

# Anaphylaxis

Vu Kiet Tran, MD, FCFP, MHSc, MBA  
University Health Network  
University of Toronto

# Case 1

- 19yo woman presents to your office because of a rash
- She ate a salad 30 minutes ago at a Thai restaurant
- She now complains of itchy palms and sensation of throat swelling
- She also complains of shortness of breath

# Case 1

- What more would you need to know?
- What features constitute the diagnosis of anaphylaxis?
- What treatment would you offer at this time?

# True or false?

- This patient is having an allergic reaction only
  - True or False?
- At this point, she just needs Diphenhydramine
  - True or False?
- Epinephrine is best given subcutaneously
  - True or False



# Case 2

- 65yo male presents in respiratory distress after eating shrimps in a restaurant
- On arrival, his BP was 90/50 and pulse was 120.
- His respiration rate is 28 and O2 saturation was 94% on RA
- He is very wheezy at the mouth
- He has a diffuse urticaria

# Case 2

- He was treated in the ED successfully and was discharged
- He now presents to your office 1-2 days later

# True or false?

- This patient is aware of his action plan should it recur
  - True or False?
- He should be prescribed an Epinephrine auto-injector
  - True or False?

# Objectives

- Recognize anaphylaxis
- Manage anaphylaxis
- Initiate treatment for anaphylaxis
- Elaborate strategy for discharge
- Prevent further episode of anaphylaxis

# Table of content

- Definition
- Pathophysiology
- Epidemiology
- Etiology
- Manifestations
- Management
- Therapy
- Prevention

# Definition

- Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death
- Sampson et al. 2006

# Definition

- Anaphylaxis  
Immediate *IgE-mediated* hypersensitivity reaction
- Anaphylactoid  
Immediate *non-IgE-mediated* hypersensitivity reaction

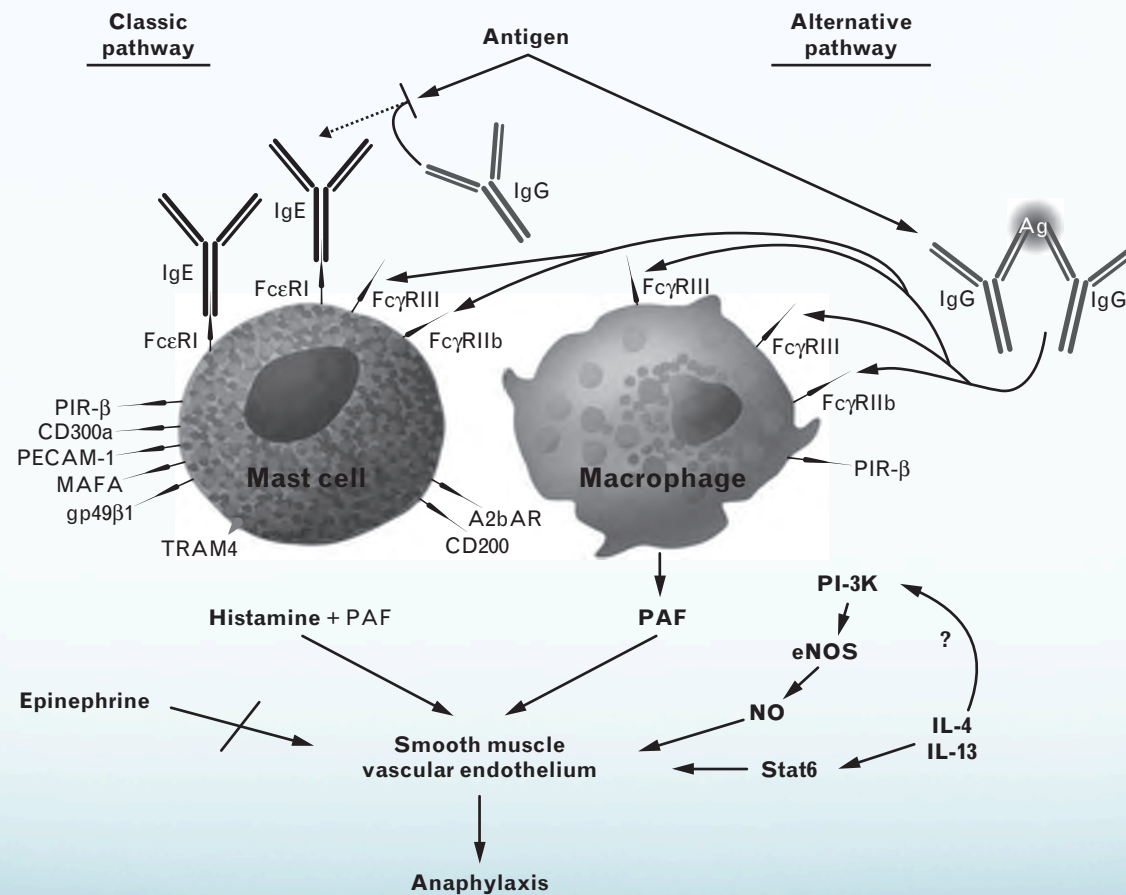
However, clinically, there is no difference between the two reactions

