Asthma and Allergy Guidelines

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Disclosures

• 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 an unapproved/investigative use of a commercial product/device in my presentation.
• I do discuss brand names of all epinephrine autoinjectors for purposes of identifying all types available but have no personal financial conflict of interest.
Outline

• Asthma
  – GINA Guidelines
  – Biologic Therapies
• Drug Allergy
  – Penicillin Allergy
• Food Allergy
  – Complementary Peanut Introduction
• Vaccine Allergy
  – Types of adverse reactions
  – Approach to patient with suspected vaccine allergy
  – COVID Vaccines

Updates in Asthma
GINA Guidelines

- The Global Initiative for Asthma (GINA) strives to increase awareness of asthma among health professionals, health authorities, and the general public
- GINA was launched in 1993 in collaboration with
  - National Heart, Lung, and Blood Institute
  - National Institutes of Health
  - World Health Organization
- They update their guidelines yearly

Concerns about SABA only treatment...

- Short acting beta agonist (SABA) as the only reliever is
  - based on older studies when asthma was thought to primarily be a disease of bronchoconstriction
- Now it is known that airway inflammation is found in most patients with asthma
  - even those with intermittent/infrequent symptoms
- Downsides of SABA only treatment
  - Regular use increases allergic responses and airways inflammation, as well as decreases response to SABA
  - Over-use of SABA (>= 3 canisters dispensed in a year) is associated with increased risk of severe exacerbations
  - Dispensing of >= 12 canisters / year is associated with increased risk of asthma related death
GINA Guidelines

• No longer prefers rescue treatment with SABA alone

• For age 12 years and older:
  – ICS-LABA for as needed symptom relief in Intermittent Asthma
  – ICS-LABA as Single-Inhaler for Maintenance and Reliever Therapy (SMART) in Mild-Moderate Persistent Asthma

• For 6-11 years:
  – Take ICS whenever SABA is taken in Intermittent asthma
  – ICS-LABA as SMART in Mild-Moderate Persistent Asthma

Why the new GINA recs?

• Reduce risk of serious asthma related exacerbations and death

• Provide consistent messaging about aims of asthma treatment, including prevention of exacerbations, across whole spectrum of asthma severity

• Avoid establishing a pattern of patient reliance on SABA early in the course of the disease

• This represents the culmination of their 12-year campaign to improve treatment of mild asthma
Pharmacokinetics of B2 agonists

<table>
<thead>
<tr>
<th>B2 agonist</th>
<th>Onset of action</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol/Salbutamol</td>
<td>5-8 min</td>
<td>4-6 hours</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>5-10 min</td>
<td>4-6 hours</td>
</tr>
<tr>
<td>Formoterol</td>
<td>2-3 min</td>
<td>12 hours</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>30 min</td>
<td>12 hours</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>5 min</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

The goal of ICS-formoterol is to offer both quick relief to reverse airway smooth muscle constriction and allow ICS to treat underlying airway inflammation.

Usual doses for rescue asthma treatment in children

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose form</th>
<th>0 to &lt;4 yrs</th>
<th>4 to 11 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol HFA MDI</td>
<td>90 mcg/puff</td>
<td>2 puffs q4-6 hrs prn</td>
<td>2 puffs q4-6 hrs prn</td>
</tr>
<tr>
<td>Levalbuterol HFA MDI</td>
<td>45 mcg/puff</td>
<td>Safety/efficacy not established</td>
<td>2 puffs q4-6 hrs prn</td>
</tr>
<tr>
<td>Albuterol breath-activated DPI</td>
<td>90 mcg/inhalation</td>
<td>Safety/efficacy not established</td>
<td>2 puffs q4-6 hrs prn</td>
</tr>
<tr>
<td>Albuterol nebulizer</td>
<td>0.63 mg/3 mL</td>
<td>0.63 to 2.5 mg q4-6 hrs prn</td>
<td>1.25 to 5 mg q4-8 hrs prn</td>
</tr>
<tr>
<td></td>
<td>1.25 mg/3 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.5 mg/3 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 mg/mL (0.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levalbuterol nebulizer</td>
<td>0.31 mg/3 mL</td>
<td>0.31 to 1.25 mg q4-6 hrs prn</td>
<td>0.31 to 0.63 mg q4-8 hrs prn</td>
</tr>
<tr>
<td></td>
<td>0.63 mg/3 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.25 mg/0.5 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.25 mg/3 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide-formoterol MDI (Combo ICS-LABA)</td>
<td>Budesonide 80 mcg-formoterol 4.5 mcg/puff</td>
<td>Safety/efficacy not established in &lt;6 years</td>
<td>1 to 2 puffs q4 hrs prn, in addition to 2 inhalations daily as maintenance (maximum total daily dose 8 puffs)</td>
</tr>
</tbody>
</table>
12 years and older

