FactSheet

Vaccines, allergy & asthma

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

- Vaccination helps children with asthma or allergic disease by reducing their likelihood of getting a serious infection which could worsen their asthma or allergy symptoms.
- Vaccines very rarely produce an allergic response, and therefore most children with allergies (e.g. to most environmental and food allergens) can safely be vaccinated.
- Advice about vaccinating people with specific allergies, such as to egg, is contained below.
- Well-performed studies show no increase in allergy or asthma due to use of routine childhood vaccines. Although asthma and allergic disease rates have increased in the past few decades, the reason for this remains unknown.
- While it has been suggested that vaccines may contribute to the rise in allergic disease because they prevent childhood infections (the 'hygiene hypothesis'), this theory does not apply to vaccine-preventable diseases.

Asthma and allergic disease rates have increased dramatically in the last few decades. The exact reasons for this increase remain unknown. Some media reports, anecdotal evidence and uncontrolled observational studies have suggested that this increase may be due to vaccines stimulating changes in the immune system which may affect the development of chronic allergic and autoimmune conditions. However, this hypothesis doesn't hold up when it comes to vaccine-preventable diseases. Moreover, several large-scale, well-controlled epidemiological studies have concluded that there is no evidence that vaccines cause allergic disease. Vaccination of persons with asthma and most allergies is very important in order to reduce their likelihood of getting a serious infection which could worsen their existing condition.

What is the proposed way that vaccines could cause allergic disease?

People with allergies have an exaggerated immune response causing increased production of allergen-specific immunoglobulin E (IgE), resulting in symptoms like wheezing, sneezing or hives. When allergens are inhaled, they are processed and presented to helper T cells which help to control IgE. One type of T cell response increases the production of allergen-specific IgE (the Th2-type response) and one decreases the production of IgE (the Th1-type response).

The two types of T cell responses are triggered by different types of infections. Th1-type responses are triggered by viral and bacterial infections and Th2-type reactions are triggered by worm and helminthic infections. Th2-type responses dominate at birth but early childhood viral and bacterial infections trigger Th1-type responses, thereby encouraging the normal balance between the two types of helper T cells.[1]

The 'hygiene hypothesis' theory,[2] which became popular in the 80s and 90s, suggests that improved hygiene has led to a delay in acquisition of early childhood infections. This, in turn, has prevented the triggering of Th1-type responses, leaving Th2-type responses dominant. Because Th2 helper cells are the ones which encourage IgE secretion, the hygiene hypothesis proposes that this is what increases the risk of developing allergic disease.

Observational studies were done in the 1980s and 1990s to examine the plausibility of the hygiene hypothesis. They concluded that there appears to be a correlation between improved hygiene and the prevalence of allergic disease. Key studies demonstrated that children from large families or children who attended day care from an early age had lower allergy rates than children who did not have extensive interaction with other children at a young age.[2,3] This was interpreted to mean that the increased prevalence of infectious pathogens and unhygienic conditions characteristic of environments

inhabited by lots of children protected children from acquiring allergies.

Some have attempted to extend the hygiene hypothesis to include vaccines, theorising that because vaccines further contribute to a delay in childhood infections they have contributed to increased allergic disease rates.[4,5] However, there are several reasons why the hygiene hypothesis does not extend to vaccines.[1]

Why is the hygiene hypothesis flawed when it comes to vaccines?

First, vaccines do not prevent the majority of childhood illnesses, most of which are mild. Only a small minority of the total infections which children encounter are prevented by vaccines. Therefore vaccines do not delay the acquisition of most childhood infections and do not affect the normal balance between Th1- and Th2-type responses as the hygiene hypothesis proposes.[6]

Second, those diseases which are vaccine preventable, such as measles and pertussis, are extremely infectious. Without vaccination, such illnesses are spread rapidly irrespective of hygiene or sanitation standards. This also does not fit with the hygiene hypothesis.[6]

Lastly, the hygiene hypothesis proposes that it is the dominance of Th2-type responses that increases the risk of developing allergic disease. Th2-type responses are triggered by worm and helminthic infections—as opposed to Th-1 type responses which are triggered by viruses and bacteria. Studies have shown, however, that children with high worm/helminth infection rates have a lower incidence of allergic disease than children who do not experience worm/helminth infections.[7] Similarly, medical conditions known to be associated with a strong Th2-type response are not associated with an increased risk of allergies,[8] and conditions which are associated with a strong Th1-type response still occur in places where the incidence of allergic disease has increased.[1]

What is the scientific evidence that vaccines do not cause allergy or asthma?

