HKIA and HKSPIAID Joint Consensus

Vaccination In Egg-allergic Individuals – A Local Guideline 2017

[FOR CONSULTATION]

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On behalf of Hong Kong Institute of Allergy and The Hong Kong Society for Paediatric Immunology

Allergy and Infectious Diseases

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Background

Vaccination is an important and effective method to develop active immunity against certain pathogens. It helps to prevent or reduce the risks of developing certain infectious diseases as well as their severities. However, the administration of certain vaccines, including influenza; measles-mumps-rubella (MMR) vaccine; and measles-mumps-rubella-varicella (MMR-V) vaccines, has historically been relatively, if not absolutely, contraindicated among egg-allergic individuals. This is because these vaccines are developed in chicken egg embryos or chicken cell fibroblasts, therefore raising the concern that egg proteins (notably ovalbumin) in these vaccines could trigger immediate allergic reactions in egg-allergic individuals. As a result, previous vaccination guidelines and vaccine product information recommended avoidance of influenza and MMR or MMR-V vaccines among individuals with history of anaphylaxis to egg exposure.

Local epidemiological studies showed that 0.4-0.7% of Hong Kong children were reported by their parents to have adverse reactions after intake of hen’s eggs. [1, 2] There is concern that administration of vaccines that could contain egg proteins, notably ovalbumin, might potentially cause allergic reactions in egg-allergic subjects. The Centre for Health Protection (CHP) recommends that mildly egg-allergic individuals can be safely administered with inactivated influenza vaccine (IIV) in primary care. But those with confirmed or suspected egg allergy who have experienced severe reactions should be seen by an allergist/immunologist for evaluation of egg allergy before administration of IIV. [3]

Recently published international guidelines have updated their recommendations regarding the administration of vaccines to egg-allergic individuals. This article summarizes the updates and aims to
provide a local recommendation for general practitioners and paediatricians. For practical reasons, this guideline will only cover influenza and MMR/MMR-V vaccines.

Yellow fever vaccine is less commonly administered and has higher egg protein content (≤ 5µg/dose*). Specialist evaluation is recommended prior to vaccination. Q fever vaccine is not available in Hong Kong and therefore is not covered in this guideline.

*Information obtained through direct communication with manufacturer

**Influenza vaccine**

Influenza vaccination is well known to be effective in preventing infections caused by influenza viruses and in reducing the risks of developing complications. Table 1 summarizes three influenza vaccines that are available in Hong Kong, which includes their product information recommendations in egg-allergic patients and the respective concentration of ovalbumin in the respective vaccine.

Moneret-Vautrin et al reported that only 1% of patients with egg allergy would develop allergic reactions at a threshold as low as 1mg. [4] As the quantity of ovalbumin in influenza vaccines is ≤1ug/dose, such a level of egg protein in influenza vaccines is very unlikely to trigger allergic response in this group of patients. Therefore, despite the product information recommendations and the trace amounts of ovalbumin present in these influenza vaccines, they should be safe to be administered to egg allergic individuals, including those with a history of anaphylaxis to egg proteins.

<table>
<thead>
<tr>
<th>Brands</th>
<th>Product Information Recommendations</th>
<th>Quantity of ovalbumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaxigrip</td>
<td>Contraindicated in patients with egg or chicken protein hypersensitivity</td>
<td>&lt;0.1ug/ml*</td>
</tr>
<tr>
<td>Fluarix Tetra</td>
<td>Contraindicated in patients with egg (ovalbumin) or chicken protein hypersensitivity</td>
<td>&lt;0.1ug/ml*</td>
</tr>
<tr>
<td>FluQuadri</td>
<td>Contraindicated in history of severe allergy reaction (e.g. anaphylaxis) to egg protein</td>
<td>&lt;0.1ug/ml</td>
</tr>
</tbody>
</table>

