ALLERGIC EMERGENCIES
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The speaker has no conflicts of interest to disclose.

Objectives for Pharmacists
- Describe the immunologic pathways to cause an allergic response
- Identify the most common triggers to cause anaphylaxis
- Choose the appropriate treatment for anaphylaxis

Objectives for Technicians
- Describe what causes an allergic reaction
- Identify the most common triggers to cause anaphylaxis
- Describe possible treatments for anaphylaxis

Patient Case
- SM is a 31 y/o female with a PMH of atopia, allergic rhinitis, asthma, eczema, and depression.
- Immunization Hx: influenza vaccine every year x 8 years
- Received influenza vaccine then briskly walked to office (~5 min walk)
- ~15 min later
  - Subjective symptoms: ‘impending doom’ feeling
  - Objective symptoms: red rash on neck and chest, chest tightness, throat tightness, shortness of breath, altered mental status

Anaphylaxis
- Lifetime prevalence ~0.05%-2%
  - Potentially underestimated
  - Definition of anaphylaxis is complex, difficult to assess in epidemiological studies
- Several guidelines
  - World Allergy Organization (WAO)
  - American Academy of Allergy, Asthma and Immunology (AAAAI) and American College of Allergy, Asthma and Immunology (ACAAI)
  - European Academy of Allergy and Clinical Immunology (EAACI)

Definition of Anaphylaxis

<table>
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<tr>
<th>WAO</th>
<th>AAAAI / ACAAI</th>
<th>EAACI</th>
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<td>'A serious life-threatening generalized or systemic hypersensitivity reaction' and 'a serious allergic reaction that is rapid in onset &amp; might cause death'</td>
<td>'An acute life-threatening systemic reaction with varied mechanisms, clinical presentations, &amp; severity that results from the sudden release of mediators from mast cells &amp; basophils'</td>
<td>'A severe life-threatening generalized or systemic hypersensitivity reaction'</td>
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Reference:
**Triggers**

- Food allergens
- Medications
- Drugs
- Insect stings
- Exercise
- Prescription or non-prescription medications
- Vaccines
- Other environmental antigens

**Influencing Factors**

- Age
- Sex
- Personal history
- Family history
- Occurrence of previous anaphylaxis

**Pathophysiology**

- **Anaphylactic Reaction**
  - Immediate release of histamine
  - Smooth muscle contraction
  - Vascular leakiness
  - Basophil and mast cell degranulation

**Clinical Presentation**

- **Onset**
  - Any allergen: within 2 hours
  - Food allergen: within 30 min
  - Parenteral medication or insect sting: < 30 min
- **Multiple organ systems affected**
  - Skin/urticaria (80-90%)
  - Respiratory tract (70%)
    - More common in pediatrics
  - Gastrointestinal tract (30-45%)
    - More common in adults
  - Cardiovascular (10-45%)
    - More common in adults
  - Central nervous system (10-15%)

**Biphasic Allergic Reaction**

- A second reaction occurring after initial recovery
- Occur: 1 to 72 hours later
- Usually: 4 to 12 hour
- Occurs in up to 20% presenting with anaphylaxis
- More severe than initial reaction
- Account for 25% of fatal/near-fatal food reactions and 23% of drug/biologic reactions
- Rarely occurs without initial hypotension or airway obstruction
Signs and Symptoms

Gastrointestinal
- Abdominal pain, nausea, vomiting, diarrhea, dysphagia

Cardiovascular system
- Chest pain
- Tachycardia, bradycardia (less common), other arrhythmias, palpitations
- Hypotension, feeling faint, urinary or fecal incontinence, shock
- Cardiac arrest

Central nervous system
- Aura of impending doom, uneasiness, throbbing headache (pre-epinephrine), altered mental status, dizziness, confusion, tunnel vision

Other
- Metallic taste
- Cramps & uterine bleeding from contractions in pregnancy

Skin, subcutaneous tissue, mucosa
- Flushing, itching, urticaria, angioedema, morbilliform rash, pilor erection

Respiratory
- Nasal itching, congestion, rhinorrhea, sneezing
- Throat itching & tightness, dysphonia, hoarseness, stridor, dry staccato cough
- Lower airways: increase respiratory rate, SOB, chest tightness, deep cough, wheezing/bronchospasm, decrease peak expiratory flow
- Cyanosis
- Respiratory arrest

Anaphylaxis Definition
1. Acute onset of illness with cutaneous and/or mucosal involvement AND at least one of the following:
   a. Respiratory compromise
   b. Cardiovascular compromise
2. Two or more of the following occur rapidly after exposure to a likely allergen
   a. Involvement of skin or mucosa
   b. Respiratory compromise
   c. Cardiovascular compromise
   d. Persistent GI symptoms
3. Hypotension after exposure to known allergen

Differential Diagnosis
- Acute asthma
- Syncope
- Anxiety/panic attack
- Acute generalized urticaria
- Aspiration of a foreign body
- Cardiovascular event (MI, PE)
- Neurologic event (seizure, CVA)
- Shock
- Nonallergic angioedema
- Systemic capillary leak syndrome
- Red man syndrome
- Pheochromocytoma
- Flushing syndrome

