Anaphylaxis

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Disclosures

• None
Objectives

- Gain an understanding of the mechanisms and pathophysiology of anaphylaxis
- Identify the symptoms of an anaphylactic reaction
- Explain the differences between a vasovagal response and a true anaphylactic reaction
- Explain current treatment algorithms for anaphylaxis
Definitions

• Anaphylaxis – An Immune mediated IgE response to an antigen

• Anaphylactoid – A non IgE mediated response that presents with the same clinical signs/symptoms

An Anaphylactic reaction can therefore be due to either IgE or Non IgE mediated processes.
Differential Diagnosis

• Vasovagal response

• Anxiety

• Anaphylaxis
  - Large local reactions
  - Systemic reactions
Vasovagal Reaction

- Reflexive and involuntary process directed by the nervous system
- Bradycardia (slow and thready pulse)
- Vasodilation of systemic arterioles (lower extremities)
- Resultant relative hypo-perfusion of the cerebral vasculature
- Deprivation of oxygen to brain with fainting (seizure activity, slurred speech)
Symptoms of Vasovagal Reaction

- Bradycardia
- Blood pressure may be normal or slightly lower
- Diaphoresis and pallor
- Brief loss of consciousness
- Brief seizure disorder
- Unlike anaphylaxis, there will be no itching, rash, wheezing, cough or feeling of doom.
Differential Diagnosis in dramatic patient collapse

- Vasovagal reaction
- Acute anxiety with hypoventilation syndrome
- Myocardial infarction
- Pulmonary embolism
- Systemic mast cell disorders
- Acute foreign body aspiration
- Seizure disorder
- Acute hypoglycemia
- Acute poisoning
Treatment of vasovagal response

• 1st step is to recognize or possibly anticipate the patient who is prone to vasovagal responses
• Once started, the vagal efferent pathway will occur
• Lay patient down, preferably with legs/feet elevated
• Cool towel/cloth over forehead
• Check vital signs to ensure stability/clearance
• Ensure that patient is not in a position to fall out of exam chair/table
• Reassurance
• Prevention (ensure proper hydration and nutrition prior to medical/surgical office procedures)
Anaphylaxis

• In 1902, Portier and Richet attempted to prophylax dogs to anemone venom by providing serial immunizations

• Animals reacted fatally to previous non-lethal doses

• They coined the term “anaphylaxis” which was the opposite of what they were trying to achieve “prophylaxis”
Anaphylaxis

- Allergen immunotherapy injections
- Foods (peanut, shellfish)
- Insection venoms
- Latex
- Allergy skin testing (100 times less common than anaphylaxis from immunotherapy)
- Idiopathic causes
Anaphylactoid Reactions

- Non-IgE mediated immune responses
- Complement activation
- Mast cell degranulation
- Clinically similar to anaphylaxis
- May occur upon first exposure to foreign substance
- Exercise, NSAIDS/drugs, radio-contrast agents
Anaphylaxis

• An immediate IgE mediated reaction due to basophil and mast cell degranulation
• Complement activation
• Signs and symptoms occur within 30 minutes of exposure
• If occurring in the allergy testing and treatment scenario, this is referred to as a “systemic reaction”
Anaphylaxis: Signs and Symptoms

- **Cutaneous**
  - 90%
  - Urticaria
  - Angioedema
  - Flushing
  - Itching without rash

- **Respiratory**
  - 60%
  - Dyspnea, wheeze
  - Upper airway angioedema
  - Rhinitis

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## Anaphylaxis: Signs and Symptoms

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdominal</strong></td>
<td>30%</td>
<td>Nausea, vomiting, Abdominal pain, cramps, diarrhea</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>30%</td>
<td>Tachycardia, hypotension, dizziness, syncope</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>1-8%</td>
<td>Headache, sub-sternal pain, seizure</td>
</tr>
</tbody>
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## Anaphylaxis vs Vasovagal response

