Case Report

37 y/o WF
- Hx of stable asthma, allergic rhinitis
- Non smoker
- Meds: albuterol PRN, cetirizine, budesonide/formoterol, emestine, fluticasone intranasal

Is this anaphylaxis?

What would you do at this point?
- A. Reassure patient to reduce anxiety and give oral antihistamine
- B. Reassure patient to reduce anxiety & observe
- C. Encourage patient to lie down and give epinephrine 1:1000
Case Report
37 y/o WF
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  - D. Administer oral antihistamine, start IV and give IV methylprednisolone

Case Report
37 y/o WF
➢ Is this anaphylaxis?
➢ What would you do at this point?
  - A. Reassure patient to reduce anxiety and give oral antihistamine
  - B. Have patient walk around and cool off
  - C. Encourage patient to lie down and give epinephrine 1:1000
  - D. Administer oral antihistamine, start IV and give IV methylprednisolone

Definitions
➢ Anaphylaxis: a life-threatening syndrome resulting from the sudden release of mast cell and basophil mediators into the circulation
  - Immunologic
    • IgE Mediated
    • Non-IgE mediated (anaphylactoid)
  - Non-Immunologic
➢ Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.
JACI 2005;115:548-91

Clinical Definition
Criterion 1
➢ An individual has skin symptoms or swollen lips and either:
  - Difficulty breathing or
  - Reduced blood pressure (< 100 mm HG systolic or > 30% decrease)
JACI 2005;115:584-91

Clinical Definition
Criterion 2
➢ An individual had exposure to a suspected allergen and two or more of the following:
  - Skin symptoms or swollen lips
  - Difficulty breathing
  - Reduced blood pressure
  - GI symptoms with suspected food allergy (such as vomiting, diarrhea, cramping)
JACI 2005;115:584-91

Clinical Definition
Criterion 3
➢ An individual had exposure to a known allergen and experiences reduced blood pressure (< 100 mm Hg in adults or a decrease in systolic BP by > 30%)
JACI 2005;115:584-91
Anaphylaxis Definition WAO
WAO Journal, July 2008

- Acute and potentially lethal multisystem allergic reaction in which some or all of the following signs and symptoms occur:
  - Diffuse erythema
  - Hypotension
  - Pruritus
  - Cardiac arrhythmia
  - Urticaria/angioedema
  - Feeling of doom
  - Bronchospasm
  - Variety of other Sxs
  - Laryngeal edema (rhinorrhea, warmth, abdominal pain, uterine cramps)

Case Report

37 y/o WF
- Rxed with 0.2cc IM epinephrine 1:1000 and placed in a supine position
  - 5 minutes later O2 sats decreased, BP decreased to 90/60
  - 0.3cc IM epinephrine given with O2, bronchodilator Rx and IV saline started
  - Slight improvement, additional epinephrine given and transported to ED

Mast Cell and Basophil Mediators

- Preformed
  - Histamine
  - Tryptase
  - Chymase
  - Histamine releasing factor
  - Other cytokines
- Newly generated
  - PGD2
  - LTB4
  - LTC4, LTD4, LTE4
  - PAF

Introduction

- Platelet-activating factor (PAF) mediates life-threatening manifestations of anaphylaxis. So, too, does PGE₂.
- The influence of epinephrine on PAF has not been elucidated.


Clinical Implications

- Our findings in vitro are consistent with clinical observations showing that epinephrine is most effective when administered early in anaphylaxis and less effective with the passage of time.

Objective

- Using human vascular smooth muscle cells, the effect of epinephrine addition on the action PAF-mediated prostaglandin E\textsubscript{2} (PGE\textsubscript{2}) release was examined.

Vadas P, Perelman B. *J Allergy Clin Immunol* 2012;129:1329-33

Results

- HVSMC stimulated with PAF released PGE\textsubscript{2} in a concentration- and time-dependent manner.
- Preincubation of HVSMC with epinephrine before PAF suppressed PGE\textsubscript{2} release.
- Treatment with epinephrine after PAF stimulation was less effective in suppressing PGE\textsubscript{2} release.

Vadas P, Perelman B. *J Allergy Clin Immunol* 2012;129:1329-33

Conclusions

- PAF induced PGE\textsubscript{2} release from HVSMCs in a concentration- and time-dependent manner.
- Early addition of epinephrine controlled PAF-induced release of PGE\textsubscript{2}.
- Epinephrine most effective when administered before stimulation with PAF and less effective with time after PAF stimulation.

