Anaphylaxis in the Clinic: Are you prepared?

Michael Zachariisen, M.D.

Conflict of Interest: none

Have you read this book?
A. Yes
B. No
C. I can’t remember
D. I only watch movies

Objectives:
- Causes of allergic reactions seen in the office setting
- Recognizing signs and symptoms
- Respiratory symptoms common/serious
- Appropriate management
Your Anaphylaxis Experience

A. I have not witnessed or treated a pt with anaphylaxis
B. I have witnessed/treated anaphylaxis and felt comfortable and confident
C. I have witnessed/treated anaphylaxis and felt a little uncomfortable.
D. I have personally experienced anaphylaxis!

Case 1

22 y/o male drank “fruit juice”
Within 20 min: nausea and abdominal pain
Itching then hives over neck, back, axillae, groin
Flushing, lip swelling and labored breathing.
He walks into your clinic!

What do you do?

A. Ask him to sit in the waiting room and fill out paperwork.
B. Obtain a detailed history & check vital signs.
C. Administer Benadryl 50 mg orally
D. Administer epinephrine and oxygen
E. Administer oral prednisone
Case 2
A 6 y/o has sore throat, fever, abdominal pain and exudate on tonsils. Rapid Strep+ You administer Penicillin IM.
Within 10 min., itching and mild cough. Ten min. later, hives and vomiting.

Case 2: You should
A. Administer cetirizine and call 911
B. Administer loratadine and ranitidine
C. Administer epinephrine SQ and Benadryl
D. Administer epinephrine IM and oxygen

Anaphylaxis
Clinical definition:
- Systemic allergic reaction
- 2 or more organ systems involved
- Dramatic and unanticipated
- Rapid in onset (min. to hours) after likely trigger
- Medical emergency---life threatening!
- Anaphylactoid
- Pseudoanaphylaxis
  - no longer used

Anaphylaxis no longer used
**Anaphylaxis: Early Signs & Symptoms**

- Are not always outwardly obvious in *early* stages
- Within moments, minutes or hours:
  - Shortness of breath, cough, wheezing (40-60%)
  - Hives/swelling (85-90%), flushing (55%)
  - Oropharyngeal swelling
  - Lightheadedness and CV (30-35%), HR
  - Vomiting other GI (25-30%)
  - Feeling of “impending doom”
  - Other: DIC, seizure (1-2%)

**Anaphylaxis: Early Signs & Symptoms**

In MY experience…(mostly allergy injections)

Within minutes…
- Sneezing
- Throat clearing
- Facial flushing
- Cough
- Itching of palms, soles, and axillae

**Angioedema**
Anaphylactic triggers at a clinic:

<table>
<thead>
<tr>
<th>Clinic walk in:</th>
<th>Administered in clinic:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food (most common)</td>
<td>Antibiotics (Pen 1:2500)</td>
</tr>
<tr>
<td>30% of fatalities</td>
<td>ASA, NSAIDs (1:50,000)</td>
</tr>
<tr>
<td>Venom</td>
<td>Vaccines 1: 1 million</td>
</tr>
<tr>
<td>Exercise</td>
<td>Biologicals (Xolair): 0.2%</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Blood transf: 1:20k-400k U</td>
</tr>
<tr>
<td></td>
<td>Allergy injection 1:150</td>
</tr>
<tr>
<td></td>
<td>Latex (1% of population)</td>
</tr>
</tbody>
</table>

Many Mediators Cause Anaphylactic Symptoms

- Leukotrienes
- Prostaglandins
- Kinins
- Platelet activating factor (PAF)
- Interleukins
- Tumor necrosis factor (TNF)
- Histamine

Patterns of Anaphylaxis

**Uniphasic:** symptoms resolve within minutes or hours after treatment and do **not** reoccur

**Biphasic:** symptoms reoccur 1-24 hrs after resolution of symptoms

**Protracted:** symptoms continue for hours or days
Biphasic Anaphylaxis

Antigen Exposure

<table>
<thead>
<tr>
<th>Initial Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>1-8 hours</td>
<td>1 - 24 hours</td>
</tr>
<tr>
<td>Time</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second-Phase Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic</td>
</tr>
<tr>
<td>Time</td>
</tr>
</tbody>
</table>

