Anaphylaxis: Practice Parameters and Devices

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Anaphylaxis: Practice Parameters and Devices

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11:30 a.m. – 12:45 p.m.
Disclosures

- Monaghan Medical Corporation – speaker
- Norvartis - speaker

No conflict

Objectives

Discuss
Discuss the pathophysiology and the immunologic mechanisms of anaphylaxis.

Explain
Explain guideline-based therapy, management and prevention of anaphylaxis.

Describe
Describe appropriate use of devices for the treatment of anaphylaxis.

History of Anaphylaxis

Term was coined in 1901 by Charles Richet and Paul Portier to describe a phenomenon discovered while experimenting with aqueous glycerin extracts of the sea anemone

Noble Prize in 1913 for discovering the phenomenon known as anaphylaxis
Anaphylaxis

- Up to 5% of the US population has had anaphylaxis
- Fatal outcome is rare, such that even for people with known venom or food allergy, fatal anaphylaxis constitutes less than 1% of total mortality risk
- Fatal food anaphylaxis most commonly occurs during the second and third decades
- Delayed epinephrine administration is a risk factor


Definition of Anaphylaxis

**Anaphylaxis**

"An acute, life-threatening systemic reaction with varied mechanisms, clinical presentations and severity" that results from allergic cell activation and subsequent mediator release.

"A serious allergic reaction that is rapid in onset and may cause death"

3 sets of clinical criteria to diagnose anaphylaxis

Anaphylaxis: The Facts

- Anaphylaxis is a severe, acute, and potentially fatal allergic reaction
- Several studies have documented poor adherence to anaphylaxis guidelines in emergency settings where most cases of anaphylaxis are managed
- Recent studies have suggested an increased incidence and prevalence of anaphylaxis
- Epinephrine is underused, especially in infants

**Anaphylaxis: Mechanism of Action**

- Anaphylaxis is initiated by an allergen interacting with allergen-specific IgE bound to the FcεRI receptor on mast cells, basophils, or both.
- Allergens interact with IgE molecules on 2 or more receptors of the cell surface to cause cross-linking, which leads to receptor aggregation and initiates intracellular signaling.
- If signaling is sufficiently robust, mast cell/basophil activation and degranulation develop, with the release of preformed mediators, enzymes, and cytokines, such as histamine, tryptase, and tumor necrosis factor.
- These mediators act directly on tissue to cause allergic symptoms and recruit/activate other inflammatory cells.
- Recruited cells release more mediators and stimulate the production of lipid-derived mediators such as prostaglandin D2 and cysteinyl leukotrienes, leading to amplification of the allergic reaction.

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**Pathways of Anaphylaxis**

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**Anaphylaxis**

- Immunologic
  - Idiopathic
    - IgE (FcεRI)
    - Non-IgE
  - Physical
    - Other

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Causes of Anaphylaxis: Immunologic

IgE-mediated reactions
- Food
- Drug-induced anaphylaxis
- Beta-lactams
- Latex
- Hymenoptera stings
- Seminal fluid
- Anaphylaxis with allergen immunotherapy
- Allergy skin testing

Immune aggregates
- Drugs
- Blood products

Pathophysiologic Changes in Anaphylaxis

Reference:

Diagnostic Criteria

Anaphylaxis is likely if any 1 of the following 3 criteria are met:

1. Acute onset of an illness (min to hours) with involvement of the skin, mucosal tissues, or both (hives, flushing, angioedema)

   AND AT LEAST ONE OF THE FOLLOWING:
   a. Respiratory compromise (dyspnea, wheezing, bronchoospasm, stridor; reduced PEF, hypoxemia)
   b. Reduced BP or associated symptoms of end-organ dysfunction (collapse, syncope, incontinence)

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to hours):
   a. Involvement of the skin-mucosal tissue (generalized hives, itch-flush, swollen lips-tongue-uvula)
   b. Respiratory compromise (dyspnea, wheezing, bronchoospasm, stridor; reduced PEF, hypoxemia)
   c. Reduced BP or associated symptoms of end-organ dysfunction (collapse, syncope, incontinence)
   d. Persistent gastrointestinal symptoms (abdominal pain, vomiting)

