Giving Flu Shots to Egg Allergic Children

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Disclosure Information
• I have no relevant financial relationships with the manufacturers of any commercial products and/or provider of commercial services discussed in this CME activity.
• I do not intend to discuss any unapproved/investigative use of a commercial product/device in my presentation

Objective
• Safely administer influenza vaccine to egg-allergic recipients
• Safely administer Tdap vaccine regardless of interval since last Td vaccine

Influenza vaccination of egg-allergic patients
• What is under consideration here is the approach to a patient who has had an immediate-type allergic reaction to the ingestion of eggs, but who has never received the influenza vaccine.
• If a patient has already had an apparent immediate-type reaction to this or any vaccine, the approach would be very different and would include skin testing with the suspect vaccine and vaccine ingredients.
**Influenza vaccination of egg-allergic patients**

- Patients who have IgE-mediated egg allergy have a theoretical risk of anaphylaxis if injected with influenza vaccines containing egg protein.
- Withholding influenza vaccine from egg-allergic recipients has very real risk, namely the morbidity and mortality associated with the disease.

**Influenza vaccine contains measurable quantities of egg protein (ovalbumin); does this cause systemic reactions when injected into egg-allergic patients?**

- 7 published studies involving >1600 egg-allergic subjects getting influenza vaccine without any serious reactions (no respiratory distress or hypotension), and with only a low rate of minor reactions (hives, mild wheezing).
- So, the answer appears to be no.

**But what about patients with severe egg allergy?**

- Most studies have specifically included patients with histories of severe anaphylaxis (n = 185) with egg ingestion and these patients also tolerate the vaccine.
- So, even these patients do not appear to be at risk of serious reaction.

**Does skin testing with the vaccine help predict a reaction?**

- In one study, the vaccine was withheld from patients with positive skin tests but...
- In the studies where skin testing was done, vaccinated skin test positive subjects had no reactions, or no greater rate of reactions than skin test negative subjects.
- The rate (low) of reactions (minor) is the same whether skin testing is included in the protocol or not.
- So, the answer appears to be no.

**Does dividing the dose (10% and if no reaction after 30 minutes 90%) reduce the rate of reactions?**

- In those studies that divide the dose, the vast majority of patients ultimately tolerate the 10+90%
- Studies with single dose also report no serious reactions.
- So, the answer appears to be no.

**Administration of influenza vaccine to pediatric patients with egg-induced anaphylaxis**

Fung I, Spergel JM.
(no conflicts declared)

SUBJECTS
• 56 children (mean age 4 yr 6 mo; range, 7 mo-13 yr 8 mo)
• History of anaphylaxis (NIAID/FAAN criteria) after egg ingestion

METHODS
• Skin prick tests (SPTs) with full-strength influenza vaccine
• Observed for 30 minutes and told to contact if any additional reaction

RESULTS
• 119 vaccinations given to 56 patients
• 91% of vaccines from 4 different Sanofi Pasteur lots (higher ovalbumin)
• 2/56 (4%) had reactions:
  – 1 eczema flare on wrist
  – 1 hives behind ear

CONCLUSIONS
• Influenza vaccine can be safely administered to children with a history of egg-induced anaphylaxis

Why are there no serious reactions being reported?
• In those studies reporting the ovalbumin level, vaccines used have contained as much as 0.7 mcg per 0.5 mL dose without serious reactions, so at least that much is tolerated.
• Such data on “safe” ovalbumin levels is based on analyzing content of vaccines used in various studies, not a dose-response study. Thus, it is not known what amount of ovalbumin per dose might be associated with a higher rate of reactions or more severe reactions.
Why are there no serious reactions being reported?

- So the answer is likely that there is just not enough ovalbumin in the vaccine to cause a reaction.

What about LAIV?

- Although the intranasally-administered live attenuated influenza vaccine (LAIV) contains a low amount of ovalbumin, all published studies to date have evaluated the injectable trivalent inactivated vaccine (TIV), and thus TIV rather than LAIV should be used for egg-allergic recipients.
- Also LAIV should not be used in children with asthma, which often coexists with egg allergy.

Conclusions

1. Egg allergy of any severity (including anaphylaxis) is not a contraindication to the administration of influenza vaccine, but rather a precaution. The risk of not vaccinating is greater than the risk of vaccinating.
2. Patients who report that they are egg-allergic should be referred to an allergist, where the current status of the patient’s egg-allergy (often outgrown) can be assessed by history and skin or blood tests for IgE antibody to egg, but this should not delay their influenza vaccination.
3. Skin testing egg-allergic persons with influenza vaccine prior to administration is not recommended because of its low sensitivity and specificity in predicting serious reactions to vaccine administration.
4. Dividing the dose of vaccine is also not required because the majority of even severely egg-allergic patients can tolerate the full vaccine dose without severe reaction.
5. All influenza vaccines available in the US contain low amounts of ovalbumin.
Conclusions

6. Influenza vaccine should be administered to those who are egg-allergic in a setting where anaphylaxis can be recognized and immediately treated should it occur and patients should remain under observation for at least 30 minutes after vaccination.

7. Egg-allergic patients with a history of hives only after egg ingestion can receive influenza vaccine in a primary care provider’s office provided the appropriate personnel and equipment are available, while those with a history of more severe reactions to egg ingestion should receive their vaccine in an allergist’s office.

References:

ACIP


AAP


Gelatin

- Gelatin is added to many vaccines as a stabilizer
- Gelatin in vaccines is bovine or porcine, which are extensively cross-reactive
- Responsible for many anaphylactic reactions to MMR, varicella, and Japanese encephalitis vaccines.
- Vaccine makers in Japan and Germany removed gelatin or changed to a less allergenic gelatin with a decrease in allergic reactions
• A history of allergy to the ingestion of gelatin should be sought before giving a gelatin-containing vaccine; negative history may not exclude an allergic reaction to gelatin injected with the vaccine.