Number of Pts Experiencing Anaphylaxis Subtypes

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protracted</td>
<td>7</td>
</tr>
<tr>
<td>Biphasic</td>
<td>5</td>
</tr>
<tr>
<td>Uniphasic</td>
<td>13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td>15</td>
</tr>
</tbody>
</table>

Frequency of the Need for Two Injections Regardless of Cause

<table>
<thead>
<tr>
<th>Subtype</th>
<th>% of Pts Requiring a 2nd Dose of Epi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protracted</td>
<td>20%</td>
</tr>
<tr>
<td>Biphasic</td>
<td>15%</td>
</tr>
<tr>
<td>Uniphasic</td>
<td>8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% of Pts Requiring &gt; 1 Dose of Epinephrine During Anaphylactic Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
</tr>
</tbody>
</table>

Varghese M et al. AAAAI 2006;
Median Time to Respiratory or Cardiac Arrest

- **FOODS**: 30 min
- **VENOMS**: 15 min
- **IATROGENIC REACTIONS**: 5 min

Patients at Risk
- Prior history of anaphylaxis!
- Asthma
- Meds: beta-blockers
- Cardiovascular disease
- Mastocytosis
- Older age, insect stings, iatrogenic
- Pt who do **not** perceive these risk factors

Survey Question: Your office/clinic

A. has an Anaphylaxis Protocol and we have had reactions in our office
B. has an Anaphylaxis Protocol but we have **NOT** had any reactions
C. does **NOT** have a protocol but we have had reactions
D. does **NOT** have a protocol and thank goodness no one has had a reaction!
Anaphylaxis Protocol

Medications
- Epinephrine: 1:1000 MDV
- Oxygen
- Diphenhydramine 50 mg/mL IM/IV
- Cetirizine syrup (1 mg/mL)
- Ranitidine 150 mg oral
- Cimetidine 300 mg IV/IM
- Albuterol 0.083% for nebulizer
- Ipratropium 0.02% for nebulizer
- Solumedrol 125 mg IV
- IVF (NS or LR): 1 L bag

Equipment
- Stethoscope
- BP cuffs
- Pulse oximeter
- Tourniquet
- Syringe and needles
- Jet nebulizer
- IV board, oral airway

Anaphylaxis Kit

Equipment | Medications
---|---
Stethoscope | Epinephrine: 1:1000 MDV
BP cuffs | Oxygen
Pulse oximeter | Diphenhydramine 50 mg/mL IM/IV
Tourniquet | Cetirizine syrup (1 mg/mL)
Syringe and needles | Ranitidine 150 mg oral
Jet nebulizer | Cimetidine 300 mg IV/IM
IV board, oral airway | Albuterol 0.083% for nebulizer

Anaphylaxis: Acute Office Treatment

- Epinephrine IM (0.15-0.5 cc)
- Recline and elevate legs
- Oxygen
- Antihistamines (H1, H2)
  - Diphenhydramine IV or IM (0.5, 1, 1.5)
  - Cimetidine 300 mg IM or IV slowly (20-40 mg/kg)
- IV Fluids: “wide open”
- Albuterol nebulizer
- Steroids: IV or po
- Aminophylline 5 mg/kg, Methylene blue*, Glucagon 1 mg IV
- IV pressors
  *1.5 mg/kg (120 mg) bolus of 4% infused, followed by 1 hr of continuous infusion of another 120 mg diluted in dextrose 5% in water
Actions of Epinephrine: Antagonize Effects of All Mediators

Epinephrine

- Antagonize Effects of All Mediators
- Vasoconstriction
- Peripheral vascular resistance
- Mucosal edema
- Insulin release
- Chronotropy
- Bronchodilation
- Vasodilation
- Glycogenolysis
- Mediator release

α₁-adrenergic receptor
α₂-adrenergic receptor
β₁-adrenergic receptor
β₂-adrenergic receptor


Epinephrine IM: Time to Onset

Maximum pharmacodynamic effect occurs before 10 min


Antihistamines: Time to Suppression

Time to 50% suppression

Fexofenadine: 51.7 min
Diphenhydramine: 79.2 min

**H2-Blockers in Anaphylaxis**

**H2-antihistamines for treating anaphylaxis with and without shock: systematic review.**

**BACKGROUND:** Although H2-antihistamines are often given for anaphylaxis, uncertainty about effectiveness.

**OBJECTIVE:** To assess benefits & harms of H2-antihistamines in treating anaphylaxis.

**METHODS:** Systematic review of randomized controlled trials/quasi-randomized controlled trials comparing H2-antihistamines with placebo or no intervention in pts with anaphylaxis.

