APAAACI Task Force
Module on COVID-19
Vaccine Adverse Reactions
SARS-COV 2
Rapid virus replication & delayed IFN-I response

Upcoming IFN-I response & accumulation of IMM s

IFN-I stimulated pathology & T cell apoptosis

**SARS-CoV**

**pDC**

**IFN-I**

**IMMs**

**CCR2 ligands**

**influx**

**pathology**

**TNF, IL-6, IL-1β, iNOS others**

**T cell apoptosis**

- **rescue**
  - early IFN-I treatment
  - lack of IFN-I signaling
  - IMM depletion
  - cytokine neutralization
- **disease**
  - exuberant inflammatory response
  - severe lung immunopathology
  - impaired T cell response
COVID-19 and Asthma

Mucosal membranes
- ↑ ACE2 and TMPRSS2

SARS-CoV2 infection

Innate immunity
- ↑ IL-6 and TNFα
- ↓ Type I/III IFN
- ↑ Inflammatory macrophages

Adaptive immunity
- ↑ CD8+ cytotoxic T cells
- ↑ T lymphocyte exhaustion and Lymphocytopenia
- ↑ Cytokine Storms

M1
Inflammatory macrophages

Aberrant anti-virus immunity

M0
Macrophages

Trained immunity

M2
Reprogrammed macrophages

RV and Allergens

Mucosal membranes
- ↓ ACE2 and TMPRSS2

Innate immunity
- ↓ Type I/III IFN
- ↑ MBL and SP-D
- ↑ Reprogramed macrophages
- ↑ ILC2s and iNK cells

Adaptive immunity
- ↑ CD4+ T helper cells

Anti-virus effect by Rx
- ICS +LABA
- Anti-IgE;
  Azithromycin

Wang JY, Pawankar R et al. Allergy 2020)
Epidemiology

• Estimates of allergic reactions to vaccines including immediate hypersensitivity reactions, range from 1 in 50,000 to 1 in 1,000,000 doses
• Anaphylaxis: estimated 1 per 100,000 to 1 per 1,000,000 doses for most commonly administered vaccines
• Rates mostly from paediatric studies (childhood immunizations)
• True rate of allergic reactions is unknown because most reactions are not reported.
Classification (ICON 2016)

- Immediate non-allergic reactions
  - Local, injection site reactions (swelling, redness, and/or soreness) and constitutional symptoms, especially fever (common)

- Immediate allergic reactions
  - Limited: e.g. bronchoconstriction, rhinoconjunctivitis, gastrointestinal symptoms, generalized urticaria and/or angioedema; onset within minutes-4 hours
  - Anaphylaxis

Section 2.5. Anaphylaxis
Richard F. Lockey, Stephen F. Kemp, Philip L. Lieberman, Aziz Sheikh

Key Statements

- Epinephrine (adrenaline) at appropriate doses, injected intramuscularly into the mid- anterior lateral thigh, is the drug of choice to treat anaphylaxis.

- There is lack of consensus about the definition and diagnostic features of anaphylaxis and this definition contributes to the variability in its identification, treatment and the use of epinephrine.

- The variability and severity of anaphylaxis is somewhat dependent on the route by which the allergen or inciting agent is delivered, e.g., parenteral versus oral administration; the former is commonly associated with more severe reactions.

- There are a variety of other terms which describe anaphylaxis and which cause confusion, especially with its definition and treatment. These include: generalized systemic reaction; systemic allergic reaction; constitutional reaction; and serious hypersensitivity reaction.

- The illustrations in the World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis, published in 2011 and updated in 2012, are ideal for all physicians and other healthcare professionals.¹ ²

- Anaphylaxis includes both allergic and non-allergic etiologies.
International Consensus (ICON): allergic reactions to vaccines


World allergy organization anaphylaxis guidance 2020

Anaphylaxis (WAO 2020)

Anaphylaxis is highly likely when any one of the following 2 criteria are fulfilled:

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

AND AT LEAST ONE OF THE FOLLOWING:

a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)

c. Severe gastrointestinal symptoms (eg, severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens

2. Acute onset of hypotension\(^a\) or bronchospasm\(^b\) or laryngeal involvement\(^c\) after exposure to a known or highly probable allergen\(^d\) for that patient (minutes to several hours), even in the absence of typical skin involvement.