<table>
<thead>
<tr>
<th>Anaphylaxis</th>
<th>Vasovagal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Pulse</td>
<td>Slow Pulse</td>
</tr>
<tr>
<td>Low Blood pressure</td>
<td>Normal BP</td>
</tr>
<tr>
<td>Warm/red skin</td>
<td>Pallor/sweating</td>
</tr>
<tr>
<td>Wheezing, cough</td>
<td>No cough/wheeze</td>
</tr>
<tr>
<td>Urticaria, itching</td>
<td>No urticaria/itching</td>
</tr>
<tr>
<td>Feeling of doom</td>
<td>No feeling of doom</td>
</tr>
</tbody>
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Mechanisms of Anaphylaxis

- Mast cell and basophil degranulation release histamine, leukotrienes, prostaglandins and other mediators

- Vasodilation and increased vascular permeability result in massive intravascular volume depletion and peripheral tissue edema

- Hypotension

- Tachycardia

- Cardiac output drops

- Airway edema with resultant stridor and airway obstruction
Acute and Late allergic reaction
Early and Late Phase Reaction

- **Early Phase Reaction**
  - Immediate
  - Urticaria
  - Vasodilation/Extravasation
  - Bronchoconstriction
  - Mucous secretion

- **Late Phase Reaction**
  - 4-6 Hours
  - Eosinophils infiltrate
  - Fibrin deposition
  - Monocyte infiltration
  - Tissue damage
Risk factors for Fatal Anaphylaxis following allergy immunotherapy

• Uncontrolled asthma
• Dose increase phase of immunotherapy
• High sensitivity measured at initial testing
• Previous history of anaphylaxis/prior injections
• Active allergen season (priming prior to allergy injection)
• New vial
• Error (wrong vial, wrong dose, wrong administration, faulty equipment, no observation)
Most common risk factors for IT related Anaphylaxis

- Buildup immunotherapy: 90%
- Active Asthma: 46%
- New vial/first injection: 10%
- Prior systemic reaction: 7%
- Vial prepared in another office: 6%
- Beta blocker treatment: 4%
- Error (wrong patient vial): 3%

Classification of Anaphylaxis Severity

Ring and Messner
- Grade 1: cutaneous manifestations
- Grade 2: mild respiratory and CV effects
- Grade 3: severe multisystem involvement
- Grade 4: respiratory collapse and cardiac arrest

Brown
- **Mild**: generalized rash, urticaria, periorbital edema, angioedema
- **Moderate**: dyspnea, stridor, wheeze, nausea/vomiting, diaphoresis, chest/throat tightness, abdominal pain
- **Severe**: hypoxia, hypotension, neurologic compromise, cyanosis, confusion, collapse, incontinence

Brown SGA. JACI. 2004; 114:371-6
Equipment to Treat Anaphylaxis

- Exam Chair/Table (allowing for reverse Trendelenberg)
- BP cuff, stethoscope, pulse oximeter
- Tourniquet
- Oxygen & Mask, Ambu Bag
- Suction device, oral and intubation tray
- IV set-up (Pole, tubing, angiocaths, tape, fluids)
- Syringes, needles
- Inhalers, relevant drugs and dosing/mixing sheets
Medications to Treat Anaphylaxis

• Epinephrine
• Diphenhydramine injectable
• Ranitidine or cimetidine injectable
• Corticosteroid injectable
• Aerosolized Beta agonist (albuterol)
• IV fluids
• Dopamine, Glucagon, Atropine, Ipratropium
Emergency Cart

- 50% Dextrose Injection, USP, 25 g (0.5 g/mL)
- 8.4% Sodium Bicarbonate Injection, USP, 50 mEq (1 mEq/mL)
- 2% Lidocaine HCL Injection, USP, 100 mg/5mL
- 2 g Lidocaine (8 mg/mL)
- Atropine Sulfate, inj., USP, 1 mg (0.1 mg/mL)
- Epinephrine inj., USP, 1:10,000, 1 mg (0.1 mg/mL)
- 400 mg Dextrose (1600 mg/mL)
- 0.9% Sodium Chloride inj., 10 mL
- 0.1% Sterile H2O for drug dilution, 20 mL

Alcohol pads

Hurricane Spray topical anesthetic oral or mucosal application

Vasopressin

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Treatment of Anaphylaxis

• The Key is →→

• Epinephrine, oxygen, and volume replacement are the most important interventions

• Remember the A, B, Cs…….
Treatment of Anaphylaxis

• Death occurs during anaphylaxis due to a delay in administration of epinephrine with resultant severe respiratory and cardiovascular collapse.