**RESULTS:** Failed to identify any eligible studies for inclusion in systematic review.

**CONC:** Well-designed randomized controlled trials investigating the role of H2-antihistamines in anaphylaxis treatment are urgently needed.


---

**Anaphylaxis Treatment Record**

- Hx of asthma or previous anaphylaxis
- Signs & symptoms
- VS, Med doses and times

---

**Anaphylaxis: Factors that intensify reaction**

- Presence of asthma
- Underlying cardiac disease
- Concomitant therapy with:
  - Beta blockers
  - MAO inhibitors
  - ACE inhibitors
- Delay in administration of Epi/or SQ
### Anaphylaxis: Outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>Poor</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose of Antigen</td>
<td>Large</td>
<td>Small</td>
</tr>
<tr>
<td>Onset of symptoms</td>
<td>Earlier</td>
<td>Later</td>
</tr>
<tr>
<td>Initiation of treatment</td>
<td>Late</td>
<td>Early</td>
</tr>
<tr>
<td>Route of exposure</td>
<td>Parenteral</td>
<td>Oral</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Presence of underlying disease</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### Anaphylaxis: Differential Diagnosis

- Vasovagal syncope (low HR)
- Anxiety with hyperventilation or globus hystericus
- Vocal cord dysfunction
- Seizure
- Factitious

### Anaphylaxis: Differential Diagnosis (cont)

- Aspiration
- Primary Cardiac Event: MI, arrhythmia
- Pulmonary embolism
- Systemic mastocytosis
- Hereditary angioedema (no hives!)
Anaphylaxis Evaluation

<table>
<thead>
<tr>
<th>ER</th>
<th>Allergy Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>Detailed History</td>
</tr>
<tr>
<td>Exam</td>
<td>Exam</td>
</tr>
<tr>
<td>Serum tryptase</td>
<td>Serum IgE (preferred)</td>
</tr>
<tr>
<td>CBC</td>
<td>Skin testing</td>
</tr>
<tr>
<td>ECG</td>
<td>Baseline serum tryptase</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td></td>
</tr>
</tbody>
</table>

Serum Tryptase Level:

Normal is <11.4 ng/mL

May not increase in food-induced anaphylaxis!

Which statement about Anaphylaxis is true?

A. A second episode of anaphylaxis will be worse than the first
B. Antihistamines can adequately treat anaphylaxis
C. Epinephrine is dangerous especially in elderly
D. Epinephrine is a drug of abuse in schools
E. The more rapid the onset of anaphylaxis, more likely to be severe
Anaphylaxis: Management

Avoidance/Education
Medication
• Epinephrine
• Antihistamine
• Corticosteroids
Medical ID bracelet
Written Anaphylaxis Action Plan
Avoid beta-blockers
Pre-treatment protocols (RCM)
Specific Treatment (VIT)

Case 1

22 y/o male drank “fruit juice”
Within 20 min: nausea and abdominal pain
Itching then hives over neck, back, axillae, groin
Flushing, lip swelling and labored breathing.
He walks into your clinic!

Case 1: Mango Anaphylaxis

Treated with: Epi IM x 2, oxygen, Benadryl IM,
Prednisone and observed. Rapid response!

Additional History:
Drank mango juice
Skin test: + mango
Case 2: Penicillin Anaphylaxis
A 6 y/o with Strep pharyngitis with immediate Penicillin reaction.

Treatment:
- Epinephrine IM
- Benadryl IM then po every 6 hours
- Zantac bid x 1 week
- Solumedrol IV and prednisone taper over 1 wk
- Sent to ER and observed overnight.

Take Home Messages
- Have an Anaphylaxis Plan/Protocol
- Practice the Plan!
- Have a “Crash cart” or “box”
- Epinephrine IM & Oxygen: preferred treatment
- Don’t delay!
- May require ≥2 doses of Epi due to severity
- Antihistamines don’t treat anaphylaxis!
- Order Serum Tryptase soon!

The diagnosis and management of anaphylaxis 2010
ER diagnosis and management of anaphylaxis 2014