STARTING TREATMENT
in adults and adolescents 12+ years with a diagnosis of asthma

FIRST ASSESS:

Confirmation of diagnosis

Symptoms most days, or waking at night once a week or more?

Low dose ICS-LABA + as-needed SABA

Low dose ICS-LABA + as-needed SABA

As-needed ICS-LABA

CONTROLLER and PREferred RELIEVER

Symptoms: Reduce the risk of exacerbations compared with using a SABA reliever

As-needed low dose ICS-buformoterol

Low dose ICS-LABA + as-needed SABA

Low dose ICS-LABA + as-needed SABA

As-needed low dose ICS-buformoterol

As-needed low dose ICS-buformoterol

As-needed low dose ICS-LABA

RELIEVER: As-needed low-dose ICS-buformoterol

As-needed ICS-LABA

As-needed ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

12 years and older

STARTING TREATMENT
in adults and adolescents 12+ years with a diagnosis of asthma

Track 1 is preferred if the patient is likely to be poorly adherent with daily controller ICS-containing therapy is recommended even if symptoms are infrequent, as it reduces the risk of severe exacerbations and need for OCS.
6-11 years

**SUGGESTED INITIAL CONTROLLER TREATMENT**

in CHILDREN 6-11 years with a diagnosis of asthma

**FIRST ASSESS:**
- Confirmation of diagnosis
- Symptom control & modifiable risk factors (including lung function)
- Comorbidities
- Inhaler technique & adherence
- Child and parent preferences and goals

**START WITH:**

**STEP 1**
- Take ICS whenever SABA taken

**STEP 2**
- Daily low dose ICS

**STEP 3**
- Low dose ICS-LABA or medium dose ICS or very low dose MRT

**STEP 4**
- Medium dose ICS-LABA or low dose ICS-LABA or low dose MRT

**STEP 5**
- Short course OCS may also be needed for patients presenting with severely uncontrolled asthma

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**STARTING TREATMENT**

Children 6-11 years with a diagnosis of asthma

**ASSESS:**
- Confirmation of diagnosis
- Symptom control & modifiable risk factors (including lung function)
- Comorbidities
- Inhaler technique & adherence
- Child and parent preferences and goals

**START HERE IF:**
- Symptoms most days, waking at night & once a week and low lung function

**STEP 1**
- Low dose ICS taken whenever SABA taken

**STEP 2**
- Daily low dose inhaled corticosteroid (ICS)

**STEP 3**
- Low dose ICS-LABA, or medium dose ICS, or very low dose ICS-LABA or very low dose MRT

**STEP 4**
- Medium dose ICS-LABA or low dose ICS-LABA or medium dose MRT

**STEP 5**
- Refer for phenotypic assessment to determine if higher dose ICS-LABA or add-on therapy, e.g., anti-IgE

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**ASSESS:**
- Symptoms recent or flare within a week or low lung function

**START HERE IF:**
- Symptoms more than once a week or more

**STEP 1**
- Daily inhaled corticosteroid (ICS) and long-acting beta2 agonist (LABA)

**STEP 2**
- Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken

**STEP 3**
- Low dose ICS-LABA, or medium dose ICS, or very low dose ICS-LABA or very low dose MRT

**STEP 4**
- Medium dose ICS-LABA, or low dose ICS-LABA or medium dose MRT

**STEP 5**
- Refer for expert advice

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Overview of Biologics in Asthma

