

## Case Report

37 y/o WF

- Hx of stable asthma, allergic rhinitis
- Nonsmoker
- Meds: albuterol PRN, cetirizine, budesonide/formoterol, emetine, fluticasone intranasal

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- Received maintenance allergy immunotherapy injection (Rx'd for 2yr)
  - Described a sensation of warmth with minimal generalized itching and nausea 10 minutes after injection
  - BP 100/60, Pulse 88, Resp 16 nonlabored
  - No rash, chest without wheeze

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- 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

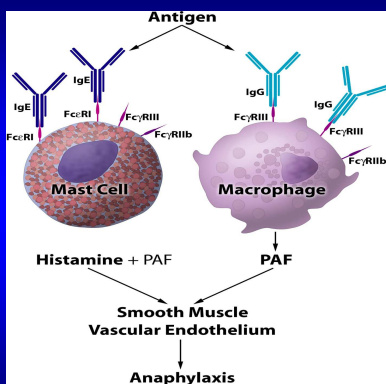
WAO Journal, July 2008

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

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- Rxd 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



JACI 2005;115:450

## 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 PGE<sub>2</sub>.
- The influence of epinephrine on PAF has not been elucidated.

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

## 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.

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

## Objective

- Using human vascular smooth muscle cells, the effect of epinephrine addition on the action PAF-mediated prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) release was examined.

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

## Results

- HVSMC stimulated with PAF released PGE<sub>2</sub> in a concentration- and time-dependent manner.
- Preincubation of HVSMC with epinephrine before PAF suppressed PGE<sub>2</sub> release
- Treatment with epinephrine after PAF stimulation was less effective in suppressing PGE<sub>2</sub> release.

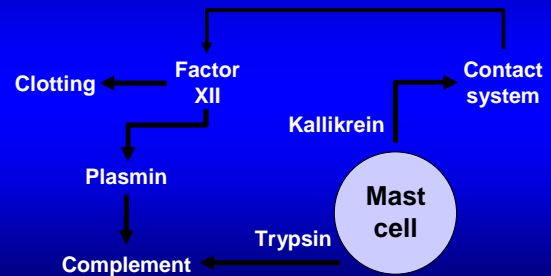
Vadas P, Perelman B. *J Allergy Clin Immunol* 2012;129:1329-33

## Conclusions

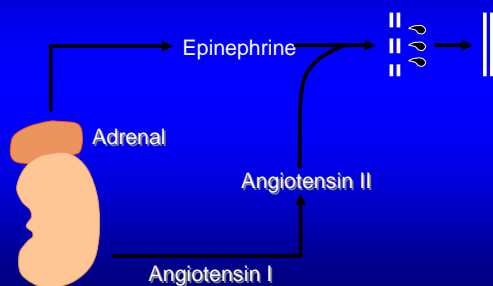
- PAF induced PGE<sub>2</sub> release from HVSMCs in a concentration- and time-dependent manner.
- Early addition of epinephrine controlled PAF-induced release of PGE<sub>2</sub>.
- Epinephrine most effective when administered before stimulation with PAF and less effective with time after PAF stimulation.

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

## Pathway Activation During Anaphylaxis



## Endogenous Compensatory Mechanisms



## 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?

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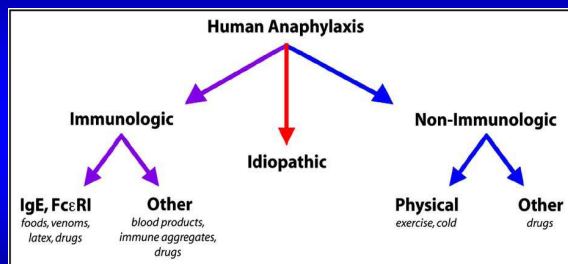
### Risk Factor if Atopic

Agents given orally  
Idiopathic  
Exercise  
Latex  
Radiocontrast

### Not Risk Factor

Most parenteral  
Penicillin  
Insulin  
Hymenoptera  
Most drugs

## Terminology



Simons FER. JACI 2006;117:367-377.

## 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

### Non-organic Disease

- Panic attacks
- Vocal cord dysfunction
- Munchausen stridor
- Globus hystericus

### Miscellaneous

- Hereditary angioedema
- Pheochromocytoma
- Red man syndrome
- Capillary leak syndrome

### Miscellaneous cont'd

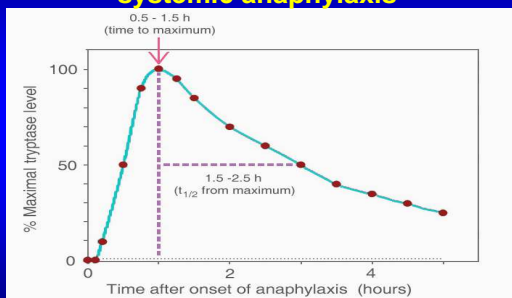
- "Restaurant syndromes"
- Other forms of shock
- Seizure
- Transfusion

## Tryptase in Anaphylaxis

- Peaks 60-90 minutes after symptom onset and remains elevated for up to 5hr
- 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

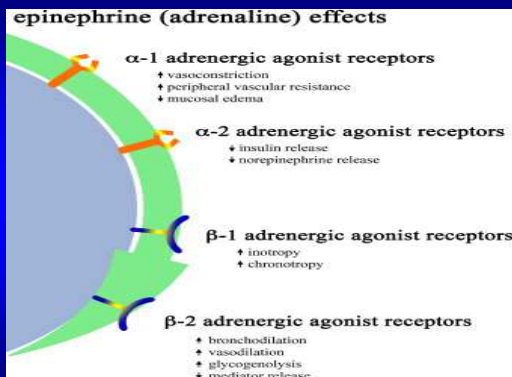
## Time course for the appearance of tryptase in serum or plasma during systemic anaphylaxis



Working Group of the Resuscitation Council (UK) January 2008

## 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



	Onset of shock	After a few minutes without treatment	Prolonged shock
Systemic vascular resistance	↘	↘	↗
Cardiac output	↗	↘	↘
Systolic volume	↗	↘	↘
Cardiac rate	± ↗	↗	↗
Central venous pressure (CVP)	Stable	↘	↘
Pulmonary capillary wall pressure (PCWP)	Stable	↘	↘

Nicolas F, Villers D, and Blanloeil Y. Crit Care Med. 1984;12(2):144-145.

## 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.