Several large studies have concluded that there is no evidence to support the hypothesis that vaccines contribute to an increased risk of allergic disease. DeStefano et al. reviewed records of more than 18,000 children and concluded that the children who had been vaccinated (with diphtheria-tetanus-pertussis, oral polio, *Haemophilus influenzae* type b, hepatitis B and measles-mumps-rubella) were no more likely to have asthma than those who had not been vaccinated.[9] In a study of more than 600 children, Nilsson et al. found that those vaccinated with pertussis (DTP) vaccine were at no greater risk of acquiring asthma or other allergic diseases than children who had not received DTP vaccine.[10] This study also concluded that children who had experienced natural pertussis infection were actually at higher risk of acquiring allergic diseases than those who had not been infected. The evidence from the majority of recent robust epidemiological studies conducted on extensive study populations suggests that there is no increased risk of allergic disease associated with childhood vaccination.[11]

Is there an established link between any specific vaccine and allergy or asthma?

The BCG (bacille Calmette-Guérin or tuberculosis) vaccine has been the most studied in regards to the risk of allergy. No studies have found an increased risk of allergy from the BCG vaccine.[11] In fact, some evidence suggests that BCG may have a protective effect against allergic disease[12] and a research team led by Melbourne's Murdoch Childrens Research Institute is currently embarking on a large randomised trial to investigate this further.[13]

Several early studies of the pertussis vaccine reported increased asthma diagnoses among those who had been vaccinated compared with those who had not.[14,15] However, these early studies were not as robust as later, larger and more well-controlled studies which have found no association between the pertussis vaccine and allergy.[9,16,17]

Studies of the measles-mumps-rubella (MMR) and poliomyelitis vaccines have found no link between these vaccines and allergy.[9,16] Most studies have also concluded that the *Haemophilus influenzae* type b (Hib) vaccine is not associated with any increase in the prevalence of allergic illness. Two studies of Hib vaccine suggested a small but significant increase in the prevalence of asthma;[9,18] however, one of these studies acknowledged their findings could have been influenced by methodological problems.[9]

Because research into whether or not vaccination is associated with an increased prevalence of allergy/asthma has used different methods and study populations, and because there is still much that is not well understood about allergy and the immune system, conflicting messages have been picked up and promoted in the media. To date, however, the vast majority of epidemiological studies, and especially those conducted on larger study populations, have concluded that there is

no increased risk of allergy or asthma associated with vaccination.[11]

Can people with allergic conditions be vaccinated?

There is no concern about vaccinating children or adults who have allergies to common environmental substances such as dustmites, pets or foods. In fact, it is usually advisable to vaccinate people with allergies or asthma to prevent serious diseases which may worsen their allergy/asthma. For example, influenza may be more serious and result in more complications among people with severe asthma, and therefore seasonal influenza vaccination is highly recommended for these people.[19]

It is extremely rare for vaccines to trigger allergic responses or anaphylaxis (a rapid and severe form of allergic reaction). The risk of vaccine-related anaphylaxis following one dose of vaccination has been found to be less than 1 case per 1 million doses.[20] Nevertheless, healthcare providers should always assess each individual for a history of allergies and be prepared to discuss the risk of an allergic reaction and treat it should it occur.

Concern about allergy and vaccination often relates to allergies to antibiotics, gelatin, yeast and egg proteins. Antibiotics are sometimes used in the manufacture of vaccines to prevent bacterial contamination. However, antibiotics such as the penicillins and the sulphonamides, which are linked to the majority of allergic reactions, are not the ones used in vaccine manufacturing. Antibiotics that are used in vaccine production include neomycin, streptomycin, polymyxin B, chlortetracyline and amphotericin B. Of these, only neomycin is used in detectable quantities and thus far no severe allergic reactions to neomycin have been documented.[6]

Immunisation providers should check the current edition of *The Australian Immunisation Handbook*[19] and/or the vaccine product information for the contents of each vaccine. Further advice on vaccinating an individual with a known allergy to an antibiotic contained in a vaccine should be obtained from a specialist clinic.