Updates in Drug Allergy
Hypersensitivity reactions

<table>
<thead>
<tr>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
<th>Type IV a</th>
<th>Type IV b</th>
<th>Type IV c</th>
<th>Type IV d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune reactant</td>
<td>IgG</td>
<td>IgG</td>
<td>IgG</td>
<td>IgG</td>
<td>5,6, 5-44, 13</td>
<td>CCL-5, IL-17</td>
</tr>
<tr>
<td>Antigens</td>
<td>Soluble antigen</td>
<td>Soluble antigen</td>
<td>Soluble antigen</td>
<td>Soluble antigen</td>
<td>Soluble antigen</td>
<td>Soluble antigen</td>
</tr>
<tr>
<td>Effector</td>
<td>Mast cell activation</td>
<td>Fcγ-receptors (neutrophils, NK cells)</td>
<td>FcγR-1 cells</td>
<td>Complement</td>
<td>Mast cell activation</td>
<td>Eosinophils</td>
</tr>
<tr>
<td>Example of hypersensitivity reaction</td>
<td>Allergic rhinitis, asthma, systemic anaphylaxis</td>
<td>Some drug alls (e.g., penicillin)</td>
<td>Serum sickness, Anaphylaxis</td>
<td>Tuberculin reaction, contact dermatitis (with nickel)</td>
<td>Chronic asthma, chronic allergic rhinitis, Maculopapular exanthema with eosinophilia</td>
<td>Contact dermatitis, Maculopapular and bullous</td>
</tr>
</tbody>
</table>

Important questions for drug allergy

- When was the reaction?
- What medication is suspected?
- What was the timing between taking the drug and symptom onset? Minutes, hours, days?
- What were the symptoms?
  - If a rash, did they take a picture?
- What treatment was used?
- How long did symptoms last?
- Have they had the drug or similar drugs since?
Penicillin Allergy

- 80% lose prior sensitivity within 10 years
- Using a PCN product can reduce rate of broad-spectrum antibiotic use

Why test for PCN?

- Patients with a PCN allergy are more likely to…
  - Receive quinolones, clindamycin, and vancomycin
  - Longer hospitalizations
  - Higher prevalence of C difficile
  - Higher prevalence of MRSA and VRE

- Positive Impact
  - Reducing cost
  - Reducing use of broad-spectrum antibiotics
  - Reducing length of hospital stay
  - Reducing complications from alternative
PCN Testing

• Low risk patients can be given the drug via oral challenge without skin testing
  – Delayed onset, benign, non-urticarial rashes
  – GI upset
  – Headaches

• High risk patients
  – Recommend evaluation by allergist
    • Skin testing with possible oral challenge to amoxicillin

Intra-family Cross-Reactivity
PCN Allergy in the Pregnant Patient

- Consider allergy testing for all patients with a history of a penicillin allergy
  - ACOG Committee Opinion report on Prevention of Group B Streptococcal Early-Onset Disease in Newborns

- In 2021, Wolfson et al., largest study on pregnant patients to date
  - 209 of 220 had their penicillin allergy label safely removed
  - Those who had an in-person evaluation by an allergist were less likely to receive alternative antibiotics (vancomycin, clindamycin, gentamicin) for GBS prophylaxis in the peripartum period

ACOG 2020
Wolfson 2021

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PCN Allergy in the Pregnant Patient

**Prenatal assessment**

- Not allergic to penicillin
  - Penicillin G or Ampicillin
  - LOW risk
  - Cefazolin
    - If susceptible, Clindamycin
    - If Clindamycin-resistant, Vancomycin

- Allergic to penicillin
  - HIGH risk
  - Check clindamycin susceptibility
    - If susceptible, Clindamycin
    - If Clindamycin-resistant, Vancomycin

- Unknown risk
  - Options: 1) PCN allergy testing, 2) Cephalosporin, 3) Clindamycin if susceptible, 4) Vancomycin if not susceptible to clindamycin

ACOG 2020
Management of Type I IgE Mediated Hypersensitivity

- What happens if the patient is determined to be penicillin allergic?
  - History of type 1 IgE mediated hypersensitivity and/or positive allergic sensitization

- Need to determine if
  - 1) there is no other alternative agent to use
  - 2) urgency to use penicillin products

- If yes to above, then the allergist will consider a drug desensitization to the desired penicillin product

Updates in Food Allergy
Food Reactions

- Intolerance – your body cannot break down the food for some reason
  - GI symptoms (pain, cramping, vomiting, or diarrhea)
  - Eat small amounts – do okay

- Allergy – your body mistakes that food for something harmful, IgE-mediated
  - Immune response – localized or systemic reaction
  - Can be triggered by eating a microscopic amount or even with touch or inhalation of the particles

- Eight types of food account for > 90% of allergic reactions:
  - milk, eggs, peanuts, tree nuts, fish, shellfish, soy, and wheat

- This is consistent with the finding that allergens belong to a very restricted number of protein families
- Prevalence in children is 7-8%

Who is high risk?