Vadas P, Perelman B. *J Allergy Clin Immunol* 2012;129:1329-33

Pathway Activation During Anaphylaxis

- Clotting
  - Factor XII
  - Kallikrein
  - Complement
  - Trypsin

- Mast cell

- Contact system

Endogenous Compensatory Mechanisms

- Epinephrine
  - Adrenal
  - Angiotensin II
  - Angiotensin I

Causes of Anaphylaxis

- IgE Dependent
  - Food: peanut, tree nut, crustaceans, fish, seeds
  - Medication: antibiotic, muscle relaxant, protamine
  - Venom
  - Latex
  - Allergen vaccine (immunotherapy)
Causes of Anaphylaxis Not IgE Mediated
- Radiocontrast media
- Renal dialysis
- Sulfonated polyacrylonitrile, cuprophane, polymethacrylate with or without ACE inhibitor
- Ethylene oxide
- Opioids, NSAIDs, Muscle relaxants
- Exercise
- Idiopathic

Anaphylaxis Syndromes
- Idiopathic
  - Monoclonal mast cell activation syndrome
- Exercise induced
- Food-dependent exercise induced
  - Oysters, shrimp, celery, wheat
- Sensitivity to Anisakis simplex
  - Parasite ingested with raw fish
- Covert food allergen: peanut, mites in flour, carmine, soy, casein, bee pollen

Is atopy a risk factor for anaphylaxis?
- Risk Factor if Atopic
  - Agents given orally
  - Idiopathic
  - Exercise
  - Latex
  - Radiocontrast
- Not Risk Factor
  - Most parenteral
  - Penicillin
  - Insulin
  - Hymenoptera
  - Most drugs

Terminology
- Human Anaphylaxis
  - Immunologic
  - Idiopathic
  - Non-Immunologic
  - IgE, FcεRI
  - Foods, venoms, latex, drugs
  - Other
    - Inhaled products, immune aggregates, drugs
  - Physical
    - exercise, cold
  - Other
    - drugs

Mast Cell Activation Syndrome (Monoclonal)
- Associated with idiopathic anaphylaxis and more severe manifestations of anaphylaxis from Hymenoptera
- Basal tryptase > 11.5 ng/ml
- May be form fruste of systemic mastocytosis (Eur J Clin Invest 2007;37:435)
Differential Diagnosis

**Anaphylaxis**
- Exercise
- Cold, heat, sunlight
- Idiopathic

**Vasopressor Reactions**
- Flush syndromes (carcinoid, menopause)
- Medullary carcinoma thyroid
- Autonomic epilepsy
- Vasovagal reaction

**Excess Endogenous Histamine Production**
- Systemic mastocytosis
- Urticaria pigmentosa
- Leukemia
- Hydatid cyst

**Miscellaneous**
- "Restaurant syndromes"
- Other forms of shock
- Seizure
- Transfusion

**Non-organic Disease**
- Panic attacks
- Vocal cord dysfunction
- Munchausen stridor
- Globus hystericus

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**Tryptase in Anaphylaxis**
- Peaks 60-90 minutes after symptom onset and remains elevated for up to 5 hr
- Beta tryptase is secreted during anaphylaxis but elevated in 20-60%
- Ratio of total tryptase (alpha + beta) to beta > 20 suggests mastocytosis (not available clinically)

_JACI 2000;106:65_

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**Time course for the appearance of tryptase in serum or plasma during systemic anaphylaxis**

*Working Group of the Resuscitation Council (UK) January 2008*

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**Severe Anaphylaxis: Additional Mechanisms**
- Complement activation
  - Decreased C3, C4; Increased C3a
- Coagulation pathway activation
  - Decreased Factor V, VIII and Fibrinogen
- Kallikrin-kinin contact system activation
  - Decreased HMW kininogen
  - Increased bradykinin

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**Epinephrine (adrenaline) effects**

Major causes of death

- 214 deaths reported by Pumphrey in which the cause was determined in 196
- 88 shock
- 96 asphyxia (49 lower airway, 22 upper, 25 both or unspecified)
- 7 DIC
- 5 Epinephrine overdose
- Severity previous reaction not predictive

Pumphrey RSH: Clin Exp Allergy 2000;30,1144

Thank you.