Table 2. Amended criteria for the diagnosis of anaphylaxis. PEF, Peak expiratory flow; BP, blood pressure. a. Hypotension defined as a decrease in systolic BP greater than 30% from that person’s baseline, OR i. Infants and children under 10 years: systolic BP less than (70 mmHg + [2 x age in years]) ii. Adults and children over 10 years: systolic BP less than <90 mmHg. b. Excluding lower respiratory symptoms triggered by common inhalant allergens or food allergens perceived to cause “inhalational” reactions in the absence of ingestion. c. Laryngeal symptoms include: stridor, vocal changes, odynophagia. d. An allergen is a substance (usually a protein) capable of triggering an immune response that can result in an allergic reaction. Most allergens act through an IgE-mediated pathway, but some non-allergen triggers can act independent of IgE (for example, via direct activation of mast cells). Adapted from (26)
Anaphylaxis (WAO 2020)

Anaphylaxis is highly likely when any one of the following two 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-uvula)

2. Acute onset of hypotension* or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement.

Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP*

Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person’s baseline

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A. Airway/Breathing: Respiratory compromise.
- (e.g. dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

B. Circulation: Reduced BP or associated symptoms of end-organ dysfunction.
- (e.g. hypotonia [collapse], syncope, incontinence)

C. Other: Severe gastrointestinal symptoms.
- (e.g. severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens

PEF, Peak expiratory flow; BP blood pressure.

*Hypotension defined as a decrease in systolic BP greater than 3% from that person’s baseline, OR
- i. Infants and children under 10 years: systolic BP less than (70 mm Hg + [2 x age in years])
- ii. Adults: systolic BP less than < 90 mm Hg

* Laryngeal symptoms include: stridor, vocal changes, odynophagia.

Anaphylaxis (WAO 2020)

Immunologic Mechanisms (IgE Dependent)
- Foods
  - Peanut
  - Soybean
  - Egg
  - Fish
  - Tree nuts
  - Melon
  - Milk
  - Shellfish
  - Sesame
  - Fruits
- Medications
  - B-Lactam antibiotics
  - 600 NSAIDs
  - Biologic agents

Nonimmunologic Mechanisms (Direct mast cell activation)
- Physical factors
  - Exercise, cold, heat, sunlight
- Ethanol
- Medications
  - Opioids

Idiopathic Anaphylaxis (No apparent trigger)
- Previously unrecognized allergen?
- Mastocytosis / clonal mast cell disorder?

Immunologic Mechanisms (IgE independent)
- Radiocontrast media
- NSAIDs
- Dextran (e.g. HMW)
- Biologic agents

*Trigger anaphylaxis by more than one mechanism.
** NSAIDs, non-steroidal anti-inflammatory drugs
*** HMW, high molecular weight
Anaphylaxis (WAO 2020)

Age-Related Factors*
- Infants: Cannot describe their symptoms
- Adolescents and young adults: Increased risk-taking behaviors
- Labor and delivery: Risk from medications (e.g., antibiotic to prevent neonatal group B strep infection)
- Elderly: Increased risk of fatality from medication and venom-triggered anaphylaxis

Concomitant Diseases*
- Allergic rhinitis and eczema
- Asthma and other respiratory diseases
- Cardiovascular diseases
- Psychiatric illness (e.g., depression)
- Mastocytosis / clonal mast cell disorders

Co-Factors that Amplify Anaphylaxis*
- Exercise
- Acute infection (e.g., a cold or fever)
- Emotional stress
- Disruption of routine (e.g., travel)
- Premenstrual status (females)

Concurrent Medications / Ethanol / Recreational Drug use*
- β-adrenergic blockers, ACE inhibitors**, NSAIDs**
- Ethanol / sedatives / hypnotics / antidepressants / recreational drugs (potentially affect recognition of anaphylactic triggers and symptoms.)

* Age-related factors, concomitant diseases, and concurrent medications potentially contribute to severe or fatal anaphylaxis. Co-factors potentially amplify anaphylaxis. Multiple factors and co-factors likely contribute to some anaphylactic episodes.
** ACE, angiotensin-converting enzyme.
*** NSAIDs, Non-steroidal anti-inflammatory drugs

Tryptase and Histamine Dynamics

- Tryptase levels provide a more precise measure of involvement of mast cells than clinical presentation\(^1\)
- Total serum tryptase may remain elevated acutely for 6+ hours\(^2\)
  - Peaks at 1 hour: obtain blood sample within 3 hours
- Normal serum tryptase value is \(<10\) ng/mL; the higher the value, the higher the sensitivity\(^3\)
- Positive predictive value of serum tryptase can be 92.6\%\(^3\)
  - Negative predictive value is only 52\%
- Plasma histamine begins to rise within 5 minutes but remains elevated for 30 to 60 minutes\(^4\)
  - Because of longer half-life, serum tryptase is preferred

Action of Epinephrine

Epinephrine

- $\alpha_1$-adrenergic receptor
- $\alpha_2$-adrenergic receptor
- $\beta_1$-adrenergic receptor
- $\beta_2$-adrenergic receptor
Respond Quickly!