Gelatin is used as a stabilising agent in some vaccines, including the MMR and varicella vaccines. The gelatin used in vaccines, however, is different from the gelatin used in foods and is highly purified and hydrolysed (broken down by water). Gelatin used as a vaccine stabiliser may be of porcine origin as opposed to gelatin of bovine origin that is typically used in foods.[21,22] Because the gelatin used in food differs from that used in vaccines, and because the incidence of severe allergic reaction to gelatin is extremely low, estimated at 1 case per 2 million vaccine doses, the risk of a severe reaction to gelatin in a vaccine is low.[22] However, those with a gelatin allergy should seek expert advice before receiving vaccines containing gelatin.

Yeast proteins are used in some vaccines, for example, hepatitis B. Yeast has only very rarely been associated with vaccine-related allergy. However, because yeast is found in breads and bread products – to which many people have an 'intolerance' – this has caused some people to be unnecessarily concerned about a possible allergic response to yeast proteins in vaccines.[6]

Finally, people who are allergic to latex may be at risk during vaccination – not because of the vaccine, but because latex may be present in the equipment used for vaccination. It should be noted that natural latex is rarely contained in vaccine vial stoppers. If an individual has a latex allergy, product information sheets should be consulted to determine whether latex is present in the vaccination equipment. If there are any doubts about the potential for latex exposure from a vaccine, it is advisable that individuals consult a specialist clinic for further advice and management.

For more detail on allergy related to vaccine components, including egg, please refer to the NCIRS Vaccine components fact sheet and *The Australian Immunisation Handbook*.[19]

What about egg allergy?

Egg allergies, because they are fairly prevalent, are a common concern for parents. However, egg allergy should not be considered a contraindication for receiving the majority of vaccines.

There are some vaccines though (yellow fever, Q fever and influenza) that are made in eggs, and the measles and mumps components of the MMR vaccine, and one of the rabies vaccines, are cultured using chicken fibroblast cell cultures.

The table below provides a summary of advice on the use of these vaccines in individuals who have an egg allergy.

Although, as mentioned above, it is extremely rare for vaccines to trigger an allergic response or anaphylaxis, staff administering any vaccine should always be prepared to respond to an episode of anaphylaxis should it occur.

Advice for use of vaccines in individuals with egg allergy

Vaccine type	Method of manufacture	Advice for use
MMR	Cell-based culture (measles and mumps components in chicken fibroblasts)	Can be given to all individuals with egg allergy
Influenza	Egg-based culture (most vaccines)	Can be given to most individuals with egg allergy, including potentially those with anaphylaxis to eggs. See ASCIA guidelines and *The Australian Immunisation Handbook*[19,23]
Yellow fever	Egg-based culture	Contraindicated in persons with known severe allergy to eggs. Seek specialist advice.
Q fever	Egg-based culture	Contraindicated in persons with known severe allergy to eggs. Seek specialist advice.
Rabies	Cell-based culture – human diploid cells (HDCV) or purified chick embryo cells (PCECV)	Use HDCV only in individuals with egg allergy.

MMR vaccine

There is no residual egg allergen detectable in the MMR vaccine and large numbers of people with egg allergy have safely received the MMR vaccine.[23]

Influenza vaccines

Until recently, a history of anaphylaxis or severe allergic reaction to egg was a contraindication to receiving influenza vaccine. However, a number of recent studies have concluded that people with severe egg allergy – including anaphylaxis – can be safely vaccinated with vaccines containing less than 1 μg of ovalbumin per dose.[23-25] Because of manufacturing changes, the majority of influenza vaccines used in Australia contain less than 1 μg of ovalbumin per dose.[23] For those with an egg allergy, this quantity should be verified in the vaccine product information. Detailed information on influenza vaccination of individuals with an allergy to eggs can be found in the Australasian Society of Clinical Immunology and Allergy (ASCIA) guidelines.[23]

Other vaccines

Yellow fever, Q fever and one of the rabies vaccines are contraindicated in people with an egg allergy. For individuals with an egg allergy who require these vaccines, it is advisable to seek specialist immunisation advice from an immunologist, allergist or specialised immunisation clinic.[19] For example, an individual with an egg allergy who requires rabies vaccine should receive the human diploid cell vaccine (HDCV; Mérieux Inactivated Rabies Vaccine) and not purified chick embryo cell vaccine (PCECV; Rabipur Inactivated Rabies Virus Vaccine).[19]