FIRST LINE TREATMENT

Epinephrine
- Dosing:
  - Adults: epinephrine (1:1000) 0.3 mg IM
  - Pediatrics: epinephrine 0.01 mg/kg (up to 0.3 mg) IM
- Given intramuscular in the anterolateral thigh
- Mechanism of action:
  - α1-adrenergic receptor: Vasoconstriction
  - α2-adrenergic receptor: Insulin release
  - β1-adrenergic receptor: Inotropy, Chronotropy
  - β2-adrenergic receptor: Bronchodilation, Vasodilation, Mediator release

Intramuscular vs. Subcutaneous Epinephrine in Adults
- 6-way cross-over study
- Healthy 18-35 y/o men
- Adverse Effects:
  - Pallor
  - Tremors
  - Palpitations
  - HA
  - Shivers

Epinephrine Absorption in Pediatrics
- Single dose, parallel-group
- 17 children (4-12 y/o)
  - Ave age: 8 ± 1 y/o
  - Epinephrine SQ 0.01mg/kg (max 0.3 mg)
  - Ave wt.: 32 ± 3 kg
  - Mean dose: 0.27 ± 0.04 mg
  - EpiPen® IM 0.3 mg
  - Ave wt.: 27 ± 2 kg

Epinephrine Absorption in Pediatrics
- Adverse Effects:
  - Tremor (16/17)
  - Pallor (14/17)
  - Headache (4/17)
  - Tingling–extremities (3/17)

Epinephrine and Obesity
- Chart review of pts presenting to ED for anaphylaxis
- Focus on total number of epinephrine doses and BMI categorization
- 321 pts in 4 different EDs
  - 261 children
  - 60 adults
- No difference in need for additional doses in:
  - Adults vs. children (P=0.94)
  - When administered adjunct medications (P=0.38)
  - Including corticosteroids
  - Obesity vs. non-obesity
    (OR 1.22; 95% CI 0.77-1.93; P=0.4)
  - Adjusted for age and sex

Outdated EpiPen®
- Epinephrine is inherently unstable
  - Oxidized by O₂ & light
  - Turning pink - brown due to the formation of melanin
- 28 EpiPen® & 6 EpiPen® Jr
  - 1-90 mo past expiration
- Bioavailability in rabbits
- Epinephrine content by spectrophotometric method

SECOND-LINE TREATMENTS
Glucocorticoid Steroids
- Adult: hydrocortisone 200 mg IV/IM x 1 or methylprednisolone 50 – 100 mg IV/IM x 1
- Pediatrics: hydrocortisone 1-2 mg/kg IV/IM x 1 (max 100 mg) or methylprednisolone 1-2 mg/kg IV/IM x 1 (max 60 mg)
- Cochrane systematic review of randomized controlled trials
- Often used inappropriately as first-line medications in place of epinephrine in ED
- Potentially prevent biphasic anaphylaxis
- Found zero randomized controlled trials assessing use in anaphylaxis
- Cannot recommend for or against the use of steroids in anaphylaxis


Other Second-line Treatments
- Beta-2 agonist
  - Adults and Pediatrics: albuterol 2-6 puffs or 2.5 mg nebulized q 20 min prn or 15 mg/hr continuous nebulization
- H1- and H2-antihistamines
  - H1: Adults: diphenhydramine 50 mg IV/IM/PO x 1
  - H1: Pediatrics: diphenhydramine 1-1.25 mg/kg IV/IM/PO (max 50 mg)
  - H2: Adults: famotidine 20 mg IV/IM/PO x 1
  - H2: Pediatrics: famotidine 0.5 mg/kg IV/IM/PO x 1 (max 20 mg)
- O2 supplementation
- Fluid resuscitation


After-anaphylaxis Management
- Consensus of all three guidelines:
  - All patients should be given a script for epinephrine auto-injector
  - Education from a trained healthcare professional
    - Recognizing signs and symptoms
    - Avoiding triggers
    - Appropriate use of epinephrine auto-injector
    - Medical alert ID
  - Follow-up with an allergist/immunologist trained in anaphylaxis
    - Allergen sensitivity testing
    - Desensitization protocols


Self Assessment Question
Which cell type is responsible for the monophasic or initial allergic response?
A. Mast cell
B. Histamine
C. Eosinophil
D. Neutrophil

Self Assessment Question
In patient SM, who a 31 y/o female with a PMH of atopia, allergic rhinitis, asthma, eczema, depression. She just received the flu shot prior briskly walked back to her office prior and subsequently experiencing symptoms of an acute allergic emergency.
What predisposing factor or trigger put her at risk for anaphylaxis?
A. Previous exposure to the flu vaccine
B. Exercise
C. Depression
D. All of the above

Self Assessment Questions
What is the best treatment option for SM?
A. Epinephrine 0.3 mg IM in anterolateral thigh and go back to work
B. Epinephrine 0.3 mg SQ in anterolateral thigh and go straight to the emergency room
C. Epinephrine 0.3 mg IM in anterolateral thigh and go to the emergency room
D. This is not anaphylaxis and should be treated with glucocorticoid steroids and an H1-antihistamine
References