- The following are at high risk of developing allergic disease:
  - A patient with family history of atopy
  - A patient with personal history of atopy
    - Especially with moderate-severe eczema

- How can we prevent these patients from developing a food allergy?
  - Introduction of highly allergenic foods in infancy

Gupta 2013

Togias 2017
Fleischer 2021
Prevention of Peanut Allergy

<table>
<thead>
<tr>
<th>Addendum guideline</th>
<th>Infant criteria</th>
<th>Recommendations</th>
<th>Earliest age of peanut introduction</th>
</tr>
</thead>
</table>
| 1                  | Severe eczema, egg allergy, or both                 | - Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC.  
|                    |                                                     | - Based on test results, introduce peanut-containing foods.                     | 4-6 months                           |
| 2                  | Mild-to-moderate eczema                             | Introduce peanut-containing foods                                               | Around 6 months                      |
| 3                  | No eczema or any food allergy                       | Introduce peanut-containing foods                                               | Age appropriate and in accordance with family preferences and cultural practices |

Peanut introduction during infancy

Does the infant have any of the following:  
- Confirmed or suspected IgE-mediated food allergy  
- Severe, moderate, or mild atopic dermatitis

No

Does the infant/child have any of the following:  
- Family history of atopic dermatitis

No

Yes

Is evaluation by an allergy specialist possible before six months of age?

No

Test IgE level prior to peanut introduction

<0.35 kU/L

0 to 2 mm wheal

Yes

Suggest introduction of peanut at home  
- An alternative if the caregiver and/or clinician are concerned about introduction

≥0.35 kU/L

2 to 7 mm wheal

Yes

Suggest supervised in-office feeding  
- An alternative if the caregiver and/or clinician are concerned about introduction

≥8 mm wheal

Yes

Suggest supervised oral food challenge  
- Probably allergic

Togias 2017
Updates in Vaccine Allergy

Safety monitoring systems


v-safe is a smartphone-based tool that monitors for you after your COVID-19 vaccination. Your participation helps keep COVID-19 vaccines safe — it’s you and your health!

If you get vaccinated in the last 6 weeks, you can participate in v-safe.

It takes just a few minutes to register and get started. If you need it, your smartphone can help you answer if the COVID-19 vaccine you received. This information is used to help keep your COVID-19 vaccine safe. If you cannot find your costs, please contact your healthcare provider.

Register for v-safe

Enter your information about yourself and follow the prompts to set up your v-safe.

CDC 2020
Adverse effects by immunologic mechanism

<table>
<thead>
<tr>
<th>Mechanism Category</th>
<th>Antibody mediated</th>
<th>T cell mediated or mixed</th>
<th>Immune deficiency</th>
<th>Normal Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen</td>
<td>excipient vaccine</td>
<td>vaccine</td>
<td>vaccine</td>
<td>vaccine</td>
</tr>
</tbody>
</table>

**Adverse event (mechanism):**
- Immediate hypersensitivity (IgE mediated)
- Local vasculitis (IgG immune complexes)
- Delayed hypersensitivity
- Delayed hypersensitivity
- Mixed - CD4+ CD8+ T & B cell mediated inflammation
- Local tenderness, warmth, fever, irritability
- Infection due to live vaccine strain

**Examples:**
- Egg, gelatins, or alpha gal immediate hypersensitivity
- Arthus Reaction
- Metal, antimicrobial contact allergy
- Delayed smallpox reaction
- Guillain-Barré syndrome, other demyelinating conditions
- Disseminated rotavirus, varicella
- Large local reaction

**Predisposing factors:**
- Pre-existing allergy to component of vaccine (see table 3)
- Previous receipt of certain vaccines, shallow injection technique
- Pre-existing allergy to component of vaccine (see table 3)
- Possible genetic variation in antigen presentation/processing
- Pre-existing primary or secondary immunodeficiency
- Normal response