• There is no absolute contraindication to epinephrine administration in the treatment of anaphylaxis.

• ABCs (Epinephrine, Oxygen, Fluids)
  - Assess the airway, breathing, circulation and level of consciousness prior to moving forward.
  - Epinephrine administration, replacement of intravascular volume and oxygen are the highest priority.
When in Doubt, Epinephrine Comes Out!

- Use 1:1000 dilution (1mg/ml) Aqueous epinephrine
- Adult dosage (IM injection or SQ 0.2 to 0.5ml)
- Children (IM injection or SQ: 0.01mg/kg, maximum 0.3mg dosage)
- May repeat epinephrine injection every 5 minutes as necessary to maintain blood pressure and control symptoms
Additional Therapeutic Measures:  
Call for Help/911

• Depending on patient’s response to Epinephrine injection:
  • 1. Place patient in recumbent position/elevate legs
  • 2. Establish/maintain the airway
  • 3. Oxygen
  • 4. IV fluid replacement with venipuncture
  • 5. May need IV epinephrine (monitoring)
  • 6. H1 antagonists/diphenhydramine
  • 7. H2 antagonists/cimetidine/ranitidine
  • 8. Consider inhaled b-agonists/albuterol
  • 9. Consider Vasopressor IV (dopamine)
  • 10. Consider systemic gluco-corticosteroids
  • 11. Prepare patient for ER transfer (observation for delayed/late reaction)
Anaphylaxis management

• Consider placing tourniquet above the site of allergy injection
• May injection 1% lidocaine with 1:100,000 epinephrine at the site of allergy injection to retain antigen in localized area and limit systemic distribution
**Airway Breathing Circulation**

- Consider ventilatory assistance with use of a facemask or ambu-bag
- Consider oral-endotracheal intubation or emergent cricothyroidotomy
- Administer oxygen in patients with prolonged reactions and those receiving multiple doses of epinephrine
- If pre-existing heart disease, administer oxygen
- Pulse oximetry and use of ABGs when available can help guide oxygen need/therapy
Airway **Breathing** Circulation

- Normal saline via intravenous line for intravascular volume depletion

- The effects of histamine and resultant extravascular leakage may move 50% of the intravascular volume into the peripheral tissues (severe edema)

- 1 to 2 liters of normal saline at a rate of 5-10ml/kg in the first 5 minutes

- Up to 7 liters of crystalloid may be necessary

- Children should receive 30ml/kg of crystalloid in the first hour
Airway Breathing Circulation

- IV administration of epinephrine (can lead to lethal cardiac arrhythmias)
- Should only use if patient has profound hypotension or cardiac arrest
- Failure to respond to intravenous volume replacement
- Failure to respond to several injected doses of epinephrine
- Ideally, need monitoring of blood pressure, pulse, and EKG activity
- If these monitoring functions are not available, the physician must determine if IV epinephrine is necessary
IV Dosing of Epinephrine (Adults)

- Aqueous epinephrine 1:1000, 0.1 to 0.3ml in 10 ml of normal saline
- Administer IV over several minutes and repeat as necessary
- May add 1mg (1ml) of a 1:1000 dilution of epinephrine to 250 ml of D5W to yield a concentration of 4mg/ml
- Infuse at a rate of 1 to 4ug/min (15 to 60 drops per minute with a microdrop apparatus (60 drops per minute = 1ml = 60ml/h), increasing to maximum of 10ug/min
- If an infusion pump is available, a 1:100,000 (1mg in 100ml of saline) can be prepared
- Start with 30 to 100ml/h (5-15ug/min), titrate up or down to clinical response or toxicity/side effects of epinephrine
IV dosing of epinephrine in Children

- Use a dosage of 0.01mg/kg (0.1ml/kg of a 1:10,000 solution, maximum dosage is 0.3mg)
- Alternate pediatric dosage by the “rule of 6” is as follows:
  - 0.6 x body weight (in kilograms) = the number of milligrams diluted to a total of 100ml of saline; then 1ml/h delivers 0.1ug/kg/min.
Preventing Anaphylaxis in the Office

