Five things to know about anaphylaxis

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Disclosures

• None relevant to this presentation
Five things to know

• Recognize anaphylaxis and its mimickers
• Appreciate the co-factor effect
• Outline emergency management of anaphylaxis
• Confidently demonstrate the use of an epinephrine auto-injector
• Outline the long term management of anaphylaxis
Anaphylaxis:

- Is a generalized reaction of rapid onset, with a wide range of signs and symptoms
- Usually lasts less than 24 hours
- Is potentially fatal

Trace amounts of allergen can trigger a severe reaction.
Triggers of anaphylaxis

- IgE-mediated anaphylaxis:
  - Foods, insect venoms, medications (NSAIDs, beta lactams, biologic agents) latex, radiocontrast media
- Non-IgE mediated anaphylaxis:
  - Radiocontrast media, medications (NSAIDs, biologic agents)
- Direct mast cell activation
  - Physical factors (exercise, cold, heat, sun), ethanol, medications (opioids)
- Idiopathic anaphylaxis
Mediator Effects

- **Histamine**: vasodilation, increased vascular permeability, heart rate, cardiac contraction, glandular secretion
- **Prostaglandin D2**: bronchoconstriction, pulmonary and coronary vasoconstriction, peripheral vasodilation
- **Leukotrienes**: bronchoconstriction, increased vascular permeability
- **PAF**: bronchoconstriction, increased vascular permeability
- **TNF-α**: activation of neutrophils, recruitment of other effector cells, enhanced chemokine synthesis

PAF = platelet activating factor
TNF-α = tumor necrosis factor-α
Prevalence

• True prevalence of anaphylaxis is unknown but estimated at 2% (from food + insect stings)
• Based on epinephrine prescriptions:
  • 0.95% in the general population
  • >1.44% in children under 17 years of age
  • 314,440 – 476,625 Canadians affected

Epinephrine dispensing patterns for an out-of-hospital population: (Simons FE et al JACI 2002)
Diagnosis

- Three criteria (95% sensitivity for diagnosis)
Anaphylaxis is highly likely when

Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING:

Sudden respiratory symptoms and signs

Sudden reduced BP or symptoms of end-organ dysfunction

Simons et al, J Allergy Clin Immunology 2011;127(3):587-593
Anaphylaxis is highly likely when

Two or more of the following that occur suddenly after exposure to a likely allergen or other trigger for that patient (minutes to several hours):

- Sudden skin or mucosal symptoms and signs
- Sudden respiratory symptoms and signs
- Sudden reduced BP or symptoms of end-organ dysfunction
- Sudden gastrointestinal symptoms

Simons et al, J Allergy Clin Immunology 2011;127(3):587-593
Anaphylaxis is highly likely when

Reduced blood pressure (BP)
after exposure to a known allergen for that patient
(minutes to several hours)

**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

Simons et al, J Allergy Clin Immunology 2011;127(3):587-593
Signs and symptoms

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cutaneous</strong></td>
<td></td>
</tr>
<tr>
<td>Urticaria and angioedema</td>
<td>85-90</td>
</tr>
<tr>
<td>Flushing</td>
<td>45-55</td>
</tr>
<tr>
<td>Pruritus without rash</td>
<td>2-5</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></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><strong>Dizziness, syncope, hypotension</strong></td>
<td>30-35</td>
</tr>
<tr>
<td><strong>Abdominal</strong></td>
<td></td>
</tr>
<tr>
<td>Nausea, vomiting, diarrhea, cramping pain</td>
<td>25-30</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>5-8</td>
</tr>
<tr>
<td>Substernal pain</td>
<td>4-6</td>
</tr>
<tr>
<td>Seizure</td>
<td>1-2</td>
</tr>
</tbody>
</table>

*On the basis of a compilation of 1865 patients reported in references 1 through 14.
†Percentages are approximations.
‡Children may have a lower frequency of cutaneous symptoms in anaphylaxis.
### Differential Diagnosis