- Administer epinephrine quickly
- Activate EMS – 911
- Then, call emergency contacts
# Adrenaline auto-injector world wide availability

<table>
<thead>
<tr>
<th>Area</th>
<th>Country</th>
<th>EpiPen/Fastjekt</th>
<th>Anapen</th>
<th>Twinject</th>
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# Vaccine Components

<table>
<thead>
<tr>
<th>Components</th>
<th>Type</th>
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<tbody>
<tr>
<td>Active immunizing antigens and conjugating agents</td>
<td>Toxoids, live-attenuated viruses, killed viruses or portions of virus, viral proteins, carrier proteins and antigens</td>
</tr>
<tr>
<td>Culture media (protein/peptides)</td>
<td>Hen’s egg, horse serum, murine and simian cells, kidney cells of dog, yeast</td>
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<tr>
<td>Additives</td>
<td>Antibiotics</td>
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<tr>
<td></td>
<td>Neomycin, chlortetracycline, gentamicin, streptomycin, erythromycin, kanamycin, polymyxin B, amphotericin B</td>
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<tr>
<td></td>
<td>Preservatives</td>
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<td>Thimerosal, 2-phenoxyethanol, phenol, benzethonium chloride</td>
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<td>Stabilizers</td>
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<tr>
<td></td>
<td>Gelatin, human serum albumin, amino acid mix, glutamate, glycine, monosodium glutamate, sucrose, lactose, sorbitol, ascorbic acid, phosphate, polysorbate 80/20, polygeline</td>
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<tr>
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<td>Adjuvants</td>
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<tr>
<td></td>
<td>Aluminum salts, MF-59, ASO4 (deacylated monophosphoryl lipid A+ aluminum hydroxide)</td>
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<td></td>
<td>Inactivation residues</td>
</tr>
<tr>
<td></td>
<td>Formaldehyde, beta-propiolactone, formalin, gluteraldehyde</td>
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<tr>
<td></td>
<td>Contamination</td>
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<td></td>
<td>Latex</td>
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</table>

Vaccine Components

Excipients

- **Preservatives**, to prevent contamination e.g. thimerosal
- **Adjuvants**, to help stimulate a stronger immune response e.g. aluminum salts
- **Stabilizers**, to keep the vaccine potent during transportation and storage e.g. sugars or gelatin

Residual trace amounts of materials used during the manufacturing process and removed

- **Cell culture materials**, used to grow the vaccine antigens e.g. egg protein, various culture media
- **Inactivating ingredients**, used to kill viruses or inactivate toxins e.g. formaldehyde.
- **Antibiotics**, used to prevent contamination by bacteria e.g. neomycin.

https://www.vaccinesafety.edu/components-Excipients.htm
# Vaccine Immune Mediated Reactions

<table>
<thead>
<tr>
<th>Immune mediated reaction</th>
<th>Frequent clinical manifestation</th>
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</thead>
<tbody>
<tr>
<td><strong>IgE mediated</strong></td>
<td>Urticaria, angioedema, rhinoconjunctivitis, bronchospasm, anaphylaxis, gastrointestinal disorders (diarrhea, abdominal cramping, vomiting)</td>
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<tr>
<td><strong>Minutes to &lt;4 hours</strong></td>
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<tr>
<td><strong>Immune complex (IgG)</strong></td>
<td>Vasculitis, myocarditis</td>
</tr>
<tr>
<td><strong>T-cell mediated</strong></td>
<td>Maculopapular exanthema, eczema, acute generalised exanthematosus pustulosis (AGEP), erythema multiforme</td>
</tr>
<tr>
<td><strong>48-72 hours, rare</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Non-IgE mediated (pseudoallergic)</strong></td>
<td>Urticaria, angioedema, anaphylactoid reactions, gastrointestinal disorders</td>
</tr>
<tr>
<td><strong>Autoimmune/inflammatory</strong></td>
<td>Thrombocytopenia, vasculitis, polyradiculoneuritis, macrophagic myofasciitis, rheumatoid arthritis, Reiter’s syndrome, sarcoidosis (juvenile), bullous pemphigoid, lichen planus, Guillain-Barré syndrome, polymyalgia</td>
</tr>
</tbody>
</table>