**Evaluation:** Thorough history and causality assessment

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**What are the expected side effects from vaccination?**

- Usually occur within a few hours of vaccination
- Resolve within minutes-hours-days
- Local
  - Pain, swelling, redness at site of injection
- Systemic
  - Fever, chills, malaise, headache, muscle pain
- Treatment:
  - Supportive: rest, hydration, Tylenol or NSAIDs
Delayed Adverse Effects

Delayed reactions

- Several hours-days after administration
- Often T-cell mediated (Rarely IgE mediated)
- All vaccines can cause minor, self-limited side effects
  - Reflective of a normal immune response
  - Not a contraindication to receiving further doses of the vaccine
- Rare sequelae
  - Serum sickness and SSLR
  - Papular rash, SJS, TEN, EM Major, AGEP, Erythema nodosum, Granuloma annulare, Bullous pemphigoid
  - Pruritic persistent nodules with aluminum containing vaccines, due to delayed Type IV hypersensitivity
  - Guillain Barre Syndrome, Encephalopathy
Non-IgE mediated reactions

- Arthus reaction
  - A localized type III hypersensitivity reaction
  - Painful local swelling and erythema
  - Can start a few hours-days after
  - Risk factors: shallow injection, previously vaccinated
  - Reported with tetanus, diphtheria and hepatitis B vaccines

Minor delayed reactions due to SARS-CoV-2 vaccines

- “COVID vaccine arm”
- Delayed (several days) large local reaction
- Either a Type III or IV hypersensitivity
- Treatment:
  - supportive, oral antihistamines, topical steroids, Tylenol/NSAIDs
- Not a contraindication to second dose
  - May recur, may need supportive treatment
Minor delayed reactions due to SARS-CoV-2 vaccines

• Lymphadenopathy
  – Temporary, mild
  – Usually axillary or supraclavicular, typically same side as vaccine administration
  – Due to activation of adaptive immune system in local lymph notes (Not a Type I Hypersensitivity)
  – Society of Breast Imaging stated:
    • For scheduling screening exams:
      – If possible, and when it does not unduly delay care, consider scheduling screening exams prior to the first dose of a SARS-CoV-2 vaccination or 4-6 weeks following the second dose of a SARS-CoV-2 vaccination.

Immediate Adverse Effects
 Immediate reactions

- Symptoms within 4 hours of administration
- Typically IgE mediated
  - Often within minutes, almost always within 1 hour
  - Can involve various combinations of up to 40 symptoms and signs
    - Most common symptoms and signs are cutaneous (urticaria, angioedema), respiratory (wheezing), cardiovascular changes (hypotension)
    - Severe form is anaphylaxis
- Can be non-IgE mediated
- Can be non-immune

Anaphylactic reactions to vaccines

- Estimated rate of anaphylaxis is 1 per million doses in general for vaccines
  - About 220 million doses of vaccines are distributed in US per year
- Anaphylactic reactions to vaccines are rare, although potentially life-threatening
  - Immunoglobulin E (IgE)-mediated reactions
  - Often due to vaccine components rather than microbial products
Criteria for anaphylaxis

Anaphylaxis is highly likely when any ONE of the following three criteria is fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, swollen lips, tongue, or oropharynx)

2. AND AT LEAST ONE OF THE FOLLOWING:
   A. Respiratory compromise (e.g., dyspnea, wheeze, bronchospasm, stridor, hypoxemia)
   B. Reduced BP* or associated symptoms of end-organ dysfunction (e.g., hypotonia, collapse, syncope, incontinence)

3. TWO OR MORE OF THE FOLLOWING that occur rapidly after exposure to a LIKELY allergen for that patient (minutes to several hours):
   A. Involvement of the skin mucosal tissue (e.g., generalized hives, 8th-flush, swollen lips, tongue, or oropharynx)
   B. Respiratory compromise (e.g., dyspnea, wheeze, bronchospasm, stridor, hypoxemia)
   C. Reduced BP* or associated symptoms (e.g., hypotonia, collapse, syncope, incontinence)
   D. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)