• Persons who react to gelatin on ingestion should be evaluated by an allergist prior to administration of gelatin-containing vaccines.

• If the history is consistent with an immediate-type allergic reaction to gelatin confirmed by skin tests or serum specific IgE, skin test with vaccines prior to administration.
  – If negative, give in usual manner but observe for 30 minutes afterward.
  – If positive, give vaccine in graded doses

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Gelatin Content</th>
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<tbody>
<tr>
<td>Influenza (FluMist, Virosome)</td>
<td>2.0 microgram per 0.5 ml dose</td>
</tr>
<tr>
<td>Influenza (Shivax, MedImmune Vaccine, Maryland)</td>
<td>2.0 microgram per 0.5 ml dose</td>
</tr>
<tr>
<td>Measles, Mumps, Rubella (MMR) or (Measles, Mumps, Rubella, Merck, Whitestown, New Jersey)</td>
<td>15.0 microgram per 0.5 ml dose</td>
</tr>
<tr>
<td>Combined, Mumps, Rubella, Varicella-Zoster Virus Vaccine, Merck</td>
<td>1.0 microgram per 0.5 ml dose</td>
</tr>
<tr>
<td>Rabies (Biovaccine, Sienta, Berkeley, California)</td>
<td>12.0 microgram per 1.0 ml dose</td>
</tr>
<tr>
<td>Typhoid Vaccine (Pasteur, TYP21) or (Ty21), Binx, Connaught Laboratories</td>
<td>capsule</td>
</tr>
<tr>
<td>Hepatitis A Vaccine (VAERX, Black)</td>
<td>12.0 microgram per 0.5 ml dose</td>
</tr>
<tr>
<td>Yellow Fever (YF VAX, Sanofi Pasteur)</td>
<td>7.5 microgram per 0.5 ml dose</td>
</tr>
<tr>
<td>Pneumococcal (PCV13, Sanofi Pasteur)</td>
<td>12.5 microgram per 0.5 ml dose</td>
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• Hepatitis B vaccines are grown in *Saccharomyces cerevisiae* (baker's yeast or brewer's yeast) and contain residual yeast protein

• However, adverse reactions to these, if any, appear to be rare

• Human papillomavirus vaccine may also contain residual yeast protein

• Yeast allergy itself is very rare but, if a patient has a history of clinical reactivity to Baker's or Brewer's yeast and a positive skin test to *Saccharomyces cerevisiae*, skin test them with yeast-containing vaccines prior to administration.
  – If negative, give in usual manner but observe for 30 minutes afterward.
  – If positive, give vaccine in graded doses

• The “rubber” in vaccine vial stoppers or syringe plungers may be dry natural rubber (DNR) latex or synthetic rubber.

• Those made with DNR pose a theoretical risk to the latex allergic

• A review of > 160,000 VAERS reports found only 28 cases of possible immediate-type allergic reactions after receiving a DNR-containing vaccine, and these may have been due to other components
• Latex content of vaccine packaging is provided is updated at: http://www.cdc.gov/vaccines/pubs/pinkbo ok/downloads/appendices/B/latex-table.pdf

• Patients with latex allergy can safely receive vaccines from vials with non-DNR stoppers.
• If the only available preparation has a latex stopper, the stopper should be removed and the vaccine drawn up directly from the vial without passing the needle through the stopper.
• If the only available vaccine contains latex in the packaging that cannot be avoided, such as in a prefilled syringe, the vaccine can still be administered but the patient should be observed for at least 30 minutes afterward.

Interval between Td and Tdap

• Due to increasing rates of pertussis in adolescents and adults, new vaccines were recommended in 2006 for those 11 to 64 years of age to provide not only booster doses for tetanus and diphtheria (Td), but to pertussis as well (Tdap).
• To provide protection for the adolescents and adults and any younger children or infants they may have contact with.

• The recommended interval between doses of Td had been 10 years, with shorter intervals thought to be associated with increased rates of Arthus reactions.
• However, in a recent study, the rates of injection site reactions to Tdap were no different in those vaccinated less than 2 years than in those vaccinated more than 2 years after previous Td.
• Another study found no higher rates of injection site reactions whether a Tdap-containing vaccine was administered one month after a Td-containing vaccine or placebo.

Table 1: Guidance for tetanus and diphtheria toxoids (Td) and tetanus toxoid reduced diphtheria toxoid (Tdap) (courtesy of the Advisory Committee on Immunization Practices (ACIP) for Tetanus, Diphtheria, and Pertussis Vaccine Recommendations for Persons 7 Years of Age and Older) (source: http://www.cdc.gov/vaccines/recs/srertd.htm)

<table>
<thead>
<tr>
<th>Td</th>
<th>Tdap</th>
<th>Td</th>
<th>Tdap</th>
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<tbody>
<tr>
<td>10y</td>
<td>No</td>
<td>1y</td>
<td>No</td>
</tr>
<tr>
<td>2y</td>
<td>No</td>
<td>1y</td>
<td>No</td>
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<tr>
<td>0</td>
<td>Yes</td>
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This includes those age 7 to 10 and ≥65 years of age in whom the vaccine has been found to be safe and immunogenic.

Interval between Td and Tdap

• Thus, with the pertussis disease burden continuing to be substantial, it is now recommended that Tdap be given to all adolescents and adults regardless of interval since the last Td.

Conclusion
ACIP reference on Tdap
interval after Td


Changes you may wish to make in practice

- Administer annual influenza vaccine to children with suspected or confirmed egg allergy, either in your office under observation or refer to an allergist.
- When indicated, administer Tdap regardless of interval since the last tetanus or diphtheria toxoid-containing vaccine.