Table 1 – Summary of influenza vaccines available in Hong Kong

*Information obtained through direct communication with manufacturer

Our view is supported by numerous international guidelines on administering influenza vaccines to egg-allergic individuals summarised in Table 2.
<table>
<thead>
<tr>
<th>Authorities (Country)</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| ASCIA (Australia) [5] | - Presence of egg allergy does not increase the risk of allergic reactions to the influenza vaccines.  
- Entire vaccine can be administered in community vaccination clinics as a single dose followed by 15 – 20 minutes waiting period. Longer waiting period (30 minutes) may be warranted if there is significant parental or health professional anxiety.  
- The immediate availability of medical practitioner care is recommended and staff should be familiar with the recognition and treatment of anaphylaxis.  
- Should there be anaphylaxis to influenza vaccine itself, further vaccination should be avoided without specialist allergy assessment.  
- The followings are NOT RECOMMENDED:  
  o Split dosing  
  o Allergy testing with the vaccine or to egg prior to administration  
  o Ingestion of egg as a pre-condition to administering the vaccine;  
  o Vaccination in specific hospital-based vaccination clinics  
  o Allergy specialist review before influenza vaccination unless anaphylaxis to the influenza vaccine itself has occurred previously |
| CDC (USA) [6] | - Any licensed and recommended flu vaccines are recommended to egg-allergic individuals who have experienced only urticaria.  
- Egg-allergic individuals who had other symptoms, such as angioedema, respiratory distress, lightheadedness, or recurrent emesis; or who required epinephrine or another emergency medical intervention, may receive any licensed and recommended flu vaccine. Flu vaccines should be administered in an in-patient or out-patient medical setting.  
- Vaccine administration should be supervised by a healthcare provider who is able to recognize and manage severe allergic conditions.  
- A previous severe allergic reaction to flu vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine. |
| AAAAI (USA) [7] | - Influenza vaccines should be administered to individuals with egg allergy of any severity, just as they would be to individuals without egg allergy (Evidence level A/B)  
- No special precautions beyond those recommended for the administration of any vaccine to any patient are necessary for administration of influenza vaccine to egg-allergic individuals (Evidence level A/B)  
- Use of non-egg-based influenza vaccines (ccIIV3 or RIV3) in egg-allergic individuals in the age groups for which they are approved is acceptable but not medically necessary or preferred (Evidence level C/D)  
- Live attenuated influenza vaccine (LAIV) may be administered to patients with egg allergy of any severity in the age group for which it is approved (ages 2-49 years), in particular countries and seasons when LAIV is recommended as an agent (based on effectiveness in prior seasons). |
| AAP (USA) [8] | - IIV administered in a single, age-appropriate dose is well tolerated by recipients with an egg allergy of any severity. Special precautions for egg-allergic recipients of IIV are not warranted, because the rate of anaphylaxis after IIV administration is no greater than in egg-allergic than in non-egg allergic recipients from other universally recommended vaccines. |
- All children with an egg allergy of any severity can receive an influenza vaccine without any additional precautions beyond those recommended for any vaccine
- Patients who refuse to receive an egg-based vaccine may be vaccinated with an age-appropriate recombinant or cell-culture product
- Quadrivalent live attenuated influenza vaccine (LAIV4) is not recommended for use in any setting in the United States during the 2017–2018 influenza seasons.

**AAP (USA) [9]**

- Approximately 1% of children have immunoglobulin E (IgE)-mediated sensitivity to egg, and of those, a rare minority has a severe allergy
- Recent data have shown that IIV administered in a single, age-appropriate dose is well tolerated by most recipients with a history of egg allergy
- More conservative approaches in children with a history of egg allergy, such as skin testing or a 2-step graded challenge, no longer are recommended.
- No data have been published on the safety of administering LAIV to egg allergy recipients
- Clinicians should determine whether the presumed egg allergy is mild or severe reaction. Paediatricians should consult with a allergist for children with a history of severe reaction
- Standard immunization practice should include the ability to respond to acute hypersensitivity reaction. Influenza vaccine should be given to children with mild egg allergy with the following preconditions: i) appropriate resuscitate equipment must be available; ii) the vaccine recipient should be observed in the office for 30 minutes after immunization
- Providers may consider the use of ccIIV3 or RIV3 vaccines produced via non-egg based technologies for adult with egg allergy in settings in which these vaccines are available and otherwise age appropriate. Because there is no known safe threshold for ovalbumin content in vaccines, ccIIV3, which does contain trace amount of ovalbumin, should be administered according to the guidelines for other IIVs. In contrast, RIV3, which contains no ovalbumin, may be administered to people with egg allergy of any severity who are 18 years or older and do not have any contraindications.
- However, vaccination of individuals with mild egg allergy should not be delayed if RIV3 or ccIIV3 are not available. Instead, any licensed, age-appropriate IIV should be used

**BSACI (UK) [10]**

- Children with egg allergy can safely be vaccinated with Fluenz Tetra in any settings
- Children who have previously required admission to an intensive care unit for severe anaphylaxis to egg should be referred to a specialist for immunization in hospital.
- Fluenz Tetra should not be administered to a child with current or recent acute wheezing in the 72 hours preceding vaccination, or who have required oral steroids in the previous 2 weeks
- Facilities and staff trained to recognize and treat anaphylaxis should be available.