3. Reduced BP after exposure to known allergens for that patient (min to several hours)

Anaphylaxis: Diagnostic Pitfalls

- Symptoms may be masked by current medications
- Initial reaction to new allergen
- Uncommunicative patient
- Failure to recognize non-specific clinical signs
- Mistaking anaphylaxis for a progressing asthma exacerbation in a known asthmatic
- Vitals/blood pressure taken after treatment initialized (epinephrine)

*Health care providers must be competent in recognizing anaphylaxis so appropriate treatment can be quickly administered

Simons JACI. Lee and Vadas CEA 2011

Time Course of Anaphylaxis

Uniphasic anaphylaxis
- Most common, 80-90%
- Peaks within minutes to hours after exposure, then resolves after treatment

Biphasic anaphylaxis
- Anaphylaxis symptoms resolve with subsequent return of symptoms without further exposure to the trigger
- Can occur hours later
- Occur in 1-35% of anaphylaxis

Protracted anaphylaxis
- Symptoms can last hours to days and is extremely rare

Biphasic Anaphylaxis

Antigen Exposure

Initial Symptoms
Asymptomatic
Symptomatic
Second-Phase Symptoms
1 - 24 hours
Clinical Manifestations

These organ systems are rich in allergic cells and are highly sensitive to the effects of mast cell mediators.

- **Cutaneous System**: 80-90%
- **Respiratory System**: Up to 70%
- **Gastrointestinal System**: Up to 45%
- **Cardiovascular System**: Up to 45%

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Patient-Reported Organ System Involvement in Anaphylaxis

<table>
<thead>
<tr>
<th>Organ System Involvement Reported by Patients with Anaphylaxis in Most Recent Reaction (N=344)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>76%</td>
</tr>
<tr>
<td>Skin</td>
<td>73%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>31%</td>
</tr>
<tr>
<td>Neurological</td>
<td>40%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>17%</td>
</tr>
</tbody>
</table>


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Cutaneous

- Urticaria (hives)
- Angioedema
- Erythema (flushing)
- Pruritus
Respiratory

- Upper Airway
  - Nasal congestion
  - Sneezing
  - Hoarseness
  - Cough
  - Oropharyngeal or laryngeal edema

- Lower Airway
  - Dyspnea
  - Bronchospasms
  - Wheezing
  - Chest tightness
  - Pulmonary edema

Gastrointestinal

- Nausea
- Vomiting
- Diarrhea
- Abdominal pain

Cardiovascular

- Hypotension
- Dizziness
- Syncope
- Tachycardia
- Hypotension

...affects about one third of patients

Cardiovascular disease does not “forbid” the use of epinephrine in the treatment of anaphylaxis

Other Symptoms

Headache, substernal pain, sense of impending doom and seizure occur less frequently.

Essential Features of History

- Detailed history of ingestants (foods/drugs) taken within 6 hours
- Activity at the time of the event
- Location of the event (home, school, work, indoors/outdoors)
- Exposure to heat or cold
- Any related sting or bite
- Time of day or night
- Duration of event
- Recurrence of symptoms after initial resolution
- Exact nature of symptoms: cutaneous, determine whether flush, pruritus, urticaria, or angioedema
- Relation between the event and menstrual cycle in women
- Medical care given and what treatments were administered
- How long before recovery occurred and was there a recurrence of symptoms after a symptom-free period

Patient Factors that Increase Risk of Anaphylaxis

- Age
  - Infants: Under recognition, underdiagnosis, no appropriate epinephrine auto-injector dose
  - Adolescents and young adults: Risk-taking behavior
  - Pregnancy: During labor and delivery, antibiotic prophylaxis against neonatal group B streptococcal infection is a common trigger
  - Elderly: Risk of fatality from medication and venom-triggered anaphylaxis
- Comorbidities
  - Asthma and other respiratory diseases, especially if severe or uncontrolled
  - CVD—Including hypertension
Patient Factors that Increase Risk of Anaphylaxis Severity and Fatality

