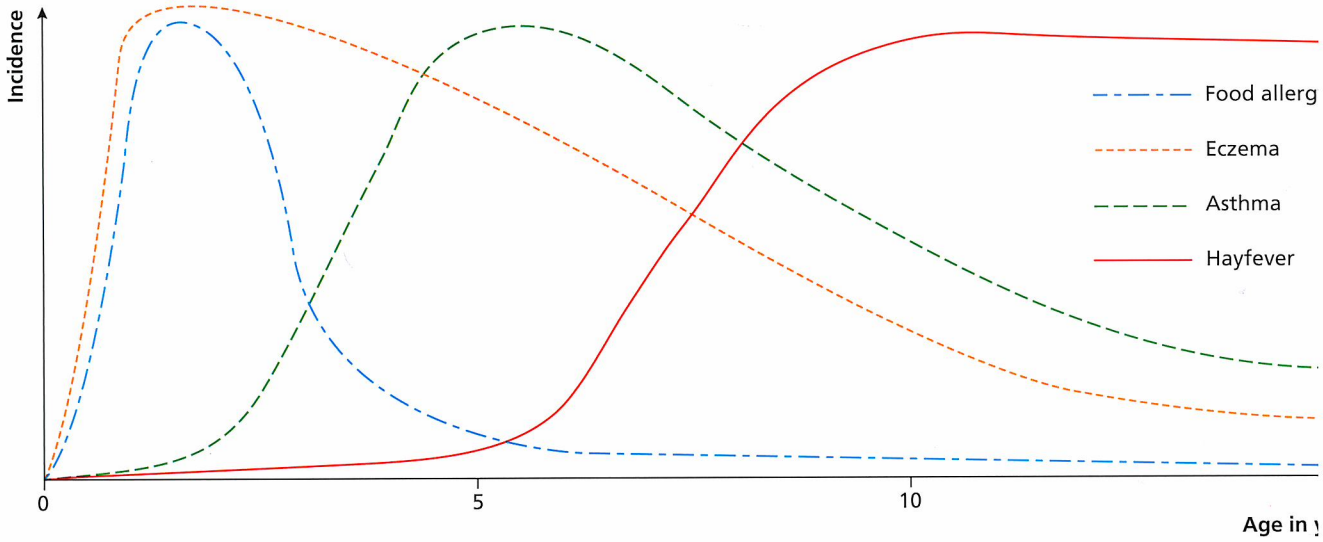


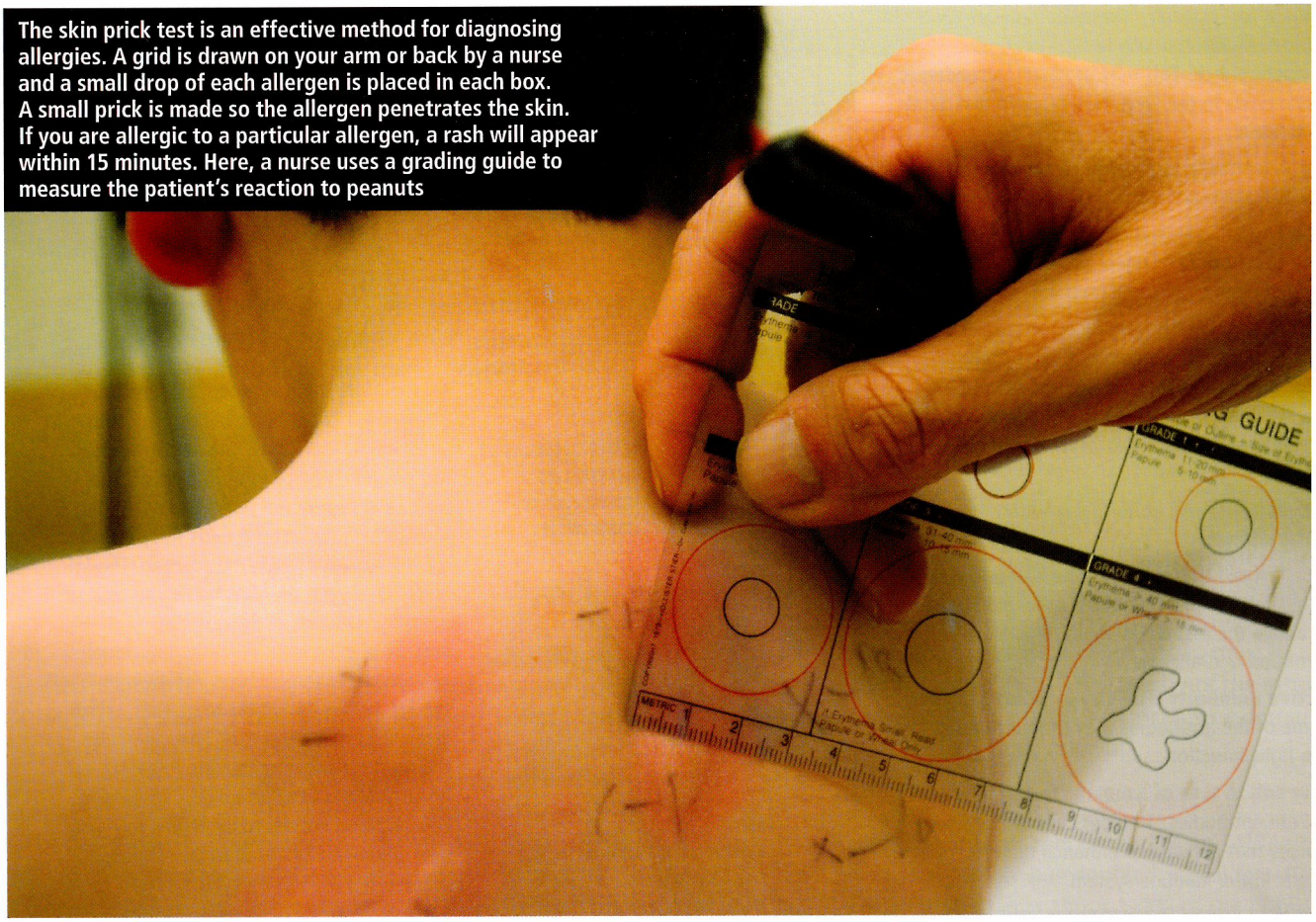
Figure 1 The allergic march. Having one atopic condition increases the risks of developing another

other regions of the world. As a consequence they get less exposure to dirty environments and their array of microorganisms, including bacteria and other infectious agents.

According to this hypothesis, exposure to such microorganisms is important for the natural development of **protective immunity**. This is why children in Western countries are more prone to developing allergies than they would be normally. Children who are prone to one allergy often develop other allergies too — this is called 'the allergic march' because these allergies usually occur in a particular sequence. Most of these a reactions appear in childhood but then ir spontaneously with age, although the reasc this remain unclear (see Figure 1).