**World Allergy Organization [11]**

- Egg allergy does not appear to impart an increased risk of an anaphylactic reaction to immunization with either inactivated or live attenuated influenza vaccines
- Immediate hypersensitivity reactions such as urticaria are no more common in egg-allergic than non-egg allergic vaccine recipients
- Any age approved influenza vaccine can be used in any patient irrespective of egg allergy status and that special precautions are not required

| **Table 2** – Summary of overseas authorities’ recommendations on administrating influenza vaccines to egg-allergic individuals. |
**Strength of Recommendation**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Implications</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Directly based on category I evidence</td>
</tr>
<tr>
<td>B</td>
<td>Directly based on category II evidence or extrapolated recommendation from category I evidence</td>
</tr>
<tr>
<td>C</td>
<td>Directly based on category III evidence or extrapolated recommendation from category I or II evidence</td>
</tr>
<tr>
<td>D</td>
<td>Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence</td>
</tr>
<tr>
<td>LB</td>
<td>Laboratory Based</td>
</tr>
<tr>
<td>NR</td>
<td>Not Rated</td>
</tr>
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</table>

**MMR/MMR-V Vaccines**

MMR-V vaccines are safe and effective at preventing mumps, measles, rubella and varicella. The local vaccination schedule recommends the first dose to be administered at 1 year old and second dose is administered at Primary 1. [12] Table 3 summarizes two MMR-V vaccines available in Hong Kong, including their product information recommendations to egg-allergic patients and the respective quantity of ovalbumin in the vaccines. Table 4 summarizes overseas authorities’ recommendations on administering MMR/MMRV vaccines to egg-allergic individuals.

<table>
<thead>
<tr>
<th>Brands</th>
<th>Product Information Recommendations</th>
<th>Quantity of ovalbumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Priorix-Tetra (GSK)</td>
<td>Individuals who have experienced anaphylaxis after egg ingestion should be vaccinated with extreme caution, with adequate treatment for anaphylaxis on hand should such a reaction occur.</td>
<td>May contain traces of egg proteins. Amount not measured in final product.*</td>
</tr>
<tr>
<td>ProQuad</td>
<td>Persons with a history of anaphylactic, anaphylactoid, or other immediate reactions subsequent to egg ingestion may be at an enhanced risk of immediate - type hypersensitivity reactions. The potential risk - to - benefit ratio should be carefully evaluated before considering vaccination in such cases.</td>
<td>Internal analysis done for ProQuad for its egg protein content but manufacturer refused to disclose the information as it is considered proprietary.*</td>
</tr>
</tbody>
</table>

Table 3 – Summary of MMR-V vaccines available in Hong Kong.

*Information obtained through direct communication with manufacturer*
**Table 4 – Summary of overseas authorities’ recommendations on administrating MMR/MMR-V vaccines to egg-allergic individuals.**

**Our Recommendations**

1. Influenza and MMR/MMR-V vaccines can be safely administered, and are recommended, to egg-allergic individuals for disease prevention. They are recommended to be administered in out-patient/ambulatory settings.

2. Should there be any significant concerns from patients, parents or healthcare professionals, healthcare professionals who are capable of recognizing signs and symptoms of allergic reactions can provide 15 – 30 minutes of monitoring after vaccination.
3. Children who have previously required admission to an intensive care unit for severe anaphylaxis to egg should be referred to a specialist for immunization in hospital.

4. Individuals who developed or are suspected to have developed allergic reactions to the vaccine or other vaccine components (such as gelatin or neomycin), should not undergo further vaccination to these products. Referral to an allergy specialist for further evaluation can be considered.

References:


7. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology, and the American College of Allergy, Asthma and Immunology Administration of Influenza Vaccines to Egg-Allergic Recipients: A Practice Parameter Update – 2017


10. British Society for Allergy and Clinical Immunology Paediatric Committee 2015/16 Influenza vaccine recommendations for children with egg allergy.


