Immunisation of the egg-allergic child

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Paediatric Refresher Course 2011
Background

Egg allergy

• Type 1 IgE-mediated allergy to hen’s egg common in infancy and childhood (± 2%)

• Major allergens in egg white: ovomucoid (Gal d 1), ovalbumin, ovotransferrin, lysozyme

• Other allergens (egg yolk): livetin, apovitellin
Egg allergy

- May react to raw but not cooked egg
- May react to contact with egg or egg fumes while being cooked
- Small number cross react with eggs of other birds (duck, quail) or poultry (chicken, turkey)
Diagnosis

• **History**
  family history, history of atopy, ingestion, timing of development of symptoms

• **Symptoms/signs**
  urticaria, angioedema, bronchospasm, rhinitis, vomiting, anaphylaxis
Diagnosis

Special investigations

• Skin prick tests (commercial product and raw egg)
  Negative predictive value >90%
  Positive predictive value >95% if wheal ≥5mm in age <2yrs
  >7mm in age >3yrs

• Blood tests – Cap-Rast for egg white +/- yolk
  95% chance of clinical reaction if IgE >2ku/L in age <2yrs
  >7ku/L in age >2yrs

• Food ingestion challenge test
Management

Avoidance – difficult; hidden ingredient in many foods

- Asian dishes
- Baked goods
- Battered food
- Binding for rissoles, patties, meatloaf
- Biscuits
- Cakes
- Cake mixes
- Confectionary eg. marshmallows
- Croissants
- Crumbed foods
- Custards
- Dessert mixes
- Dips
- Egg noodles and pasta
- Fried rice
- Health drinks
- Ice cream, frozen desserts and sherbets
- Icings
- Malted chocolate drinks, eg. Ovaltine
- Marshmallow

- Mayonnaise
- Melts
- Meringue
- Milk puddings
- Mock or butter cream
- Mousse
- Muffins and muffin mixes
- Naan bread
- Nougat
- Pasta
- Pie fillings
- Prepared soups, clear soups, consommes
- Processed meats
- Puddings
- Rissoles, sausages
- Salad dressings
- Some breads, breaded foods
- Shiny glaze on baked goods
- Tarts and pastry
- Vegetarian meat substitutes
Terms that imply that product contains

- Albumin
- Globulin
- Lecithin
- Livetin
- Lysozyme
- Vitellin
- Words starting with "ova" or "ovo," such as ovalbumin or ovoglobulin
Non-food products that may contain egg

- Shampoo
- Medications
- Cosmetics
- Finger paints
Management

- Anaphylaxis precautions - medic alert, antihistamine, adrenaline

- Education of family/school

- Ongoing monitoring for development of tolerance

- New research – introduction of egg protein at 4-6 months may prevent egg allergy


- (Trials – specific oral tolerance induction)
Vaccination

• Vaccines have had a dramatic effect on the prevalence of communicable diseases

• Most people have no allergic reaction to vaccination

• Incidence of anaphylaxis <1 per million doses (all vaccines)


• Most anaphylaxis occurs in non-egg allergic children
Potential allergens in vaccines

- **Gelatine** — MMR, DTaP, varicella, influenza, typhoid, yellow fever, Japanese encephalitis, measles
- **Neomycin** — MMR, polio, rabies
- **Aluminium** — DTaP, hep A+B, Hib, pneumococcal, HPV, anthrax
- **Streptomycin** — inactivated polio
- **Yeast** — hep B, HPV
- **Latex** — contaminant from stopper/gloves
- **Lactose**
- **Polymyxin B**
- **Egg**
Vaccines and egg allergy

**Vaccines produced in embryonated eggs**
(may contain egg-protein)
- **Yellow fever** - most likely to contain egg protein
- **Influenza** - varies by year and batch
- **Rabies**

**Vaccines produced in chick fibroblast cell cultures**
(no significant egg protein)
- **MMR/measles**
MMR/measles

- Anaphylaxis after MMR is rare
- Reported in both egg allergic and non-allergic
- Gelatine may cause a reaction
- Neomycin may cause a reaction
- Minute quantity of egg protein insufficient to cause allergic reaction
MMR/measles

• Studies report uneventful MMR immunization in egg-allergic individuals and in those with positive MMR skin tests

• Others report occasional adverse reactions despite preceding MMR skin testing and graded challenge.

• Skin testing with MMR vaccine in egg-allergic individuals is no longer recommended
MMR

• 1227 egg-allergic patients received MMR

• 2 had symptoms suggesting an allergic reaction (both from same case report)

• Better studies - no patient reacted

• Combined data indicate that 99% of egg-allergic children can safely receive MMR vaccine
MMR

- MMR given to 140 children with egg allergy
  (double-blind placebo-controlled food challenges to egg or recent anaphylaxis due to egg AND a positive skin test)

- No reactions

MMR

- MMR given to 54 children with egg allergy (positive skin test and either a positive food challenge or history of severe or recent anaphylaxis)

- No reactions

MMR

- MMR given to 500 children with egg allergy
  (convincing history of egg allergy and positive skin test to egg)

- No reactions

Rabies

- 3 types of vaccines

1) Purified chick embryo cell culture vaccine - PCEC
   (Rabipur, Rabhuvax, RabAvert)

2) Human diploid cell vaccine - HDCV
   (Merieux Inactivated Rabies vaccine, Imovax-Rabies, Rabivac)

