Anaphylaxis

- Acute, life-threatening reaction often resulting from exposure to an offending agent
- Result of immunologic (IgE mediated) or non immunologic reactions
- Results from the release of chemical mediators from mast cells, basophils, and other inflammatory cells
- Any delay in recognition of the symptoms may result in fatal outcome

Incidence & Prevalence of Anaphylaxis

- Exact incidence is unknown
- Appears to be increasing
- Lifetime prevalence is 0.05% to 2%
- Largest # of cases is among children and adolescents
- underreported
Anaphylaxis – Clinical Manifestations

- Cutaneous (90%) – itching, flushing, hives, angioedema
- Respiratory (40-60%) – cough, dyspnea, hoarseness, stridor, wheezing, laryngeal edema
- Cardiovascular (30-35%) – dizziness, hypotension, shock

Anaphylaxis – Clinical Manifestations (cont)

- Gastrointestinal (25-35%) – nausea, vomiting, diarrhea, abdominal pain
- Neurological (5-8%) – headache, seizure, loss of consciousness

Risk Factors for Anaphylaxis

- Being female – increase for latex, aspirin, and muscle relaxants
- Route of administration (parenteral)
- Time since last reaction
- Constancy of administration
- Atopy in some instances, e.g. anaphylaxis to latex and food

Kemp Arch Int Med 1995 155:1749-54
**Differential Diagnosis of Anaphylaxis**

- Vasovagal reaction – pallor, diaphoresis, bradycardia, hypotension, faint feeling
- Carcinoid syndrome – flushing, abdominal cramps, diarrhea, bronchospasm
- Pheochromocytoma – adrenal gland tumor that secretes catecholamines, causes headache, sweating, palpitation, tremor and chest pain
- Hereditary angioedema
- Vocal cord dysfunction

**Differential Diagnosis of Anaphylaxis**

- Restaurant syndromes
  - Monosodium glutamate (MSG)
  - Sulfites
  - Scrombroidosis
- Systemic mastocytosis
- Urticaria pigmentosa
- Urticaria vasculitis
- Panic attacks
- Munchausen’s stridor

**Anaphylaxis - Mediators**

- Histamines and leukotrienes
  - Smooth muscle contraction
  - Increase vascular permeability
  - H1 + H2-vasodilatation
- Neutral Proteases (tryptase, chymase)
  - Cleavage of complement components
  - Chemoattractants
  - Activation and degranulation of mast cells
Anaphylaxis – Mediators (cont’d)

- Proteoglycans (heparin, chondroitin sulfate)
- anticoagulation
- Inhibition of complement
- Activation of kinin pathway
- Chemoattractant for eosinophils
- Nitric oxide
- Increase vascular permeability and dilation

Anaphylaxis – Immunologic Mechanism

- IgE mediated
- Allergen enters the body, combines with IgE antibodies on the surface of mast cells and basophils
- These cells degranulate and release mediators causing signs and symptoms of anaphylaxis

Examples of IgE Mediated Triggers

- Foods (e.g. shellfish, tree nuts, peanuts)
- Medications (B-lactam antibiotics)
- Insect stings
- Latex
- Allergen Immunotherapy
Anaphylaxis – Other Immunologic Mechanism

- Immune aggregates (type II)
  - Intravenous immunoglobulin
  - Dextran
- Autoimmune mechanism
  - Some patients with IA
- Complement activation
  - Blood transfusion

Anaphylaxis – Non immunologic Causes

- Nonspecific degranulation of mast cells and basophils
  - Medications: opioids, RCM, vancomycin
  - Physical: exercise, cold or heat

Common Causes of Anaphylaxis

- Food – most commonly peanuts, eggs, fish, shellfish, milk and tree nuts
- Medications – penicillin, cephalosporins, aspirin, NSAID, anesthetic agents, opiates, muscle relaxants
- IV radiographic contrast media – 0.2% for ionic agents and 0.04% for lower osmolality, nonionic agents
Common Causes of Anaphylaxis (cont)

- Latex – 8-17% of health care workers experience some form of allergic reactions
- Insect stings (fire ant, bee, wasp, hornet, yellow jacket) – 40-100 deaths per year in U.S.A.

Food Induced Anaphylaxis

- Children – most common foods implicated are peanuts, tree nuts, fish, shellfish, milk and eggs
- Adults – shellfish is most common
- Reactions: minutes to couple of hours
- Unpredictable cross reactivity with other foods
- Most useful diagnostic test is skin test and food challenges

Food Anaphylaxis – Risk Factors

- Accidental ingestion
- Unstable asthma
- Not recognizing early symptoms
- Epinephrine not available or expired
- Use of antihistamine only for treatment
Anaphylaxis to Foods - Prevention

- Education on avoidance and management of accidental ingestion
- Staff at school should be trained for the use of epinephrine
- Most reactions occur outside of home, importance of carrying epipen and educated on the use

Anaphylaxis to drugs

- Penicillin - most common
- Skin testing with penicillin reagents yields negative result in 90% of patients with a hx or penicillin allergy
- Negative predictive value of penicillin skin test is 97% to 99%, positive value is at least 50%
- Allergic cross-reactivity between penicillin and cephalosporins is low

- Aspirin and NSAID second most common cause
- Medication specific
- Do not cross-react with structurally unrelated aspirin or other NSAID
- Aspirin sensitivity may be IgE mediated without cross reaction to NSAID
- NSAID cross reactivity is not IgE mediated
Anaphylaxis due to Insect Stings