CDC MMWR of SARS-CoV-2 vaccines

- Rate of reported anaphylaxis has been extremely rare
  - VAERS data from 7/31/2021:
    - 66 of 213 cases confirmed as post-vaccination anaphylaxis with day 0-1 ED visit
      - BNT162b2 vaccine (N=37): 5 per million doses
      - mRNA-1273 vaccine (N=26): 4.9 per million doses
      - Ad26.COV2.S vaccine (N=3): 7.6 per million doses
    - All cases fully recovered with treatment
    - Most occurred within 30 minutes of vaccine administration
    - Most had self-reported a history of allergies, but no consistent type of allergy

  Sampson 2006
  Reber 2017

  CDC 2021
Non-allergic reactions that mimic anaphylaxis

<table>
<thead>
<tr>
<th>Anxiety or Immune activation</th>
<th>Vasovagal reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Minutes</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Tachycardia, HTN, globus sensation, flushing without urticaria</td>
</tr>
<tr>
<td>Important Features</td>
<td>Can be due to anxiety or innate immune activation from vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Resolves with rest +/- supportive care</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- In these situations, it can help to draw tryptase level within 2 hours of reaction to differentiate from anaphylaxis
- If not proven to be anaphylaxis, should consider getting 2nd dose

Acute Management of Vaccine Reactions
Example of a vaccine reaction protocol

Injectable epinephrine
Assessing reactions to vaccines

• Detailed history to help determine causality
  – Signs and symptoms during the reaction with timing
  – Drugs or substances taken before vaccination
  – Medications needed to treat the reaction
  – Physical exam including vitals at the time of reaction

• Ancillary laboratory information
  – Within 30-90 minutes after an acute reaction
    • Serum tryptase level (mast cell marker)
    • SC5b-9 (terminal complement complex)

Follow up

• If symptoms fully resolve after first dose of epinephrine
  – Can discharge 4-8 hours after resolution of symptoms
  – Extended observation if multiple doses of epinephrine
    • To monitor for arrhythmias and late phase anaphylactic reactions

• Discharge with
  – Education on how to recognize and manage anaphylaxis
  – Potential prescription for epinephrine autoinjectors
  – Referral to allergist
Long Term Management of Vaccine Reactions

Who needs an evaluation by an allergist

- A patient who experienced...
  - An apparent allergic or other serious adverse reaction after receiving a vaccine OR
  - A suspected allergy to vaccine component
What will the allergist do?

Positive history of reactions after vaccine administration

Nonimmediate reaction

• In most cases, no allergy work-up
• If contact dermatitis or nodules, consider patch test

Immediate reaction

Positive history of reproducible allergy to vaccine excipient?

No

Yes - review vaccine excipient list and determine if allergy skin testing is necessary before vaccine administration

• Skin testing and/or in vitro IgE testing to vaccine and/or components

Positive

If additional doses required, vaccine may be given in graded doses

Negative

If additional doses required, vaccine can be given according to general recommendations

Vaccine Components

Active components
• Virus, bacteria, toxin

Culture media
• Hen’s egg
• Horse serum
• Murine or simian cells
• Kidney cells of dog
• Yeast

Inactive residues
• Formaldeyde
• Beta-propiolactone
• Formalin
• Gluteraldehyde
• Casein

Contaminants
• Latex

Adjuvants
• Aluminum salts
• MF-59 (squalene salt)
• ASO4 (monophosphoryl lipid A and aluminum hydroxide)

Stabilizers
• Gelatin, Polgylene
• Human serum albumin
• Amino acid mix, Glycine
• Glutamate, MSG
• Sucrose, lactose, sorbitol
• Ascorbic acid
• Phosphatase
• Polysorbate 80/20

Antibiotics
• Neomycin, Gentamicin, Streptomycin, Kanamycin
• Chlortetracycline
• Erythromycin
• Polymyxin B
• Amphotericin B

Preservatives
• Thimerosal
• 2-phenoxyethanol
• Phenol
• Benzenethionium chloride
Allergy testing

Examples of testing used to assess specific vaccines suspected of causing allergic reactions

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Skin testing</th>
<th>In vitro IgE testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP, Td, Tdap</td>
<td>DTaP, Td, Tdap, Tetanus toxoid, Gelatin, Milk</td>
<td>Gelatin, Milk</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Hepatitis B, Yeast</td>
<td>Yeast</td>
</tr>
<tr>
<td>Influenza</td>
<td>Influenza, Egg, Gelatin</td>
<td>Egg, Gelatin</td>
</tr>
<tr>
<td>MMR</td>
<td>MMR, Measles, Mumps, Rubella, Gelatin</td>
<td>Gelatin</td>
</tr>
<tr>
<td>Varicella or Zoster</td>
<td>Varicella or Zoster, Gelatin</td>
<td>Gelatin</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Yellow fever, Egg, Gelatin</td>
<td>Egg, Gelatin</td>
</tr>
</tbody>
</table>