**TABLE 4. Differential Diagnosis of Anaphylaxis**

<table>
<thead>
<tr>
<th>Common diagnostic dilemmas</th>
<th>Flush syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute asthma&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Peri-menopause</td>
</tr>
<tr>
<td>Syncope (faint)</td>
<td>Carcinoid syndrome</td>
</tr>
<tr>
<td>Anxiety/panic attack</td>
<td>Autonomic epilepsy</td>
</tr>
<tr>
<td>Acute generalized urticaria&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Medullary carcinoma of the thyroid</td>
</tr>
<tr>
<td>Aspiration of a foreign body</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular (myocardial infarction&lt;sup&gt;a&lt;/sup&gt;, pulmonary embolus)</td>
<td>Nonorganic Disease</td>
</tr>
<tr>
<td>Neurologic events (seizure, cerebrovascular event)</td>
<td></td>
</tr>
<tr>
<td><strong>Postprandial syndromes</strong></td>
<td><strong>Shock</strong></td>
</tr>
<tr>
<td>Scombroidosis&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Hypovolemic</td>
</tr>
<tr>
<td>Pollen-food allergy syndrome&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Cardiogenic</td>
</tr>
<tr>
<td>Monosodium glutamate</td>
<td>Distributive&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sulfites</td>
<td></td>
</tr>
<tr>
<td>Food poisoning</td>
<td>Septic</td>
</tr>
<tr>
<td><strong>Excess endogenous histamine</strong></td>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>Mastocytosis/clonal mast cell disorders&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Nonallergic angioedema</td>
</tr>
<tr>
<td>Basophilic leukemia</td>
<td>Hereditary angioedema types I, II, &amp; III</td>
</tr>
<tr>
<td></td>
<td>ACE inhibitor-associated angioedema</td>
</tr>
<tr>
<td></td>
<td>Systemic capillary leak syndrome</td>
</tr>
<tr>
<td></td>
<td>Red man syndrome (vancomycin)</td>
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<tr>
<td></td>
<td>Pheochromocytoma (paradoxical response)</td>
</tr>
</tbody>
</table>

Lieberman et al. JAACI September 2010
1. Recognize anaphylaxis and its mimickers

**Differential Diagnosis**
- Angioedema/urticaria
- Asthma
- Syncope
- Panic attack
- Acute cardiac or neurologic events
- Postprandial syndromes
  - Scombroid, MSG, sulfites, food poisoning
- Excess endogenous histamine
- Mastocytosis/clonal mast cell disorder
- Flushing syndromes
- Non-organic disease

Patient co-factors

- Patient co-factors: age-related factors, concomitant disease, and concurrent medications, which may
  - Amplify anaphylaxis
  - Impair recognition of anaphylaxis
  - Reduce epinephrine’s effect
  - Sensitize patients to epinephrine’s effect
- Up to 39% of cases of anaphylaxis may involve co-factors

2. Appreciate the co-factor effect

Up to 39% of all anaphylactic reactions are associated with cofactors in adults.

1. Patient intrinsic factors - nonimmunologic
   - eg. atopic diseases, cardiovascular disease, mastocytosis

2. Patient extrinsic factors - nonimmunologic
   - eg. drugs - ACEI, Beta blockers

3. Augmentation factors - direct immunologic modulation
   - eg. exercise, alcohol, infection, NSAIDs
Course & Severity

- Typically **uniphasic**
- Up to ~**20%** will be **biphasic**
- Patients should stay in close proximity to a hospital or where they can call 911 for the next **48 hours** after treatment for anaphylaxis
- **Protracted anaphylaxis** (rare) has poor prognosis
Severity

- Cannot always be predicted from previous reactions
- May depend on:
  - Degree of sensitivity
  - Dose of allergen
  - Route of allergen
  - Co-factors (e.g., medical conditions, medications)
• Adequate warning signs are not always present before serious reactions occur.

• Research shows that fatalities from anaphylaxis are often associated with failure or delay in use of epinephrine.
Recognizing anaphylaxis

- Patients at risk of anaphylaxis with previous severe reactions may be educated to administer epinephrine immediately after likely exposure to a known allergen, even before symptoms begin.

- Teach patients to recognize symptoms.

- Sudden onset of illness (e.g., respiratory, urticaria, flushing or swelling, dizziness or lightheadedness, abdominal pain, vomiting, etc.)
3. Outline emergency management of anaphylaxis

- Epinephrine dose is either 0.3mg or 0.15mg 1:1000 (if patient is ≥30kg get 0.3mg dose)
- Intramuscular injection to anterolateral thigh
- NO contraindications to using epinephrine during suspected anaphylaxis (if in doubt, use it!)
- Call 911 if epinephrine administered. Lie down if in shock.
- In ED: ABC's
  - oxygen
  - fluid resuscitation
  - adjunctive therapies (antihistamines, corticosteroids, bronchodilators, glucagon)
Epinephrine

- Epinephrine is the first-line treatment for anaphylaxis
- Epinephrine is an $\alpha$ and $\beta$ adrenergic receptor agonist
  - $\alpha$ increases PVR, increasing BP and coronary artery perfusion, and reverses peripheral vasodilatation
  - $\beta$-1 has inotropic and chronotropic effects so increases HR and strength of contraction

Epinephrine

- Fatality rates are highest in patients in whom treatment with epinephrine is delayed.
- There are no absolute contraindications to epinephrine administration in the setting of anaphylaxis.
- Second dose of epinephrine may be required.
- *Antihistamines must not be used as first-line treatment for anaphylactic reactions.*
After epinephrine