References

1. Offit PA, Hackett CJ. Addressing parents' concerns: do vaccines cause allergic or autoimmune diseases? *Pediatrics* 2003;111:653-9.
2. Strachan DP. Hay fever, hygiene, and household size. *BMJ* 1989;299:1259-60.
3. Krämer U, Heinrich J, Wjst M, Wichmann HE. Age of entry to day nursery and allergy in later childhood. *The Lancet* 1999;353:450-4.
4. Odent MR, Culpin EE, Kimmel T. Pertussis vaccination and asthma: is there a link? *JAMA* 1994;272:592-3.
5. Kay AB. Allergy and allergic diseases. First of two parts. *New England Journal of Medicine* 2001;344:30-7.
6. Offit PA, Moser CA. *Vaccines and your child: separating fact from fiction*. New York: Columbia University Press; 2013.
7. van den Biggelaar AH, van Ree R, Rodrigues LC, et al. Decreased atopy in children infected with *Schistosoma haematobium*: a role for parasite-induced interleukin-10. *The Lancet* 2000;356:1723-7.
8. Du Bois RM. Interferon gamma-1b for the treatment of idiopathic pulmonary fibrosis. *New England Journal of Medicine* 1999;341:1302-4.
9. DeStefano F, Gu D, Kramarz P, et al. Childhood vaccinations and risk of asthma. *Pediatric Infectious Disease Journal* 2002;21:498-504.
10. Nilsson L, Kjellman NI, Björkstén B. A randomized controlled trial of the effect of pertussis vaccines on atopic disease. *Archives of Pediatrics and Adolescent Medicine* 1998;152:734-8.
11. Sánchez-Solis M, Garcia-Marcos L. Do vaccines modify the prevalence of asthma and allergies? *Expert Review of Vaccines* 2006;5:631-40.

12. El-Zein M, Parent ME, Benedetti A, Rousseau MC. Does BCG vaccination protect against the development of childhood asthma? A systematic review and meta-analysis of epidemiological studies. *International Journal of Epidemiology* 2010;39:469-86.
13. Melbourne Infant Study: BCG for Allergy and Infection Reduction (MISBAIR). 2014. Available from: http://misbair.org.au/ (Accessed July 2014).
14. Kemp T, Pearce N, Fitzharris P, et al. Is infant immunization a risk factor for childhood asthma or allergy? *Epidemiology* 1997;8:678-80.
15. Farooqi IS, Hopkin JM. Early childhood infection and atopic disorder. *Thorax* 1998;53:927-32.
16. Anderson HR, Poloniecki JD, Strachan DP, et al. Immunization and symptoms of atopic disease in children: results from the International Study of Asthma and Allergies in Childhood. *American Journal of Public Health* 2001;91:1126-9.
17. Bernsen RM, de Jongste JC, van der Wouden JC. Lower risk of atopic disorders in whole cell pertussis-vaccinated children. *European Respiratory Journal* 2003;22:962-4.
18. Laubereau B, Grote V, Hölscher G, et al. Vaccination against *Haemophilus influenzae* type b and atopy in East German schoolchildren. *European Journal of Medical Research* 2002;7:387-92.
19. Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook*. 10th ed. Canberra: Australian Government Department of Health and Ageing; 2013.
20. Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics* 2003;112:815-20.
21. Lakshman R, Finn A. MMR vaccine and allergy. *Archives of Disease in Childhood* 2000;82:93-5.
22. University of Oxford, Oxford Vaccine Group. Vaccine knowledge project. Vaccine ingredients. Gelatin (a stabiliser). 2014. Available from: http://www.ovg.ox.ac.uk/vaccine-ingredients#gelatine (Accessed October 2014).
23. Australasian Society of Clinical Immunology and Allergy (ASCIA). Guidelines for medical practitioners: Influenza vaccination of the egg-allergic individual. September 2010. Available from: http://www.allergy.org.au/images/stories/pospapers/ascia_guidelines_influenza_vaccination_egg_allergic_individual_2010.pdf (Accessed July 2014).
24. Greenhawt MJ, Li JT, Bernstein DI, et al. Administering influenza vaccine to egg allergic recipients: a focused practice parameter update. *Annals of Allergy, Asthma and Immunology* 2011;106:11-6.
25. Erlewyn-Lajeunesse M, Brathwaite N, Lucas JS, Warner JO. Recommendations for the administration of influenza vaccine in children allergic to egg. *BMJ* 2009;339:b3680.