3) Purified vero-cell vaccine - PVRV
   (Verorab)
Rabies

• PCEC vaccines contain minute quantities of egg protein unlikely to cause clinical reaction

• But...No good safety data

Safety review of the purified chick embryo cell rabies vaccine: Data from the Vaccine Adverse Event Reporting System (VAERS), 1997-2005 Vaccine. 2007 May 22;25(21):4244-51

• Use HDCV or PVRV in egg-allergic individuals
Influenza

• Allergic reactions to influenza vaccine 0-40%

• Contain small amount of egg protein (ovalbumin)

• Egg protein varies with manufacturer and year
Influenza vaccine – current recommendations

- **CDC** - immunise all children 6mo-18yrs
- **UK** – immunise all high-risk children >6mo
- **South Africa** – current drive to immunise all children >6mo-5yrs
Influenza vaccine – recommendations in egg allergic individuals

• **Recommendation** - egg-allergic individuals should not be routinely vaccinated

• If benefits outweigh risks – refer to allergist for evaluation, skin prick testing and 2-step graded challenge or desensitisation

(graded challenge = give 10% of dose, observe for 30 minutes, give 90% of dose thereafter)
Influenza vaccine

• British Society for Allergy and Clinical Immunology guidelines for the management of egg allergy. Clinical & Experimental Allergy 2010. 40, 1116–1129

- give vaccine under guidance of allergy specialist
- analyse severity of allergy
- if benefits outweigh risks, do skin tests
- use vaccine with lowest ovalbumin content
- administer in divided doses
Influenza vaccine

• American Academy of Asthma, Allergy and Immunology 2010 guidelines for administering influenza vaccine to egg allergic recipients
Influenza

• 171 egg allergic patients vaccinated (no history of anaphylaxis)

• 115 vaccinated in 2-dose graded challenge with no vaccine skin test

• 56 vaccinated after vaccine skin test and graded challenge (3 had positive skin test)

• Tolerance equal in both groups

• 7 (4%) had mild systemic reactions - 3 in skin test group
  - 4 in non-skin test group

Influenza

- H1N1 vaccine with low ovalbumin (<0.03µg/ml)
- 758 egg-allergic individuals (no history of anaphylaxis) given single dose with no skin test
- 72 with anaphylaxis or co-existing asthma had 2-dose graded challenge with no skin test
- 2% had mild symptoms (3% of controls) – resolved with antihistamine; no anaphylaxis
- A further 3600 children then vaccinated with same schedule
- 2% developed symptoms requiring antihistamine or salbutamol and no anaphylaxis

Influenza

- 105 egg-allergic patients (all severities, including 25 with anaphylaxis)
- Those with negative skin tests received full-dose vaccine
- Those with positive skin tests received 2-step graded challenge
- **Results**: no significant reactions with either method
  - vaccine skin testing not predictive of tolerance
  - vaccine skin testing induced an irritant reaction
- All those who received the graded challenge subsequently received full booster dose of untested vaccine lot (including 7 with previous anaphylaxis)

Influenza - Conclusion

• AAAAI currently recommends vaccinating those with egg allergy (not anaphylaxis) without doing skin tests

2 approaches
1) no skin test, receive vaccine in 2-step graded challenge

2) no skin test, no graded challenge, observe for 30mins
Influenza vaccination

- Use vaccine with lowest ovalbumin concentration (see package insert)
- No consensus regarding those with severe egg allergy or previous anaphylaxis
- Multicentre trial evaluating this issue currently underway in USA
- For any provider administering vaccines, resuscitation equipment should always be available
- A period of observation should be routine
# 2010-2011 Influenza Vaccines Ovalbumin Content Levels

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Ovalbumin content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afluria</td>
<td>Merck</td>
<td>&lt; 1 μg</td>
</tr>
<tr>
<td>Agriflu</td>
<td>Novartis</td>
<td>&lt; 0.4 μg</td>
</tr>
<tr>
<td>Fluarix</td>
<td>GSK</td>
<td>&lt; 0.05 μg</td>
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<td>FluLaval</td>
<td>GSK</td>
<td>&lt; 1 μg</td>
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<tr>
<td>FluMist</td>
<td>Medimmune</td>
<td>Level not listed</td>
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<tr>
<td>Fluvirin</td>
<td>Novartis</td>
<td>&lt; 1 μg</td>
</tr>
<tr>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>Level not listed</td>
</tr>
<tr>
<td>Influvac (RSA)</td>
<td>Solvay</td>
<td></td>
</tr>
<tr>
<td>Vaxigrip (RSA)</td>
<td>Sanofi Pasteur</td>
<td>Level not listed</td>
</tr>
</tbody>
</table>
Yellow fever

Yellow Fever, countries or areas at risk, 2008

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization/CDC
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Yellow fever vaccine

• Greatest likelihood of containing sufficient amount of egg protein to cause an allergic reaction

• Also contains sorbitol and gelatine

• Several reports of anaphylaxis in egg-allergic individuals (1940’s)

• No prospective studies

• **Recommendation** – refer to allergy specialist for evaluation, skin testing and graded challenge/desensitisation
Vaccine allergy

• Do not repeat immunisation if previous anaphylaxis to the vaccine

• Recommendation – refer to allergy specialist to determine which component of the vaccine caused the reaction