Diagnosing peanut allergy

Several methods are used to diagnose peanut a A basic diagnosis is based on physical exami



The skin prick test is an effective method for diagnosing allergies. A grid is drawn on your arm or back by a nurse and a small drop of each allergen is placed in each box. A small prick is made so the allergen penetrates the skin. If you are allergic to a particular allergen, a rash will appear within 15 minutes. Here, a nurse uses a grading guide to measure the patient's reaction to peanuts

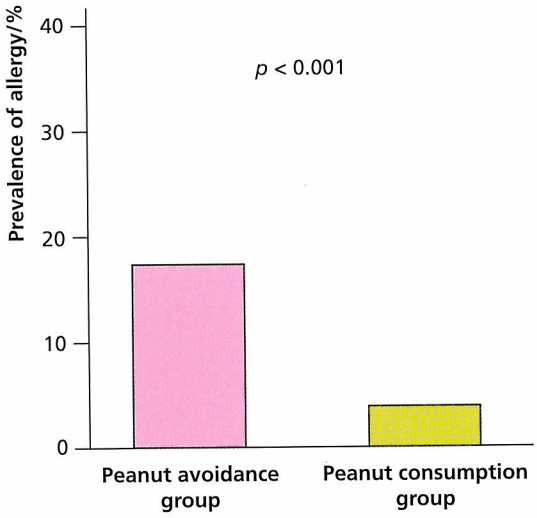


Figure 2 Prevalance of peanut allergy at 60 months of age for infants in the LEAP study

of the symptoms. The patient (or their parents) is also asked questions about previous experiences of similar symptoms, and whether they or members of their family suffer from asthma, eczema or other atopic conditions. There are, however, more specific diagnostic tests.