Vaccine Immune Mediated Reactions

• Self-reactive antibodies, created by molecular mimicry between the vaccine antigen and endogenous epitope
• Idiopathic thrombocytopenic purpura: 1 in 30,000 for measles, mumps, and rubella (MMR) vaccine
• Guillain-Barré syndrome (GBS) outbreak in 1976-1977
• Many people immunized with the swine influenza vaccine during the campaign period (approximately 0.04 per 100,000 vaccinations) developed GBS within 6 weeks following immunization
• Estimated rate of influenza vaccination-related GBS in Korea was reported to be 0-0.025 per 100,000 distributed doses which is considerably lower than 0.04 to less than one case per 100,000 vaccinations reported in previous studies
• Strong epidemiological data of an association between swine flu vaccination and GBS, the biological mechanisms remain unknown

Gelatin

- **Common cause of vaccine allergy**
- **Stabiliser**
- **When used in vaccines, gelatin is extensively cross-reactive and is of bovine or porcine origin**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Gelatin content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza (Fluzone; Sanofi Pasteur)</td>
<td>250 µg per 0.5 mL dose</td>
</tr>
<tr>
<td>Influenza (FluMist; MedImmune Vaccines)</td>
<td>2,000 µg per 0.2 mL dose</td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMRII; Merck)</td>
<td>14,500 µg per 0.5 mL dose</td>
</tr>
<tr>
<td>Measles, mumps, rubella, varicella (ProQuad; Merck)</td>
<td>11,000 µg per 0.5 mL dose</td>
</tr>
<tr>
<td>Rabies (RabAvert; Novartis)</td>
<td>12,000 µg per 1.0 mL dose</td>
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<tr>
<td>Typhoid Vaccine Live Oral Ty21a (VIVOTIF; Berna)</td>
<td>Capsule</td>
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<tr>
<td>Varicella (VARIVAX, Merck)</td>
<td>12,500 µg per 0.5 mL dose</td>
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<tr>
<td>Yellow fever (YF-VAX; Sanofi Pasteur)</td>
<td>7,500 µg per 0.5 mL dose</td>
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<tr>
<td>Zoster (ZOSTAVAX; Merck)</td>
<td>15,580 µg per 0.65 mL dose</td>
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Latex

- Latex, used to create a natural rubber latex and dry natural rubber, contains naturally occurring impurities.
- Such impurities are often responsible for recipient allergic reactions.
- **Synthetic** latex does not contain such impurities and therefore should be considered as an alternative when administering vaccinations.
- Contact type allergy is more common than latex anaphylaxis.
- Injection related latex allergies and anaphylaxis are thus very rare.
COVID-19 Vaccines

Fig. 1 | An overview of the different vaccine platforms in development against COVID-19. A schematic representation is shown of the classical vaccine platforms that are commonly used for human vaccines, and next-generation platforms, where very few have been licensed for use in humans. The stage of development for each of these vaccine platforms for COVID-19 vaccine development is shown; online vaccine trackers are available to follow these vaccines through the clinical development and licensing process.

van Riel D, de Wit E. Nat Mater 2020;19(8):810-812
COVID-19 Vaccines

<table>
<thead>
<tr>
<th>Whole-inactivated virus</th>
<th>Protein subunit</th>
<th>Adenovirus vector</th>
<th>mRNA</th>
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<tbody>
<tr>
<td>Sinovac</td>
<td>Novavax</td>
<td>The University of Oxford/AstraZeneca</td>
<td>Moderna/NIH</td>
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<td>Wuhan Institute of Biological Products/Sinopharm</td>
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<td>CanSinoBIO/Beijing Institute of Biotechnology</td>
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<tr>
<td></td>
<td></td>
<td>Johnson &amp; Johnson/Janssen Pharmaceuticals</td>
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</table>
COVID-19 vaccine doses administered per 100 people, Jan 27, 2021

Total number of vaccination doses administered per 100 people in the total population. This is counted as a single dose, and may not equal the total number of people vaccinated, depending on the specific dose regime (e.g. people receive multiple doses).