# Pathophysiology

- The IgE-dependent response consists of an allergen binding to the Fab portion of IgE, resulting in a cross-linking of FcεRI receptor present on the mast cells and basophils, activating many proteins, including protein kinases.
- The IgE-independent response is activated by IgG or complement



# Pathophysiology



# Mechanisms






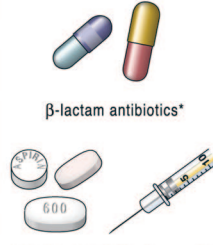






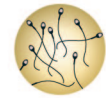




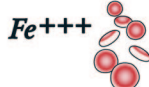
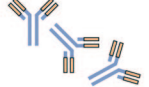
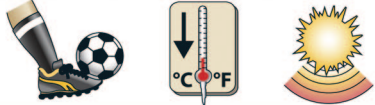



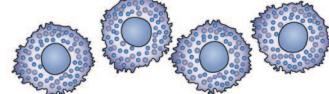
## IgE-dependent

- Insect bites
- Medications
- Latex
- Peanuts
- Tree nuts
- Shellfish and fish
- Milk
- Eggs
- wheat

## Non-IgE-dependent

- Anaphylactoid reaction
- Exercise-induced
- Idiopathic
- Radiocontrast agents
- Opiates
- NSAIDS

# Anaphylaxis mechanisms

IMMUNOLOGIC MECHANISMS (IgE dependent)					
 peanut	 tree nuts	 shellfish	 fish	 stinging insects	 β-lactam antibiotics* NSAIDs* ** biologic agents*
 milk	 egg	 soybean	 peach		
Foods		Venoms		Medications*	
 Natural rubber latex	 Occupational allergens	 Seminal fluid	 Aeroallergens	 Radiocontrast media*	
IMMUNOLOGIC MECHANISMS (IgE independent)					
 Radiocontrast media*	 NSAIDs* **	 Dextran (e.g. HMW*** iron or other source)	 Biologic agents* (e.g. some monoclonal antibodies)		
NONIMMUNOLOGIC MECHANISMS (Direct mast cell activation)					
 Physical factors (e.g. exercise, cold, heat, sunlight)	 Ethanol	 Medications* (e.g. opioids)			
IDIOPATHIC ANAPHYLAXIS (No apparent trigger)					
 Previously unrecognized allergen?	 Mastocytosis/clonal mast cell disorder?				
*Trigger anaphylaxis by more than one mechanism    **NSAIDs, non-steroidal anti-inflammatory drugs    ***HMW, high molecular weight					

# Major mediators of anaphylaxis

Mediators/cells	Action
Histamine (H1-H4)	Pruritus, tachycardia, rhinorrhea, bronchospasm, endothelial release of NO (vasodilatation and hypotension), flushing, headache
Tryptase	Activates complement and kalikrein-kinin system leading to <ul style="list-style-type: none"><li>• Angioedema</li><li>• Hypotension</li><li>• CIVD</li></ul>
Platelet Activating Factor	Systemic mast cell activation
Eosinophils	Pro-inflammatory

