Appropriate Recognition and Management of Anaphylaxis
Session F4038

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Learning Objectives

At the conclusion of this CME activity, the participant will be able to:

1. Describe and recognize anaphylaxis.
2. Identify the most common causes of anaphylaxis.
3. Understand the importance of identifying and treating anaphylaxis quickly.
4. Name the treatment of choice for anaphylaxis.
Changes You Might Make in Your Practice

1. Reach for epinephrine first when treating anaphylaxis.

2. Have anaphylaxis mock-code drills.

3. Create an anaphylaxis management plan for your patients.
From Whence “Anaphylaxis”? 

• Richet and Portier, 1902  
  • During attempts to immunize dogs to the toxin of sea anemone, dogs that previously tolerated sub-lethal doses died after being given small doses.  
  • Coined the term “anaphylaxis” (without protection).  
    • Opposite of prophylaxis.  
• Richet: 1913 Nobel Prize in Medicine.

Charles R. Richet, MD  Paul J. Portier, MD
What is Anaphylaxis?

One of three clinical scenarios:

• Acute onset (minutes-hours) of a reaction involving skin and/or mucosal tissue AND either respiratory compromise, hypotension OR symptoms of end organ dysfunction.

• Two or more of the following occurring rapidly after exposure to a likely allergen: skin/mucosal tissue, respiratory compromise, reduced blood pressure or associated symptoms, and/or persistent GI symptoms.

• Reduced blood pressure after exposure to a known allergen.

An acute multi-system reaction caused by the rapid release of mediators from tissue mast cells and peripheral blood basophils. Immunologic mechanisms can be allergic (IgE-mediated) or non-IgE-mediated. Non-immunologic anaphylactic reactions, formerly called anaphylactoid or pseudo-allergic reactions, also occur.

Johansson SGO et al JACI 2004, 113:832-6
Prevalence of Anaphylaxis

• Estimated risk in US: 1-3%.
  • 3.3 to 4 million Americans at risk.
  • 1,433 to 1,503 at risk for fatal reaction.

• 5-year review of 1.15 million Canadians.
  • 0.95% of the population had epinephrine prescribed.
  • Dispensing rates varied with age.
    • 1.44% for individuals <17 years of age.
    • 0.9% for those 17-64 years of age.
    • 0.32% for those >65 years of age.
  • Conclusion: Anaphylaxis appears to peak in childhood, and then gradually decline.

J Allergy Clin Immunol 2001;108:622
J Allergy Clin Immunol 2002;110:341-8
Arch Int Med 2001;161,15-21
Incidence of Anaphylaxis

- Estimates range from 10-100 per 100,000 person-yrs.
- 1983-87: 21 per 100,000 person-yrs. (95% confidence interval: 17 - 25).
  - Occurrence rate: 30 per 100,000 person-yrs.
- 2000: 49.8 per 100,000 person-yrs.
  - Increased over time.
  - Highest in children (70/100,000 person-yrs).

Risk Factors for Anaphylaxis

Risk factors

• Atopy  Time since reaction
• Age    Economic status
• Gender  Season
• Route and constancy of administration

Not risk factors

• Race
• Geography
• Chronobiology

J Allergy Clin Immunol. 2001;105
## Anaphylaxis Risks If You Are Atopic

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Not Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Idiopathic</td>
<td>• Penicillin</td>
</tr>
<tr>
<td>• Exercise</td>
<td>• Insulin</td>
</tr>
<tr>
<td>• Latex</td>
<td>• Muscle relaxants</td>
</tr>
<tr>
<td>• Radiocontrast media</td>
<td>• Hymenoptera venom</td>
</tr>
</tbody>
</table>

Gender and Risk of Anaphylaxis

- Females > males
  - Age 15 and older
  - Overall
  - Latex
  - Muscle relaxants
  - Aspirin/NSAIDs
  - Idiopathic

- Males > females
  - Younger than 15 yrs.

Diagnosing Anaphylaxis

Clinical diagnosis.
Careful history to identify cause.
Confirmed by elevated serum tryptase.
  • Specific for mast cell degranulation.

Refer to allergist for detailed history and specific testing.

J Allergy Clin Immunol 2005;115:S483-523
J Allergy Clin Immunol 2010,126(3):480e1-e42
Frequency of Symptoms in Anaphylaxis

Percent of children

Adapted from J Allergy Clin Immunol 2002;109:S181
Signs and Symptoms of Anaphylaxis

Skin: Flushing, urticaria, angioedema, pruritus.

Respiratory:
   Nose: Symptoms of allergic rhinitis.
   Laryngeal*: Dysphonia, stridor, dyspnea, asphyxiation, death.
   Lungs*: Wheezing, cough, chest tightness, asphyxiation, death.