- Mastocytosis and clonal mast cell disorders
- Depression and other psychiatric diseases (might impair recognition of symptoms)
- Thyroid disease (some patients with idiopathic anaphylaxis)
- Concurrent medication/chemical use
- Potentially affect recognition of anaphylaxis
- Sedatives/hypnotics/antidepressants/ethanol/recreational drugs
- Potentially increase anaphylaxis severity
- β-Blockers and ACE inhibitors

Treatment of Anaphylaxis

Treatment of anaphylaxis is epinephrine

No absolute contraindications for epinephrine during anaphylaxis

Failure or delay in giving epinephrine during anaphylaxis is associated with poor outcomes/mortality

Epinephrine is administered IM lateral thigh
Anaphylaxis Treatment

- Optimal dose of epinephrine is unknown
  - There have been no published dose-response studies documenting that the suggested dose of 0.01 mg/kg is the correct dose
  - Before the advent of automatic epinephrine injectors, the recommended doses of epinephrine varied considerably
- Severity of prior reactions does not predict severity of future reactions


Epinephrine: Mechanism of Action

Injectable epinephrine is universally agreed upon as the first-line therapy for anaphylaxis
- Mechanism of Action – acts through
  - \( \alpha \)-adrenergic receptors:
    - induce vasoconstriction
    - prevents or diminishes tissue/airway edema
    - Hypotension
    - distributive shock
  - \( \beta \)-adrenergic receptors
    - increase heart rate and cardiac contractility
  - \( \beta_2 \)-adrenergic receptors
    - Bronchodilation
    - may potentially block further release of mediators by mast cells and perhaps other effector cells

Anaphylaxis: Treatment

Assess circulation, airway, breathing and level of consciousness

If anaphylaxis is suspected, administer epinephrine IM lateral thigh

Administer aqueous epinephrine 1:1000 dilution (1mg/ml)
- Dose for adults: 0.3–0.5 mg (0.1–0.2 ml) IM
- Dose for children: 0.01 mg/kg, with max 0.3 mg IM
- Dose can be repeated in 5 minutes (or sooner) if needed
Anaphylaxis: Treatment

- Based on response call 911
- Place patient in recumbent position with feet elevated unless vomiting or in respiratory distress (in these cases may not be able to tolerate this position)
- Administer oxygen
- Consider IV fluids, maintain/establish airway
- Give additional adjunctive therapies → these therapies should NOT be used in place of epinephrine

- Antihistamines
- Leukotriene Receptor Antagonists (LTRAs)
- H2 antagonist
- Bronchodilators
- Steroids

Prevention of Further Episodes

- Anaphylaxis to a drug: patient education on possible cross-reacting agents
- Anaphylaxis to a food: patient should be educated about cross-reactivity of foods; epinephrine device
- Drugs that place patients at risk for a more severe episode or complicate therapy should be discontinued if possible
  - b-adrenergic blocking agents
  - Angiotensin-converting enzyme inhibitors
  - Angiotensin blockers
  - Monoamine oxidase inhibitors
  - Certain tricyclic antidepressants
- If the patient must be re-exposed to a drug to which an event occurred, specialized procedures such as desensitization and pretreatment can be performed
Do epinephrine auto-injectors have an unsuitable needle length in children and adolescents at risk for anaphylaxis from food allergy?


- skin to muscle distance (STMD)
- skin to bone distance (STBD)

To obtain an intramuscular injection, the STMD must be at the most the exposed needle length minus 1 mm (needle ≈ 5 mm).

- There is a risk of intramuscular injection if the STBD is less than the full exposed length of the needle and the risk of subcutaneous injection is obese subjects.
Storage of the Devices

- Epi-Pen® video
  - http://www.epipen.com/how-to-use-epipen
  - epipenforkids.com
- Auvi-Q® video
  - https://www.auvi-q.com/
- Adrenaclick®
- Generic
  - http://www.epinephrineautoinject.com/

Thank you!

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