One such test is the skin prick test. The patient's skin is pricked with different substances that commonly cause allergies to see if there is a reaction. Another test is called a 'food challenge'. It is specific for food allergies. For this test, a patient is given a small amount of the suspected allergenic food and then is checked for any symptoms that develop. This test is carried out in a specialist allergy centre with experienced medical staff because the test also tells medical staff how severe an allergic reaction could be if the child were to accidentally come into contact with that food. The most specific test measures the concentration of IgE antibodies in the patient's blood. Each test has its pros and cons — the more specific tests are better in terms of reliability, but they take longer to perform and obtain results.

Recent advances and future interventions

About one in five children who have peanut allergy grow out of it by the time they are teenagers. For the rest of those affected, this is not the case and their only option is to completely avoid foods containing peanuts. Nevertheless, recent studies have shown promising results in terms of preventative treatments for peanut allergies. Such treatments are termed immunotherapy.

Immunotherapy is based on a concept that has intrigued scientists for a long time — the concept of oral tolerance. Oral tolerance means exposing at-risk individuals to increasing amounts of the potential allergen so that they build up tolerance to the allergen rather than becoming sensitised to it. This approach has been used successfully in pollen and insect allergies. It is more risky in peanut allergy because patients run the risk of developing anaphylaxis from the exposure.

However, a recent clinical trial conducted at Kings College in London has shown that this approach can also be effective in peanut allergy. The 'Learning Early about Peanut Allergy' (LEAP) trial involved over 600 infants aged between 4 months and 11 months. These infants were all at risk of developing peanut allergy because they were known to be atopic. The infants were first given a skin prick test to see if they reacted to peanut protein. Infants who showed either a negative reaction or a weakly positive reaction in this test were then randomly assigned to one of two groups. One group avoided peanuts; infants in the other group ate up to 6 g of peanut protein per week. Infants who exhibited a severe reaction to peanuts were not included in the study because of the potential risk of severe anaphylactic shock. Infants in both groups were then re-assessed for peanut allergy when they were 12, 30 and 60 months old.

The results of this study showed that eating peanuts from an early age significantly reduced the risk of developing an allergy to peanuts. Only 3% of children who ate the peanut snack developed an allergy to peanuts at 5 years of age compared with 17% of those infants who avoided peanuts (see Figure 2). This protective effect was particularly impressive given that these infants were in a high-risk atopic group. The study then went on to show that if both groups of infants avoided peanuts for the next 12 months (until they were 6 years old), only 5% of those that ate peanuts originally developed an allergy to peanuts, compared with nearly 19% of those in the 'avoid peanuts' group. This result means that the immune system can still remember it is tolerant to peanuts and so should not make IgE antibodies against peanut proteins, even when it has not been exposed to peanuts on a regular basis for a year.

These results are very exciting because it means that there may be a way to halt the rise of peanut allergy around the world. However, we are still some time away from applying these results in real life. More studies and clinical trials must be conducted under controlled and safe environments — you should not try this at home.

Originally from Kuwait, **Mohammad Abdullah** is a third year medical student at The University of Manchester.

Further reading

For information about allergy in general and peanut allergy, see: **www.allergyuk.org** and **https://tinyurl.com/c3z3ec8**

For more information about the clinical trial 'Learning Early About Peanut Allergy', see: **www.leapstudy.com**

Skin prick test video: **www.youtube.com/watch?v=z68gDFcjUwE** (over 9 min), or: **www.youtube.com/watch?v=xWQBQbqk1ek** (not quite so long...)

Video explaining type I hypersensitivity reaction: **www.youtube.com/watch?v=2tmw9x2Ot_Q**

Key points

- Peanut allergy is the most common food allergy in the world, and is getting more common.
- Many factors cause peanut allergy.
- There is no cure for peanut allergy. The only known 'solution' is complete avoidance of all foods containing peanuts.
- Recent research into preventative therapies has shown promising results that could be of great clinical use in the future.