* Potentially fatal
Signs and Symptoms of Anaphylaxis

Gastrointestinal: Nausea, vomiting, bloating, cramping, diarrhea.

Cardiovascular*: Tachycardia, hypotension, collapse, shock, bradycardia, death.

Other: Sense of impending doom, metallic taste, urinary urgency, uterine cramps.

* Potentially fatal
Differential Diagnosis

Scombroid poisoning.
Systemic mastocytosis.
Hereditary angioedema.
Samter’s triad.
Vasovagal reaction.
Cardiac arrhythmia.
Hypoglycemia.
Psychiatric conditions.
Flushing syndromes.
SIDS.

Time to Demise in Anaphylaxis

![Graph showing the time to demise in anaphylaxis for different causes.]

## Factors Affecting Prognosis

<table>
<thead>
<tr>
<th></th>
<th>Poor Prognosis</th>
<th>Good Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Early</td>
<td>Late</td>
</tr>
<tr>
<td><strong>Initiation of treatment</strong></td>
<td>Late</td>
<td>Early</td>
</tr>
<tr>
<td><strong>Route of exposure</strong></td>
<td>Injection</td>
<td>Oral*</td>
</tr>
<tr>
<td><strong>β-blocker use?</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Underlying disease?</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

* Medications
Killers in Anaphylaxis

• Hypotension and shock.
  • Less frequent cutaneous/GI symptoms.

• Asphyxia (upper and/or lower).

• Cardiac.
  • Hypotension.
  • Tachycardia.
  • Bradycardia.
  • Myocardial infarction.
  • Empty heart syndrome.
Classification of Anaphylaxis

Adapted from Johansson, et al JACI 2004 and Simons JACI 2006

Anaphylaxis

Immunologic

- IgE (FcεRI)
  - Food, venom, latex, drugs (Type I)

- Non-IgE
  - Blood products, drugs, dextran, immune complexes (Type II and III)

Non-Immunologic

- Idiopathic

- Physical
  - Exercise, cold

- Other
  - Drugs, IV contrast, systemic mastocytosis
Not All Mast Cell Activation is IgE-Mediated
Type I vs. Type II and III Hypersensitivity Reactions

Type 1 tend to be more severe. Higher rate of hypotension and arrest.

Type 1 have higher tryptase level.

Clin Rev Allergy. 1991;9(3-4):249-258
Ann Fr Anesth Reanim. 1999;18(8):796-809
Anesthesiology 99:536,2003
Causes of Anaphylaxis in Childhood

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number of Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
<td>25</td>
</tr>
<tr>
<td>Drug</td>
<td>15</td>
</tr>
<tr>
<td>Exercise</td>
<td>5</td>
</tr>
<tr>
<td>Venom</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>20</td>
</tr>
</tbody>
</table>

Causes of IgE-Mediated Anaphylaxis

Food: Peanut, tree nuts, shellfish/fish, egg, milk.

Medications: β-lactam and other antibiotics, NSAIDs, muscle relaxants, biologicals, others.

Latex.

Venom: Bees, wasp, vespids, fire ants.

Allergen immunotherapy, skin testing (rare).

Exercise with food dependence.

Seminal fluid.

Neugut AI et al. Arch Intern Med 2001;161:15-21
J Allergy Clin Immunol 2010,126(3):480e1-e42
Causes of Non-IgE-Mediated Anaphylaxis

Radiocontrast media.

Medications: Opiates, IVIg, ACE inhibitors, vancomycin.

Cellular elements.

Physical: Exercise (without food), cold.

Idiopathic.

Mastocytosis.

Scombroid poisoning.

J Allergy Clin Immunol 2002;110:341-8
J Allergy Clin Immunol 2010,126(3):480e1-e42
Iatrogenic Causes of Anaphylaxis

Radiocontrast media.
Medications.
Latex.
Cellular elements (transfusions).
Allergen immunotherapy.
Temporal Patterns of Anaphylaxis

• Uniphasic

• Biphasic
  • Return of symptoms (any severity) 1-8 hours after apparent resolution.
  • Estimated: 2-3% of children and 5-20% of adults with severe episodes.

• Protracted
  • Up to 32 hours.
  • May not be prevented by steroids.