- 50 deaths per year
- 0.5% to 5% of the US population
- Bees, wasps, hornets, yellow jackets and fire ants

Latex-induced anaphylaxis

- Risk factors: health care workers, children with spina bifida and GU abnormalities, workers with exposure to latex
- IgE mediated
- No standard commercial extract for skin testing
- Extracts prepared from gloves for skin testing

Latex Induced Anaphylaxis (cont)

- RAST testing is less sensitive
- Use latex free gloves for procedures and in working environment
- Cross reactivity between latex and foods (banana, avocado, kiwi, chest nut)
Anaphylaxis and Allergen Immunotherapy

- Fatal reaction – 1 in 2.5 million injections
- Near fatal reactions – 1 in 1 million injections
- Systemic reactions – 0.5%
- Most within 20-30 minutes
- Systemic reactions not predicted by large local reactions

Anaphylaxis and Allergen Immunotherapy – Risk Factors

- Errors in dosage
- Administration of the wrong extract
- Uncontrolled asthma
- High allergen sensitivity
- Previous systemic reaction
- Peak pollen season
- Concurrent use of B-adrenergic blocking agents

Idiopathic Anaphylaxis

- Symptoms are identical to other types of anaphylaxis
- May account for as many as 50% of cases
- Detailed history and evaluation needed including lab and other diagnostic studies
- Rule out other causes such as mastocytosis, carcinoid, pheochromocytoma, etc
- A diagnosis of exclusion
Idiopathic Anaphylaxis

- Acute treatment is the same as for other types of anaphylaxis
- If symptoms are frequent, use of corticosteroid as prophylaxis is beneficial
- Start with prednisone 80-100mg qd until control then taper slowly by 5-10mg per month
- Daily use of antihistamines (H1 and H2)
- Some cases are due to autoantibodies to IgE-benefit from leukotriene antagonist (Zafirlukast)

Diagnosing Anaphylaxis

- Careful history to identify potential triggers
- Skin manifestations as most common
- Lab studies to aide the diagnosis
  - Skin test or RAST
  - Elevated serum tryptase level (peak 60 - 90mins, last 5 hours)
  - Elevated histamine level (15 to 60mins)

Anaphylaxis – Acute Treatment

- Epinephrine
- Oxygen
- IV fluids – rapid volume expansion
- Supine position
- Call 911
- Repeat epinephrine every 10 - 15 minutes
- Others: beta agonist, H1 & H2 antihistamines, glucocorticoid, other vasopressor, glucagon
- CPR
Biphasic/Protracted Anaphylaxis

- Exact incidence not known
- Occur more frequently when epinephrine administration is delayed
- Can occur as late as 28 hours after remission
- Risk factor: previous h/o biphasic reaction
- If at risk, recommend observation for 24 hours
- No evidence that steroids can prevent

Management of Anaphylaxis

- Recognize signs and symptoms
- Prompt recognition with immediate treatment is essential
- Place patient in supine position and elevate lower extremities
- Monitor vital signs every 2-5 mins and stay with the patient
- Epinephrine is the mainstay of the therapy

Epinephrine

- Intramuscular injection – faster peak plasma levels than SQ
- Lateral thigh – achieve higher concentration
Management of Anaphylaxis

- Administer Epinephrine 1:1000
  - Adults: 0.3-0.5ml IM q 10 mins
  - Child: 0.01ml/kg up to 0.5ml IM q 15 mins
  - Apply tourniquet proximal to the injection site
- Maintain airway
- Oxygen – 8-10 L/min

Management of Anaphylaxis

- Antihistamines
  - H1 + H2 antagonist superior to H1 alone
  - Diphenhydramine: 25-50 mg IM or IV for adults, 12.5 - 25mg PO, IM or IV for child
  - Ranitidine or cimetidine: 4mg/kg IV cimetidine, 1mg/kg IV ranitidine
  - Administer cimetidine slowly to prevent fall in blood pressure

Management of Anaphylaxis

- Hypotension
  - IV fluids: rapid volume expansion with NS or lactated Ringer's solution 1000ml to 2000ml in the first 5 mins
  - vasopressor (dopamine)
- Bronchospasm – inhaled B2 bronchodilator, consider aminophylline
Management of Anaphylaxis

- Patients on Beta blockers or refractory to treatment – consider glucagon 1mg IV bolus and continuous infusion 1-5mg per hour if needed
- Corticosteroids – hydrocortisone 5mg per kg or 250mg, solumedrol 2mg/kg or 120mg every 6 hrs, or oral prednisone 2mg/kg or 60mg per day

Possible Reasons for Lack of Response to Epinephrine in Anaphylaxis

- Rapid progression of anaphylaxis
- Delay in epinephrine administration
- Inadequate dosing of epinephrine
- Not optimal site
- Past expiration date
- Individual not supine
- On beta blocker or ACE inhibitor that prevent optimal epinephrine effect
- Comorbidity such as severe asthma

Fatalities due to Anaphylaxis

- Relatively rare but many are preventable
- Having asthma is a risk factor
- Under use of epinephrine
- Death can occur regardless of the offending agent
Case
A 23 year-old woman with a past history of seasonal allergic rhinitis presented to the allergy clinic for routine injection of allergen immunotherapy. She received her injection and after waiting for 20 minutes, she noticed itching of the palms of her hands, followed by sensation of shortness of breath. When she presented to the nurse, she appeared flushed and was sweating profusely.

Case - Questions
- What features lead to the diagnosis of anaphylaxis?
- What is the appropriate initial management?
- How should such a patient be followed after symptom resolution?

Thank you