Source: Official data collated by Our World in Data – Last updated 28 January, 14:00 (London time) OurWorldInData.org/coronavirus • CC BY

https://ourworldindata.org/
COVID-19 Vaccine Anaphylaxis

1. Allergic reactions including anaphylaxis as defined by the Brighton Collaboration Working Group was used as part of the Vaccine Adverse Event Reporting System (VAERS) where based on spontaneous reporting, 21 cases of anaphylaxis after 1,893,360 first doses of Pfizer-BioNTech (11.1 cases per million doses) were reported, with 71% of cases occurring within 15 minutes of vaccination.

2. During December 21, 2020-January 10, 2021, monitoring by the VAERS detected 10 cases of anaphylaxis after administration of a reported 4,041,396 first doses of Moderna COVID-19 vaccine (2.5 cases per million doses administered. In 9 cases, onset occurred within 15 minutes of vaccination. No anaphylaxis-related deaths were reported.

Polyethylene-glycol (PEG)

- PEG is a hydrophilic polymer frequently used as an excipient in everyday products including medicines, cosmetics, or foods
- Increased number of allergic reactions to PEG (IgE and non-IgE-mediated)
- Cross-reactivity Polysorbat 80 due to the shared chemical moiety: \(-(\text{CH}_2-\text{CH}_2\text{O})_n\)
- Skin prick testing and intradermal testing with different dilutions of PEG, basophil activation test, oral provocation testing are recommended in suspected individuals
- No commercial specific IgE assays
- ** Oxford/Astra-Zeneca COVID-19 vaccine does not contain PEG

## Current Recommendations

<table>
<thead>
<tr>
<th>Condition</th>
<th>US CDC</th>
<th>UK</th>
<th>APAAACI</th>
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<tbody>
<tr>
<td>Severe allergic reaction to currently available mRNA COVID-19 vaccine</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>Severe allergic reaction after 1&lt;sup&gt;st&lt;/sup&gt; dose mRNA COVID-19 vaccine</td>
<td>✗</td>
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<td>✗</td>
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<tr>
<td>Non-severe immediate allergic reaction to currently available mRNA COVID-19 vaccine e.g. hives, swelling, wheezing</td>
<td>✗</td>
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<tr>
<td>Non-severe immediate allergic reaction after 1&lt;sup&gt;st&lt;/sup&gt; dose mRNA COVID-19 vaccine</td>
<td>✗</td>
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<tr>
<td>Previous allergic reaction to polyethylene glycol (PEG) or polysorbate</td>
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US CDC as of 31 Dec 2020
UK MHRA & BSACI Expert Vaccine Allergy Group as of 30 Dec 2020
## Current Recommendations

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<tr>
<td>Immediate allergic reaction to other types of vaccines or injectable</td>
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<td>![Green Check]</td>
<td>![Green Check]</td>
</tr>
<tr>
<td>Anaphylaxis to other vaccines, drugs or food</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
</tr>
<tr>
<td>Allergies not related to vaccines or injectables e.g. food, pets, environmental, latex</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
</tr>
<tr>
<td>History of drug allergy/hypersensitivity</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
</tr>
<tr>
<td>Family history of severe allergic reactions</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
<td>![Green Check]</td>
</tr>
</tbody>
</table>

US CDC as of 31 Dec 2020
UK MHRA & BSACI Expert Vaccine Allergy Group as of 30 Dec 2020
Clinical Approach

Clinical history
- Positive history of reactions after vaccine administration
  - Nonimmediate reaction
    - In most cases, no allergy work-up
    - After contact dermatitis or nodules consider patch test
  - Immediate reaction
    - Skin testing (prick test and/or intradermal test) and/or in vitro IgE testing
      - Vaccine and/or its components should be tested
        - Positive
          - If additional doses required, the vaccine may be given in graded doses **
        - Negative
          - If additional doses required, the vaccine can be given according to general recommendations
- Positive history of immediate allergy to gelatin, latex or yeast*

Premedication for those with a h/o allergies

30 min prior vaccination
- Hi antihistamine
- H2 antihistamine
- Montelukast

For emergency in case of anaphylaxis
- Epipen on hand
Diagnostic Tests

1. Do you have a history of a severe allergic reaction to an injectable medication (intravenous, intramuscular, or subcutaneous)? *
2. Do you have a history of a severe allergic reaction to a prior vaccine? *
3. Do you have a history of a severe allergic reaction to another allergen (e.g., food, venom, or latex)?
4. Do you have a history of an immediate (<4 hours) or severe allergic reaction to polyethylene glycol (PEG), a polysorbate or polyoxy 35 castor oil (e.g. paclitaxel) containing injectable or vaccine?

