Anaphylaxis Update
ACAAI ANAPHYLAXIS SIMULATION SESSION

Anaphylaxis
- Diagnosis based on history and physical exam

Table 1-2
Essential features of history in the evaluation of a patient who has experienced an episode of anaphylaxis

A. Detailed history of ingestants (foods/drugs) taken within 6 h before the event
B. Activity in which the patient was engaged at the time of the event
C. Location of the event (home, school, work, indoors/outdoors)
D. Exposure to heat or cold
E. Any related sting or bite
F. Time of day or night
G. Duration of event
H. Recurrence of symptoms after initial resolution
I. Exact nature of symptoms (eg, if cutaneous, determine whether flush, pruritus, urticaria, or angioedema)
J. In a woman, the relation between the event and her menstrual cycle
K. Was medical care given and what treatments were administered
L. How long before recovery occurred and was there a recurrence of symptoms after a symptom-free period

Lieberman, Ann Allergy Asthma Immunol 2015.
Diagnosing Anaphylaxis

**TABLE 1. Clinical criteria for diagnosing anaphylaxis**

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips/tongue-uvula)
   1. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
   2. Reduced BP or associated symptoms of end-organ dysfunction (eg, 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 (eg, generalized hives, itch-flush, swollen lips-tongue-uvula) b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia) c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence) d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
   4. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
      a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP* b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person’s baseline


Campbell, Ann Allergy Asthma Immunol 2014.
Summary of signs and symptoms in 1,865 patients of all ages with multiple etiologies

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Cutaneous</td>
<td>62–90</td>
</tr>
<tr>
<td>Urticaria and angioedema</td>
<td>45–55</td>
</tr>
<tr>
<td>Flushing</td>
<td>5–10</td>
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<tr>
<td>Pruritus without rash</td>
<td>2–5</td>
</tr>
<tr>
<td>Respiratory</td>
<td>2–5</td>
</tr>
<tr>
<td>Dyspnea, wheeze</td>
<td>45–50</td>
</tr>
<tr>
<td>Upper airway angioedema</td>
<td>50–60</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>15–20</td>
</tr>
<tr>
<td>Hypotension, dizziness, syncope, diaphoresis</td>
<td>30–35</td>
</tr>
<tr>
<td>Abdominal</td>
<td></td>
</tr>
<tr>
<td>Nausea, vomiting, diarrhea, abdominal pain</td>
<td>25–30</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>5–8</td>
</tr>
<tr>
<td>Substantial pain</td>
<td>4–5</td>
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<tr>
<td>Seizure</td>
<td>1–2</td>
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</tbody>
</table>


Mechanism

LoVerde, Chest 2018.
Treatment

- **First line:** Give epinephrine IM
  - Consider IV infusion of epinephrine if not responding
  - Can give by IO if necessary
- **Second Line:**
  - Remove trigger and call for help
  - Place patient in supine position (or upright for respiratory distress)
  - Administer oxygen if needed (or to all patients with anaphylaxis)
  - Prepare for airway management if needed
  - Administer IV fluids if needed for circulatory support
  - Administer inhaled β-agonist if bronchospasm present
- **Third Line:** Antihistamines and Corticosteroids

*Campbell, Ann Allergy Asthma Immunol 2014.
Muraro, Allergy 2014.*

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Treatment

- Consider glucagon if patient on β-blocker and not responding to epinephrine
- **Monitoring:**
  - Observe patients for 4-8 hours and consider longer observation if history of risk factors for severe anaphylaxis (asthma, previous biphasic reactions, protracted anaphylaxis)
  - Prescribe auto-injectable epinephrine and provide an action plan with instructions
  - Follow-up with an allergist-immunologist

*Campbell, Ann Allergy Asthma Immunol 2014.*
Epinephrine

- First line treatment
  - Benefit of using appropriate doses of IM epinephrine far exceeds the risk
- Mechanism:
  - $\alpha$ receptors: increases peripheral vascular resistance, reverses peripheral vasodilation, improves blood pressure and coronary perfusion, and decreasing angioedema
  - $\beta_1$ receptors: positive inotrophic and chronotropic cardiac effects
  - $\beta_2$ receptors: bronchodilation, increases intracellular cAMP production in mast cells and basophils -> decreases release of inflammatory mediators


Epinephrine

- Dosing for IM:
  - 0.01 mg/kg in infants and children
  - 0.3-0.5 ml diluted 1:1000 (0.3-0.5 mg)
  - Repeat dose at 5 minute intervals
  - Intramuscular administration preferred to subcutaneous due to faster max plasma concentrations (8 min vs 34 min) and higher max plasma concentration
- Dosing for IV bolus in arrest:
  - 1 mg IV of 1:10,000 dilution
  - For children, 0.01 mL/kg to max dose of 1 mg (1:10,000 dilution)
- Dosing for IV drip:
  - 1 mg (1 ml) of a 1:1,000 concentration to 250 ml of dextrose 5% in water
  - Infuse at an initial rate of 1 mcg per minute