- Use conservative initial skin testing dilutions
- Minimize testing cross-reacting antigens
- Vial test prior to beginning any new treatment vial
- Re-test when changing manufacturer
- Use gradual and individualized dose escalation
- Consider holding or reducing injections during seasonal fluctuations, acute illness, recent severe local reaction, history of systemic reactions, or missed/delayed injections
- Double/triple check patient ID, vial ID, proper dose
- Quiet environment for vial preparation
- Beware of Beta blockers, ACE inhibitors, and MAO inhibitors
Office preparation to treat anaphylaxis

- Anaphylaxis must be considered a possibility in every patient undergoing testing or treatment
- Observation area in clinic for patients
- Basic CPR certification of staff
- Staff education in signs/symptoms of anaphylaxis
- Equipment, drugs, and instructions prepared in advance
- Hold readiness drills/mock drills (Simulation Center)
- Consider purchasing an office AED
Drug interactions and Anaphylaxis

• “Allergy skin testing or immunotherapy is inadvisable in patients who take a B blocker orally or in the form of ophthalmic eyedrops”
  
  Toogood JH. CMAJ. 1987; 136:929-933

• “Patients taking B-adrenergic blocking agents may be at increased risk when receiving allergen immunotherapy, because B-receptor blockade can make treatment of anaphylaxis more difficult. Therefore, b-adrenergic blocking agents are relative contraindications for immunotherapy”

Beta Blockers may be a problem

• Systemic beta blockade alters the balance between alpha and beta adrenergic receptors as well as cholinergic neuro-humoral mechanisms.
• Resultant effect on the regulation, synthesis, and release of anaphylactic mediators
• Beta blockade increases IgE levels
• Beta blockade alters the pharmacologic action of epinephrine with decreased effectiveness and hypertensive crisis (alpha adrenergic overdrive)
• Inhaled beta agonists will not be as effective
Other drugs that may interfere with Anaphylaxis treatment

• Selegiline
• Candesartan
• Irbesartan
• Losartan
• Valsartan
• Benazepril
• Enalapril
• Lisinopril
• Amitriptyline
• Doxepin
Steroids

• For control of late phase reactions
• Hydrocortisone  250-500mg IV/IM

• Methylprednisolone 125mg/IV/IM (or 1-2 mg/kg)
• Dexamethasone 10mg IV/IM
Anaphylaxis Treatment with Beta Blockade

- Administering epinephrine in patients on beta blockers can cause a severe hypertensive crisis.
- Give epinephrine (decreased dose, but monitor BP)
- If hypertension:
  - Phentolamine (alpha 1 and alpha 2 receptor antagonist) at 5-10mg IV every 10 minutes. Pediatric dosing (0.1mg/kg to block alpha effects)
  - Nitroglycerin or Nitroprusside
  - Consider Glucagon (1-5mg IV), atropine (0.3-0.5mg IV for bradycardia), MgSO₄
Treatment of Anaphylaxis with Beta Blockade

- Atropine 0.5mg IV, repeat every 10 minutes
- Glucagon 1-5 mg IV
- Ipratropium nebulized/MDI – dose as for COP
- Albuterol nebulized/MDI – dose as for acute asthma
Prevention of Delayed Reaction

- Transport patient as soon as stabilized
- Speak with receiving ER physician
- Should consider overnight admission due to risk of late phase or bi-phasic anaphylaxis
Learn from the Past, Look to the Future

• Hold a debriefing session for staff
• Perform a root cause analysis
• Adjust diagnostic and treatment approaches for office practice
• Review written protocols with staff
• If human error occurs, make full disclosure to patient and family
Summary

• Anapylaxis prevention is the best process

• Always be prepared

• Remember Epinephrine, Epinephrine, Epinephrine
Resources

• American Academy of Otolaryngic Allergy (AAOA) Basic and Advanced Courses (July and December respectively)
• Fall AAO-HNS and AAOA meetings with courses/primers on otolaryngic allergy.
• www.aaaai.org/practice-resources/statements-and-practice-parameters
• Consider becoming a Fellow of the AAOA
• Visit aaoa@aaoaf.org
Thank you