• Delayed

Lieberman P. Ann Allergy Asthma Immunol 2005;95:21
Biphasic Reactions

• 3-20% (or more).
• Onset 4-8 hours later (or more).
• Usually similar symptoms.
• Risks:
  • Ingested allergen.
  • Delay in onset of symptoms.
  • Severe reaction.
  • Delay in epi or > 1 epi dose.
• Comorbidities and medications.
• GOMER or SIMER?
Uniphasic Anaphylaxis

Antigen Exposure

Treatment

Initial Symptoms

Time

1-72 hours
Biphasic Anaphylaxis

Antigen Exposure

Time

1-72 hours

Initial Symptoms

1-8 hours

Late-Phase Symptoms

Treatment

Treatment
Protracted Anaphylaxis

Initial Symptoms

Antigen Exposure

1-72 hours

Time

Treatment

Treatment

Treatment
Identifying the Trigger

History, history, history.

• Timing of exposure.
• Associated factors (exercise, meds).
• Sequence of symptoms.
• Treatment.

Testing for specific IgE.

Other lab tests.

Challenge tests?
Specific IgE can confirm or refute diagnostic suspicion.

- Inhalants, foods, venom, some medications.

Lab tests for mast cell disease.

- Mastocytosis.
- Complement activation.
Interpreting Allergy Tests

Positive test ≠ allergy.

Positive test = sensitization.
  • Presence of specific IgE

Allergy = sensitization + mast cell activation with exposure.
  • Symptoms

Therefore, do not test for random or irrelevant allergens.
Types of IgE Allergy Testing

*In vivo*: Skin tests
- Choose appropriate allergens and controls.
- No antihistamines or tricyclic antidepressants.
- Positive test ≠ allergy: Correlate with history.
- Skin prick test vs. Intradermal.
  - Sensitivity/Specificity.
  - Venom, medications, aeroallergens.

*In vitro*: “RAST”
- Less sensitive, more expensive, longer to get result.
- Often harder to interpret. Positive test ≠ allergy.
- Not influenced by medications or skin disease.
Tests for Mast Cell Mediators in Anaphylaxis

Adapted from Anesthesiology. 2003;99:536. and JACI. 2010, 126(3):480e1-e42.
Random chart review (n=678) of patients with food allergy presenting to 21 North American emergency departments.

Management:

- Antihistamines: 72%.
- Systemic corticosteroids: 48%.
- Epinephrine: 16% (24% of severe reactions).
- Respiratory meds (e.g., albuterol): 33%.
- Self-injectable epinephrine at discharge: 16%.
- Referred to an allergist: 12%.

Clark S et al. J Allergy Clin Immunol 2004;347-52
The treatment of choice for anaphylaxis is:

A. Adrenaline.
B. Better give epinephrine or call your lawyer.
C. Can’t justify anything better than epinephrine.
D. Don’t give anything before epinephrine.
E. Epinephrine
F. F….well, just give the epi!
If You Remember Nothing Else Today…

WHY?
Treatment of Anaphylaxis

Onset of Action:

• Epinephrine (IM): Seconds.
• Antihistamines (IM, IV, or PO): Minutes.
• Corticosteroids: (IM, IV, or PO): Hours.
When in Doubt…

Inject Epinephrine!
Old Epinephrine is Better Than No Epinephrine

Rules from The House of God (#3)

“At a cardiac arrest, the first procedure is to take your own pulse.”

-Samuel Shem
Management of Anaphylaxis

Speed is critical:

Circulation
Airway
Breathing
Defibrillation
Epinephrine
Fluids

Management of Anaphylaxis

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Management of Anaphylaxis

Speed is critical:

- **E**pinephrine
- **C**irculation
- **A**irway
- **B**reathing
- **F**luids
- **D**efibrillation

Management of Anaphylaxis

Secondary measures:
• Patient in recumbent position; elevate legs.
• Maintain airway (intubate or cricothyrotomy).
• Oxygen, 6-8 liters/minute.
• IV fluids for severe hypotension.

Kemp SF and Lockey RF. J Allergy Clin Immunol 2002;110:341-8
Management of Anaphylaxis

• Secondary measures:
  • Epinephrine 1:1000, ½ dose into injection site.
  • Diphenhydramine or other H1-blocker.
  • Ranitidine or other H2-antagonist.
  • Albuterol nebulized solution.
  • Methylprednisolone 1-2 mg/kg per 24 hr.

• For refractory hypotension:
  • Dopamine 2-20 μg/kg/min.
  • Glucagon 20-30 μg/kg (max 1 mg in children) over 5 min. then run at 5-15 μg/min.

Kemp SF and Lockey RF. J Allergy Clin Immunol 2002;110:341-8
After the Anaphylaxis

Accidents are never planned.
  • Review the trigger and avoidance.
  • Recognize symptoms early.
  • React quickly.

Educate all caretakers.

Create a management plan.
  • Emphasize & validate self-injectable epinephrine.
Anaphylaxis Action Plans

Home/school:
• Triggers and symptoms to look for.
• Medications to use with dose and order.
• Where medications are kept and access.
• What others should do.

