When Should I Use Epinephrine? Why Am I Afraid of it?

Presented by
Jonathan Spergel, MD

FARE Clinical Advisory Board Executive Committee

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Welcome!

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Today’s Presenter

Jonathan Spergel, M.D.
Division of Allergy-Immunology,
Children’s Hospital of Philadelphia
Perelman School of Medicine at Univ. of Pennsylvania
When Should I Use Epinephrine?
Why Am I Afraid Of It?

Jonathan M. Spergel, MD, PhD
Division of Allergy-Immunology
Children’s Hospital of Philadelphia
Perelman School of Medicine at University of Pennsylvania
Adverse Reactions to Foods

Toxic reactions
- Food poisoning

Food intolerance
- Lactase deficiency

IgE/Th2-mediated
- Hives
- Anaphylaxis
- Eczema

Nontoxic reactions

Food allergy

Non–IgE-mediated
Intestinal reactions
Fatal Food Anaphylaxis

- Rare event
- Frequency: ~ 16.5-150 deaths / year
- Clinical features:
  - Respiratory symptoms prominent
  - Cutaneous symptoms may be absent
- History: often it is due to a known food allergen
- Risk factors:
  - Underlying asthma
  - Adolescents, young adults
- Key foods:
  - peanuts and tree nuts
  - Milk
- Most events occur away from home

Fatality Rate

**Table 3. Rates of hospitalization and fatalities (per 100,000 population per annum) in the United Kingdom, the United States, and Australia**

<table>
<thead>
<tr>
<th></th>
<th>The United Kingdom [25*]</th>
<th>The United States [26,27*]</th>
<th>Australia [28*,32]</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause anaphylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>1.0</td>
<td>3.7</td>
<td>7.0</td>
</tr>
<tr>
<td>Fatalities</td>
<td>0.036</td>
<td>0.043</td>
<td>0.054</td>
</tr>
<tr>
<td>Anaphylaxis: food</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>ND</td>
<td>1.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Fatalities</td>
<td>0.010</td>
<td>0.012</td>
<td>0.012</td>
</tr>
<tr>
<td>Anaphylaxis: venom</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>ND</td>
<td>0.09</td>
<td>0.46</td>
</tr>
<tr>
<td>Fatalities</td>
<td>0.005 [27*]</td>
<td>0.005 [27*]</td>
<td>0.009 [26]</td>
</tr>
<tr>
<td>Anaphylaxis: medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>ND</td>
<td>0.78</td>
<td>1.4</td>
</tr>
<tr>
<td>Fatalities</td>
<td>0.018</td>
<td>0.026</td>
<td>0.028</td>
</tr>
</tbody>
</table>

*Data for 1999.
ND, no data available.
Comparison of Fatal Food Allergy

• (15-150) ? cases a year in the US
  – 78 million children in the US
    • Estimated rate 0.005/100,000
    • 4-40? children a year
    • Actual rate is difficult to determine due to coding issues
• 872 deaths a year due automobile (Institute for Highway Safety)
• 15,780 children a year-diagnosed with cancer
  – 1960 deaths a year (NIH)
• 2624 children die by gun violence a year (CDC)
Anaphylaxis is a severe allergic reaction that is rapid in onset, and may cause death.

Anaphylaxis often begins within minutes after a person eats a problem food. Symptoms of anaphylaxis may include:

- LUNG: Short of breath, wheezing, repetitive cough
- HEART: Pale, blue, faint, weak pulse, dizzy
- THROAT: Tight, hoarse, trouble breathing/swallowing
- MOUTH: Significant swelling of the tongue and/or lips
- SKIN: Many hives over body, widespread redness
- GUT: Repetitive vomiting, severe diarrhea
- OTHER: Feeling something bad is about to happen, anxiety, confusion

OR A COMBINATION of symptoms from different body areas.
Can we predict the severity of reaction?