- Epinephrine is emergency supportive therapy only

- Patients must be immediately transported to hospital, ideally by ambulance

- Observation in an emergency facility is recommended

- New epinephrine auto-injector prescription should be provided
## Other medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen and fluid resuscitation</td>
<td>• High-flow oxygen should be administered to patients experiencing respiratory symptoms, hypoxia or hemodynamically unstable (^2)  &lt;br&gt;• Rapid fluid resuscitation should be given to restore intravascular volume (^1,2)</td>
</tr>
<tr>
<td>(H_1) – and (H_2) antihistamines</td>
<td>• Not recommended for acute management (^1)  &lt;br&gt;• Consider second line for symptomatic treatment of urticaria-angioedema and pruritus (^2)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>• Not recommended for acute management (^2)  &lt;br&gt;• Adjunctive medication, may help in an acute attack in preventing or shortening protracted reactions and in the treatment of recurrent idiopathic anaphylaxis (^1)  &lt;br&gt;• Early corticosteroids treatment is beneficial in asthma (^1)  &lt;br&gt;• Steroids do not prevent biphasic reactions (^1,2)</td>
</tr>
<tr>
<td>Bronchodilators</td>
<td>• Adjunctive medication for bronchospasms refractory to epinephrine (^1,2)</td>
</tr>
<tr>
<td>Glucagon</td>
<td>• In patients taking (\beta)-blockers - If administration of epinephrine is ineffective, glucagon can be used. Airway protection must be ensured because glucagon causes emesis (^2)</td>
</tr>
</tbody>
</table>
4. Confidently demonstrate the use of an epinephrine auto-injector

- Currently only EpiPen is available on the market (no Twinject or Allerject)
Monitoring

• At least four hours advised (but also at discretion of the emergency physician)

• Up to 20% of reactions will have a second reaction (biphasic) with the majority occurring within 10 hours (mean time)

• Second-phase reactions can occur even following administration of corticosteroids
Monitoring

• Following treatment of anaphylaxis, patients should stay within close proximity to a hospital or where they can call 911 for the next **48 hours**.
Evaluation by an allergist

History:
- Detailed clinical history helps determine the diagnostic tests
- Temporal correlation is important

Investigations:
- Skin prick tests
- Allergen specific IgE in selected cases
- Other investigations as indicated (eg. Tryptase, spirometry)
- Challenge (medications, foods)

Management:
- Education
- Emergency action plans, medicalert, epipen
- Desensitization
Panel testing is never indicated for anaphylaxis
5. Outline long term management of anaphylaxis

• Referral to an Allergist

• Prescribe epinephrine auto-injector

• Demonstrate how and when to use the Epipen

• Provide information on how to avoid the precipitating allergen (if known)

• Provide comprehensive action plan including medic alert bracelet information
Key points

• All patients who have been diagnosed with severe allergy should be given an **anaphylaxis action plan**. The plan should be shared with family members and all potential care-providers. The plan should be reviewed with the patient at each visit.

• **All patients** at risk of anaphylaxis should be prescribed sufficient epinephrine auto-injectors to ensure there is one available to them at all times.
Key points

• There is one epinephrine auto-injector available in Canada, Epipen®. It’s proper administration should be demonstrated to patients who have severe allergy.

• Training devices, which contain no medication and no needle, can be ordered at: www.epipen.ca

• Use the teach-back method with the training device when demonstrating how to use the epinephrine auto-injector. Demonstrate the administration procedure and then have the patient teach it back to you, ensuring their full understanding. Patients should be confident with the proper use of the device.
Key points

• Ensure that your patients with severe allergy are always carrying only current, **non-expired epinephrine auto-injectors, at room temperature**. Renew prescriptions regularly and educate patients to dispose of expired devices. Patient reminder programs are also available at: [www.epipen.ca](http://www.epipen.ca)

• Ensure patients know that they must go to **hospital** immediately after epinephrine administration; even if they feel better, it is still an emergency.

• Patients need close monitoring after being treated for anaphylaxis.
Resources

• Anaphylaxis Canada  www.anaphylaxis.ca
• Allergy/Asthma Information Association  www.aaia.ca
• Asthme et Allergies Québec  www.asthmeallergies.com
• Association Québécoise des Allergies Alimentaires  www.aqaa.qc.ca
• Allergy safe Communities  www.allergy safecommunities.ca
• Family Physician Airways Group of Canada  www.fpagc.com
• Safe 4 Kids: A Site for Kids Living with Anaphylaxis  www.safe4kids.ca
• Why Risk It: A Site for Canadian Youth at Risk for Anaphylaxis  www.whyriskit.ca
• Food Allergy and Anaphylaxis Network (US)  www.foodallergy.org
• MedicAlert Foundation Canada Inc.:  www.medicalert.ca