Epinephrine

- Delayed administration associated with risk of death
  - Review of 6 fatal and 7 near-fatal cases of food-induced anaphylaxis
    - All patients had asthma
    - None knew the allergen had been eaten
    - Epinephrine had been prescribed 3 of 6 kids with fatal reactions, 3 of 7 with nonfatal reactions
      - None of those with fatal reaction had it at the time of the reaction
      - Only one patient with nonfatal reaction gave herself epinephrine
    - Studies show that epinephrine is often not given or administration delayed


Epinephrine

How many doses are needed?
- Retrospective chart review of 105 anaphylactic events in allergy clinic – 35% required more than one dose of epinephrine
  - SCIT and sting challenges
- Retrospective review of SCIT reactions – 64 of 9592 injection visits with systemic reaction
  - 10/64 (16%) required more than one dose of epi
- Review of 413 patients seen for food allergy – 95 reactions for which epi was given
  - 19% required more than one dose
- Consider epi drip if no response after 3-4 doses of IM epinephrine

## Epinephrine

First line treatment
- Give if there is suspicion of anaphylaxis to reduce morbidity and mortality
- There is no contraindication
- IM is preferred route (1:1000)
- May need second dose in 10-35% of cases

## Antihistamines

- Use of antihistamines in anaphylaxis based on mechanism of action and effectiveness in other allergic diseases
- Vasodilatation, increased vascular permeability, bronchial smooth muscle contraction, and increased airway secretions mediated by histamine
- No direct evidence to support use in treatment of anaphylaxis
- Cochrane review of literature in 2007 found no studies that satisfied inclusion criteria

Lieberman, Ann Allergy Asthma Immunol 2015.
Sheikh, Allergy 2007.
Addition of H2 Blockers

- Prospective ER study of 91 patients with acute allergic syndromes treated with:
  - Diphenhydramine + placebo
  - Diphenhydramine + ranitidine
- Increased resolution of urticaria at 2 hours
- No significant difference in erythema or angioedema, blood pressure, symptom score
- Cochrane review of H2-receptor antagonists in urticaria determined very limited evidence

Fedorowicz, Cochrane Database Syst Rev 2012.

Use of Steroids

- Steroids have no role in acute management of anaphylaxis
- No strong evidence for decrease of biphasic or prolonged reactions is not supported by strong
- Patients who have complete resolution of symptoms after treatment with epinephrine do not need to be prescribed antihistamines or corticosteroids
- Cochrane review of literature in 2012 found no studies that satisfied inclusion criteria

Lieberman, Ann Allergy Asthma Immunol 2015.
Use of Steroids

- In observational study of 2,701 ED visits, there was a similar frequency of ED revisits within 7 days in the 48% of patients who had received steroids versus those who had not (5.8% vs 6.7%)

<table>
<thead>
<tr>
<th>Table 2. Outcomes and propensity score analysis.</th>
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<tbody>
<tr>
<td>Primary Outcome, Secondary Outcomes, Secondary Analysis</td>
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<tr>
<td>Full cohort (n=2,701)</td>
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<tr>
<td>Anaphylaxis (n=473)</td>
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<tr>
<td>Pneumonia (n=328)</td>
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<tr>
<td>Other or likely prolaps (n=1,368)</td>
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<td>Secondary outcomes (all examining full cohort)</td>
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Biphasic reactions

- First case report in 1984 of 3 patients with biphasic anaphylactic reactions
- Retrospective review of 100 children admitted with anaphylaxis
  - 6% with biphasic reactions
  - Increase risk with delay in epinephrine administration (48 vs. 190 minutes)
  - No differences in corticosteroid use or serious cardiovascular or respiratory symptoms
- In 103 patients with anaphylactic reactions, 19.4% with biphasic reaction
  - Average time to onset of second phase was 10 hours
  - 40% occurred more than 10 hours after initial reaction
  - Biphasic reactors received less epinephrine and less corticosteroid

Popa, Ann Allergy 1984.
Biphasic reactions

Recent studies show lower incidence:
- In ED review of 872 cases of anaphylaxis, 4.1% rate of biphasic reactions
- Risk factors: prior anaphylaxis, unknown inciting trigger, and delayed epinephrine
Causes of Anaphylaxis


**Causes of Anaphylaxis:**

- Risk factors for reactions
  - Symptomatic asthma
  - Exacerbation of allergic rhinitis
  - High degree of allergen hypersensitivity
  - Use of beta-blockers (possibly ACE inhibitors)
  - Dosing error
  - Injection from new vial
  - Previous systemic reaction

- Additional Risk factors for fatal reaction
  - Delay or failure to administer epinephrine
  - Inadequate post injection waiting period
  - Administration of injections in suboptimal settings (eg, at home)
Thank you