- Food-specific IgE and skin tests are not predictive of the severity of the reaction

<table>
<thead>
<tr>
<th>Wheal Size (mm)</th>
<th>Anaphylaxis</th>
<th>Cutaneous</th>
<th>Respiratory</th>
<th>GI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10.1 ± 0.69</td>
<td>8.21 ± 0.35</td>
<td>7.95 ± 1.5</td>
<td>8.67 ± 0.94</td>
</tr>
</tbody>
</table>

- Reaction depend on amount, overall health, concurrent illness, fasting, alcohol, exercise, stress? and other medications

Spergel et al, Annual Asthma Allergy and Immunol
WHAT HAPPENS IF YOU USE EPINEPHRINE LATE?
If use Epinephrine Late?

- Increase hospitalizations
- Increase rate of biphasic reactions
- Fatalities? (a very rare event)
Increase Hospitalizations

• Chart Review at Hasboro Hospital (Children’s) in Rhode Island
• Looked at early Epinephrine before ED
  – 384 cases of anaphylaxis
    • 234 received Epinephrine (61%)
    • 164 (70%) had prior to the ED
    • 70 (30%) had in the ED
  – Rate of Hospitalization
    • Early: 17%
    • Late: 43%

Risk of Biphasic Reactions

- There is a large range from 0.4 to 14.7%.
- In OFC, the rate is less 2% and none had more severe reactions later.
- In clinical OIT trials, no cases of biphasic reactions.
- More recent studies suggest the lower end <3%.
  - In our institution, it is less than 1% in Emergency Department.
- Corticosteroids do not decrease the risk of biphasic reactions.
- But delay of Epinephrine increase the risk.

Conclusion

• With anaphylaxis
  – You need to use Epinephrine
Mechanism of Epinephrine

Epinephrine's $\alpha_1$- and $\beta_2$- adrenergic effects prevent and relieve *life-threatening symptoms* of anaphylaxis in most organ systems.

- **Epinephrine**
  - $\alpha_1$-receptor
    - $\uparrow$ Vasoconstriction
    - $\uparrow$ BP
    - $\downarrow$ Mucosal edema (larynx)
  - $\beta_2$-receptor
    - $\uparrow$ BD
    - $\downarrow$ Mediator release

- Prevents and relieves hypotension and shock
- Relieves upper airway obstruction
- $\downarrow$ Wheezing
- $\downarrow$ Hives

**Additional pharmacologic effects:** at $\beta_1$-receptor: $\uparrow$ heart rate; $\uparrow$ cardiac contraction force

BP = blood pressure; BD=bronchodilation
Fear of Epinephrine or Lack of use?

- Anaphylaxis in America Survey:
  - Individual with >2 previous episodes:
    - 48% had emergency action plan
    - 32% intended to use their Epinephrine
    - 52% never had Epinephrine
    - 60% did not have an Epinephrine available.
Epinephrine Is Under-Utilized for Acute Treatment

• Only about 30% of individuals requiring epinephrine during a reaction actually received it. (Gold and Sainsbury, 2000)

• In fatal food-induced reactions, failure to use, delayed use, or inappropriate dose are contributing factors to death. (Sampson et al, 1992)

• Used in treatment of 62% of fatal reactions but given before cardiac arrest in only 14% of reactions. (Pumphrey, 2000)
Fear of Epinephrine Autoinjectors

• Interviewed children and family from Montreal Children’s Hospital (1229 participants)

• 672/1209 (56%) experience fear
  – Hurting the child
  – Using incorrectly
  – Adverse event

• (My families do not want to go to the ED and wait).
Hurting the Child-Side Effects

• Will the needle-hurt the child
• Damage the leg?
Side Effects of Epinephrine

• Risk mainly from IV
• IM dose in thigh
  – Increase heart rate, pallor, diaphoresis, tremor, headache, nausea
• Risk of arrhythmia and hypertension (316 cases in ED)
  – 0.8% cases had BP >120 (with double dose of IM)
  – No episodes of arrhythmia
  – One episode of angina with double dose of IM epinephrine


The Children's Hospital of Philadelphia Research Institute
2ND FEAR: USING IT INCORRECTLY
Inadequate Knowledge of Epinephrine Usage