Answer “yes” to question 4
Answer “yes” to questions 1, 2 or 3
Answer “no” to all 4 questions

Higher Risk
- History of potential anaphylaxis to an injectable medication or vaccine containing PEG, PEG derivates, or polysorbate with lack of proven tolerance since incident reaction
- History of potential anaphylaxis to oral PEG (e.g. Miralax)

Medium Risk
- History of potential anaphylaxis to a vaccine or injectable medication without PEG or polysorbate
- History of potential anaphylaxis to food, drugs, venom, or latex
- History of idiopathic anaphylaxis

Lower Risk
- History of food, drug(s), venom, or latex allergy except anaphylaxis
- Any prior reaction to vaccines except anaphylaxis
- Mastocytosis/mast cell activation
- Allergic rhinitis and asthma

Clinical Phenotyping
Expanded Skin Testing*
(May Be Ineligible for mRNA Vaccine)

Routine Vaccination with 30 Minute Observation
Routine Vaccination with 15 Minute Observation
Chlorpheniramine 4 mg x 10 tablets

Diphenhydramine 50 mg/ml injection x 2 vials

Salbutamol 0.5% respiratory solution x 10 ml x 2 units

Prednisolone 20 mg tab x 10 tablets

Epinephrine 1mg/ml injection x 5 vials

Hydrocortisone sodium succinate 100 mg injection x 2 units.
Diagnostic Tests

Expanded Skin Testing in Conjunction with Clinical Phenotyping by Allergist:
1. History of potential anaphylaxis to an injectable medication or vaccine containing PEG, PEG derivates or polysorbate
2. Patients with potential anaphylaxis to first dose of Pfizer-BioNTech or Moderna COVID-19 vaccine

Clinical Phenotyping Does Not Confirm Anaphylaxis

If Skin Testing Positive, STOP

- Ineligible for PEG/polysorbate containing vaccines
- Provide patient with a list of PEG/polysorbate containing vaccines and injectables

Skin Test Positive

Skin Prick
- PEG3350 (i.e., Miralax)
- Methylprednisolone acetate (contains PEG3350)
- Triamcinolone acetonide or Refresh Eye Drops or Prevnar (contains polysorbate 80)
- Hepatitis A or Twinrix vaccine (contains polysorbate 20)

Skin Test Negative

Intradermal
- Methylprednisolone acetate (contains PEG3350)
- Triamcinolone acetonide or Refresh Eye Drops or Prevnar (contains polysorbate 80)
- Hepatitis A vaccine or Twinrix (contains polysorbate 20)

Skin Test Negative

Challenge:
- Informed Consent
- Vaccination with 30 Minute Observation, Ideally Under Allergist Supervision
# Skin Tests

<table>
<thead>
<tr>
<th></th>
<th>PEG3350</th>
<th>Control*</th>
<th>Polysorbate 20</th>
<th>Polysorbate 80(\text{\textsuperscript{f}})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td>Miralax</td>
<td>Methyl-prednisolone Acetate (Depo-Medrol) (\text{\textsuperscript{5}})</td>
<td>Methyl-prednisolone Sodium Succinate (Solu-medrol) (\text{\textsuperscript{5}})</td>
<td>Hepatitis A vaccine or Twinrix</td>
</tr>
<tr>
<td><strong>Epicutaneous</strong></td>
<td>1:100 (1.7mg/mL)</td>
<td>40 mg/ml</td>
<td>40 mg/ml</td>
<td>1:1</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Epicutaneous</strong></td>
<td>1:10 (17 mg/mL)</td>
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<tr>
<td><strong>Step 3</strong></td>
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<tr>
<td><strong>Epicutaneous</strong></td>
<td>1:1** (170 mg/mL)</td>
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<tr>
<td><strong>Step 4</strong></td>
<td></td>
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<tr>
<td><strong>Intradermal</strong></td>
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<tr>
<td><strong>Step 5</strong></td>
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<tr>
<td><strong>Intradermal</strong></td>
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</tbody>
</table>

APAAACl Task Force

Chairs: Ruby Pawankar and Bernard Thong

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