• Whenever possible, the same vaccine from the same manufacturer that was given at the time of the reaction should be used for testing

Testing to vaccine

• Vaccine skin tests (not component testing)
  • Prick test with full strength vaccine
    • Consider dilution if history of life-threatening reaction
    • If prick test with full strength vaccine negative, move on to intradermal testing
  • Intradermal test with 0.02 mL vaccine 1:100
    • If negative, move on to challenge

• Limitations:
  • No formal studies to evaluate the positive and negative predictive values for vaccine skin tests
  • May cause irritant (false-positive), clinically irrelevant reactions
• May not be available for certain vaccines (SARS-CoV2 vaccines)
Vaccine graded challenge protocols

- Doses given at 15-minute intervals as tolerated
- Needs to be performed under direct medical supervision, equipped to handle anaphylaxis
  - Office/hospital setting, with/without IV line in place

SARS-CoV-2 Vaccines
I’m allergic to ___, should I still get the SARS-CoV-2 vaccine?

Standard 15 min observation

- Family history of severe allergies
- History of contact dermatitis
- Delayed reactions to drugs or vaccines
- Allergic rhinitis
- Asthma
- Mast cell disease

30 min observation

- History of potential anaphylaxis to:
  - Foods
  - Pollens, molds, dust mites
  - Latex
  - Insect venom
  - Drug
  - Radiocontrast dye
- History of idiopathic anaphylaxis

Refer to allergist

- Severe allergic reaction (anaphylaxis) to mRNA SARS-CoV-2 vaccine
- Allergic reaction to SARS-CoV-2 vaccine components
  - Immediate reaction to polysorbate or polyethylene glycol
- May also refer if history of allergic reaction to non-SARS-CoV-2 vaccine or injectable medication

Banerji 2020
Castells 2020
### SARS-CoV-2 vaccine components

<table>
<thead>
<tr>
<th>Vaccine Platform</th>
<th>Vaccine Name</th>
<th>Excipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA based vaccine</td>
<td>BNT162b2</td>
<td>Polyethylene glycol 2000</td>
</tr>
<tr>
<td>RNA based vaccine</td>
<td>mRNA-1273</td>
<td>Polyethylene glycol 2000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tromethamine</td>
</tr>
<tr>
<td>Adenovirus vector</td>
<td>AZD1222</td>
<td>Polysorbate 80 EDTA</td>
</tr>
<tr>
<td>Adenovirus vector</td>
<td>Ad26.COV2-S</td>
<td>Polysorbate 80</td>
</tr>
<tr>
<td>Protein subunit</td>
<td>NVX-CoV2373</td>
<td>Polysorbate 80 M1 adjuvant</td>
</tr>
<tr>
<td>Protein subunit</td>
<td>SCB-2019</td>
<td>Polysorbate 20</td>
</tr>
</tbody>
</table>

*Castells 2020
CDC 2021*

### History of allergy to polyethylene glycol (PEG) or polysorbatr allergy

- PEG is in mRNA SARS-CoV-2 vaccines
  - A possible antigen for severe allergic reaction to mRNA SARS-CoV-2 vaccines
- Polysorbate 20 or 80 are in non-mRNA SARS-CoV-2 vaccines
- Both act as a solvent, plasticizer, surfactant, base, lubricant. It stabilizes the vaccine.
Who should you refer?

- **Urgent**
  - Allergic reaction (severe/immediate) to SARS-CoV-2 vaccine
  - Allergic reaction to SARS-CoV-2 vaccine components and eligible to receive vaccine now

- **Routine**
  - Immediate allergic reaction to non-SARS-CoV-2 vaccine or injectable medication
  - Can consider referral of patient with multiple allergic conditions

Shared Decision Making

- We can help each individual patient identify their values and preferences to help guide decision making.
Thank you! If you have any questions, feel free to contact me at MLOVE2@kumc.edu.

References

References, continued


References, continued