- In 2000, Healthcare professionals and patients have inadequate knowledge about outpatient use.
  - 76% of physicians are unaware that two Epinephrine autoinjectors dose formulations exist.
  - Only 55% of patients at risk have in-date auto-injectors on hand!
  - Only 30%-40% know how to use auto-injectors correctly!
Is Epinephrine Used Correctly

- 63% of anaphylaxis cases received epinephrine in ED (2007)
- Most recent studies (2016) show up to 97% in the ED
  - (many patient got Epinephrine in the field)
- But, still low rate by EMT-17-36% of patients with anaphylaxis received Epinephrine (2014)
Epinephrine Devices

- Epipen
- AUVI-Q (returning in 2017)
- Adrenaclick
- Home kits (not recommended)
Epinephrine Dosing

- 0.15 mg and 0.3 mg
- Weight based >25 kg—0.3 mg
- Recommend for all ages (no lower limit)
Remove cap(s)
How to do?

• Swing and push orange/red tip against mid-outer thigh until it “clicks”
• Hold firmly in place for 3-10 sec (depends on the device)
• Call 911
Epinephrine mechanism
I FORGOT MY EPINEPHRINE DEVICE?
IT IS OLD DEVICE.
Stability of Epinephrine

- Review of all studies examining epinephrine in syringes, vials and ampules
- 9 studies
  - None saw any effect on extreme cold
    - 2.5°C/36.5°F x 1 month or -20°C/-4°F x 16 hours
  - Intermittent heat/cold showed no effect
    - 3 hour at 65°C, then cooling
    - Field studies (Emergency Vehicles x 1 yr)
  - Constant heat (145°F) x 100 hour lead to degradation
  - But 40°C/104°F x 1 year had no effect.
- Stable for 2 years past expiration date
Food Allergy Anaphylaxis Plan

**FOOD ALLERGY & ANAPHYLAXIS EMERGENCY CARE PLAN**

**Name:** __________________________________________  **D.O.B.:** __________________________________________

**Allergy to:** ____________________________________________________________

**Weight:** ___________________ lbs. **Asthma:** [ ] Yes (higher risk for a severe reaction) [ ] No

**PLACE PICTURE HERE**

**NOTE:** Do not depend on antihistamines or inhalers (bronchodilators) to treat a severe reaction. USE EPINEPHRINE.

**Extremely reactive to the following allergens:** ____________________________________________________________

**THEREFORE:**

[ ] If checked, give epinephrine immediately if the allergen was LIKELY eaten, for ANY symptoms.

[ ] If checked, give epinephrine immediately if the allergen was DEFINITELY eaten, even if no symptoms are apparent.

**FOR ANY OF THE FOLLOWING:**

**SEVERE SYMPTOMS**

**LUNG** Short of breath, wheezing, repetitive cough

**HEART** Pale, blue, faint, weak pulse, dizzy

**THROAT** Tight, hoarse, trouble breathing/swallowing

**MOUTH** Itchy/runny nose, sneezing

**SKIN** Itchy mouth

**GUT** A few hives, mild itch

**NOSE** Pale, blue, faint, weak pulse, dizzy

**MOUTH** Significant swelling of the tongue and/or lips

**SKIN** Many hives over body, widespread redness

**GUT** Repeated vomiting, severe diarrhea

**OTHER** Feeling something bad is about to happen, anxiety, confusion

**INJECT EPINEPHRINE IMMEDIATELY.**

2. **Call 911.** Tell emergency dispatcher the person is having anaphylaxis and may need epinephrine when emergency responders arrive.

   - Consider giving additional medications following epinephrine:
     - Antihistamine
     - Inhaler (bronchodilator) if wheezing
   - Lay the person flat, raise legs and keep warm. If breathing is difficult or they are vomiting, let them sit up or lie on their side.
   - If symptoms do not improve, or symptoms return, more doses of epinephrine can be given about 5 minutes or more after the last dose.
   - Alert emergency contacts.
   - Transport patient to ER, even if symptoms resolve. Patient should remain in ER for at least 4 hours because symptoms may return.