Your office:
• Allergy emergency practice drills.
• What others should do.
Anaphylaxis Action Plans

Hey Babysitter, Nanny, Caregiver, Teacher or Friend

Emergency Action Plan

Food Allergy Action Plan

Anaphylaxis Action Plan

ANAPHYLAXIS EMERGENCY ACTION PLAN

NAME: ____________________  AGE: _____

ALLERGIES TO: ____________________

Food allergies: Yes / No

Other health problems besides anaphylaxis:

Concurrent medications, if any:

SYMPTOMS OF ANAPHYLAXIS INCLUDE:

MOUTH: Inching, swelling of lips and tongue
SKIN: Itching, tightness/numbness
GUT: Vomiting, diarrhea, cramps
LUNG: Shortness of breath, cough, whose weak pulse, dizziness, passing out

Only a few symptoms may be present. Severity of symptoms can 
‘Some symptoms can be life-threatening!’ ACT FAST

WHAT TO DO:

1. INJECT EPINEPHRINE IN TRICEPS (check one) (Epineph. Jr. 0.15 ml) (Epineph. 0.3 mg)

Other medications/doses:

IMPORTANT: ASTHMA PUFFERS AND/OR HISTAMINE-2 BLOCKERS CAN'T BE GIVEN WITH EPINEPHRINE

2. CALL 911 OR RESCUE SQUAD BEFORE CALLING CONTACTS

3. EMERGENCY CONTACT #1: name ____________________ number ____________________

4. EMERGENCY CONTACT #2: name ____________________ number ____________________

DO NOT HESITATE TO GIVE EPINEPHRINE!

COMMENTS:

Doctor's Signature: ____________________ Patient's Signature: ____________________


North Dakota Anaphylaxis Action Plan

North Dakota Anaphylaxis Action Plan

Name: ____________________ Date: ____________________

Travel/Contact(s): Name(s): Phone Number

Emergency Contact: Phone Number

Emergency Numbers: Phone Number

Resuscitation Card Responder (omit): Phone Number

Signature of Health Care Provider:

Emergency Epinephrine Administration and Self-Administration Apparatus: This kit has been received as of not used or see next page.

Emergency Kit: Date: ____________________

Anaphylaxis or a significant allergic reaction:

Swelling of lips, face, eyes
Hives or welts
Difficult or noisy breathing
Swelling of the tongue
Swelling or tightness of the throat
Difficulty talking and/or hoarse voice
Wheeze or persistent cough
Loss of consciousness and/or collapse
Pallor and tachypnea (young children)

Action:

1. GIVE ONE TIME: 
   - Epineph. Jr. 0.15 ml for individual 33 lbs
   - Epineph. Jr. 0.3 mg for individuals > 66 lbs

2. Call ambulance. Telephone 911

3. Contact parent/care giver

Substances Causing Severe Allergic Reactions:

How to give Epineph. or Epineph. Jr.

1. Form fist around Epineph. or Epineph. Jr.

2. Place black and against upper arm

3. Press down until click is heard or felt and hold in place for 10 seconds.

4. Remove Epineph. or Epineph. Jr. and be careful not to touch the needle. Massage the injection site for 10 seconds.

Additional Instructions:

To download this action plan, go to www.nd.gov/health

How to give Epineph. or Epineph. Jr.

N.D. Dept. Health, Stop Allergy...; N.D. Health, Stop Allergy...; N.D. Dept. of Human Services

Emergency Medical Services 1-701-328-2588

N.D. Dept. of Health, Stop Allergy...; N.D. Health, Stop Allergy...; N.D. Dept. of Human Services

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For anaphylaxis information contact: Emergency Medical Services
1-701-328-2588
Equipment and Medications for Anaphylaxis Preparedness

Required:
- Epinephrine 1:1000
- Oxygen
- IV fluids (0.9 NL saline)
- Tourniquets, syringes, Large bore needles

Consider having:
- Epinephrine 1:10000 IV
- β-agonist/nebulizer
- IV pole/latex free gloves
- O₂ Sat monitor
- Vasopressor (e.g., dopamine)

Recommended:
- One-way valve facemask
- Oral airways (4-6 sizes)
- AED
- Glucagon

Optional:
- Diphenhydramine (IV/IM)
- Ranitidine (IV/IM)
- Corticosteroids (IV)

Referral to the Allergist

Trigger identification.
- History.
- Testing.

Patient education.
- Anaphylaxis in general.
- Trigger avoidance.
- Epinephrine auto-injector.

Detailed action plan.
Changes You Might Make in Your Practice

1. Reach for epinephrine first when treating anaphylaxis.
2. Have anaphylaxis mock-code drills.
3. Create an anaphylaxis management plan for your patients.
References