**MILD SYMPTOMS**

**NOSE** Itchy/runny nose, sneezing

**MOUTH** Itchy mouth

**SKIN** A few hives, mild itch

**GUT** Mild nausea/discomfort

**FOR MILD SYMPTOMS FROM MORE THAN ONE SYSTEM AREA, GIVE EPINEPHRINE.**

**FOR MILD SYMPTOMS FROM A SINGLE SYSTEM AREA, FOLLOW THE DIRECTIONS BELOW:**

1. Antihistamines may be given, if ordered by a healthcare provider.
2. Stay with the person; alert emergency contacts.
3. Watch closely for changes. If symptoms worsen, give epinephrine.

**MEDICATIONS/DOSES**

**Epinephrine Brand or Generic:** ____________________________

**Epinephrine Dose:** [ ] 0.15 mg IM [ ] 0.3 mg IM

**Antihistamine Brand or Generic:** __________________________

**Antihistamine Dose:** __________________________

**Other (e.g., inhaler-bronchodilator if wheezing):** ____________________________
When to Use-CHOP Action Plan

The Children’s Hospital of Philadelphia
3550 Market Street, Philadelphia, PA 19104-6399
DIVISION OF ALLERGY AND IMMUNOLOGY
Allergy and Asthma
www.chop.edu

TREATMENT OF SEVERE ALLERGIC REACTIONS/ANAPHYLAXIS

Name: [redacted]  MRN [redacted]  DOB: [redacted]  Date: [redacted]
Hi (redacted) [redacted]  |  WI
Current known allergies: [redacted]

High Risk for Severe reaction? Yes
What do allergic reactions look like? Signs of severe reactions or anaphylaxis are highlighted below:

- Skin: "hives" (red blotches or welts that itch), mild swelling, severe swelling
- Eyes: tearing, redness, itch
- Nose: clear discharge, itch, congestion
- Mouth: itch, lip swelling; tongue swelling
- Throat: tightness, trouble speaking, trouble breathing in
- Lungs: shortness of breath, rapid breathing, cough, wheeze
- Gut: repeated vomiting, nausea, abdominal pain, diarrhea (usually later)
- Heart/Circulation: weak pulse, loss of consciousness
- Brain: anxiety, agitation, or loss of consciousness

Epinephrine auto-injector must be available at all times.

ACTION PLAN:

1. If Riley develops ONLY HIVES or mild skin swelling, give an antihistamine. Benadryl (diphenhydramine) is preferred.
   - A) Dose: Benadryl 1 teaspoon(s) by mouth. (12.5 mg/teaspoon: approximately 1 teaspoon per 25 lbs of body weight.
   - B) Observe closely for additional symptoms for the next 6 hours: Notify responsible person.

2. If Riley develops any signs of severe reaction or anaphylaxis, IMMEDIATELY:
   - A) Give EpiPen Jr (0.15mg) into the fleshy portion of the outer thigh (see directions below)
   - B) Give Benadryl as above if Riley can swallow.
   - C) Call 911 to arrange transport to Emergency Room.

3. If wheezing is occurring, then treat with Albuterol or Xopenex if available.
Bold Symptoms-Per CHOP

- Severe swelling of the skin
- Tongue Swelling
- Throat tightness, unable to speak
- Shortness of breath, rapid breathing, coughing, wheezing
- Repeated vomiting
- Loss of consciousness
Mild Symptoms

- **CHOP/FARE plan**
  - Isolated Hives
  - Nausea
  - Itchy mouth
  - Runny nose, sneezing

- **CHOP Plan**
  - Itchy red eyes
  - Stuffy nose
  - Diarrhea
  - Abdominal pain
  - Anxiety
When to use?

- History of previous severe reaction - Lower threshold for early use
- Potential Exposure - No
- Exposure - No symptoms? - probable not
- What symptoms?
  - Isolated hives - probable not
  - Isolated GI symptoms - probable not
- Lower Respiratory/Cardiovascular - YES
- Progression of symptoms - YES
Conclusion

• There is fear and reluctant
  – How to use it?
  – When to use it?
  – Side effects
  – Should it be only for severe reactions?

• Consequences
Thank you!

Made possible through a 2016 grant from:

www.foodallergy.org