# Epidemiology

- Incidence: 4-50 cases per 100 000 people per year
- Prevalence: 0.5-2% (Lieberman et al. 2006)
- Population-based estimates are not reliable
  - Case not reported
  - Case no diagnosed
  - Data is not extensive
- Incidence seems to be increasing for last decade
- Young patients are mainly involved

# Epidemiology

- Incidence of anaphylaxis is increasing in US, Australia, UK
- Rise is the highest in the youngest age group
  - Children < 5yo had the highest rate of hospital admission
- Food being the most common trigger

# Epidemiology

- Mortality is also difficult to estimate
  - Less than 2% (Moneret-Vautrin et al. 2005)
- Fatal anaphylaxis could be responsible for > 1000 deaths per year in the US
- Half of the deaths are caused by *Penicillin*
- Young women are especially affected by *food anaphylaxis*
- Older men are especially affected by *insect bites*

# Epidemiology

- Deaths from food anaphylaxis have remained stable
- Death by insect stings have fallen by 88%
- Death from drug-induced anaphylaxis have risen 300% in the last decade



# Anaphylaxis in Children

- 80% of identified anaphylactic reactions are due a **food trigger**
  - Affects 6% of young children
  - Most commonly implicated:
    - Peanuts
    - Tree nuts (walnut, hazel, nut/filbert, cashew, pistachio, Brazil nut, pine nut, almond)
    - Fish
    - Shellfish (shrimp, crab, lobster, oyster, scallops)
    - Milk (cow, goat)
    - Chicken eggs
    - Fruit, vegetables

# Anaphylaxis in Children

- Cow's milk is the first foreign proteins ingested by infants
  - Potent allergens
  - Presence is widespread (often unlabelled)
- Sensitivity can be severe (reaction to particle inhalation)
- Severe allergy to pollen can indicate susceptibility to food anaphylaxis
  - Homologous proteins found between pollen and foods (**Profilin**)

# Causes of anaphylaxis

Causes	Comments
Food (30%)	<ul style="list-style-type: none"><li>• Most common cause of anaphylaxis in children</li><li>• Nuts, especially peanuts are the most common cause of food anaphylaxis in the US</li><li>• Tendency to be severe</li><li>• Can occur with first recognized exposure (often nuts are hidden in food)</li></ul>
Insect (11%)	<ul style="list-style-type: none"><li>• Order of <i>Hymenoptera</i><ul style="list-style-type: none"><li>• <i>Bees</i></li><li>• <i>Vespids</i> (yellow jackets, hornets, wasps)</li><li>• <i>Stinging ants</i></li></ul></li></ul>

# Causes of anaphylaxis

Causes	Comments
Drugs (22%)	<ul style="list-style-type: none"><li>• Antibiotics</li><li>• NSAIDS</li><li>• Biologics</li></ul>
Exercise-induced	<ul style="list-style-type: none"><li>• In some exercise alone can induce anaphylaxis</li><li>• Many require a co-factor<ul style="list-style-type: none"><li>• Food-dependent<ul style="list-style-type: none"><li>• Wheat</li><li>• Shellfish</li><li>• Tomatoes</li><li>• Peanuts</li><li>• Corn</li></ul></li><li>• Typically, food is ingested 4-6h prior to exercise</li></ul></li></ul>
Idiopathic (30%)	<ul style="list-style-type: none"><li>• Baseline Tryptase should be measured to exclude mastocytosis</li></ul>

# Causes of anaphylaxis

## Some Causes of Anaphylaxis and Anaphylactoid Reactions

### Foods

Bananas, beets, buckwheat, Chamomile tea, citrus fruits, cow's milk,\* egg whites,\* fish,\* kiwis, mustard, pinto beans, potatoes, rice, seeds and nuts (peanuts, Brazil nuts, almonds, hazelnuts, pistachios, pine nuts, cashews, sesame seeds, cottonseeds, sunflower seeds, millet seeds),\* shellfish\*

### Venoms and saliva

Deer flies, fire ants, *Hymenoptera* (bees, wasps, yellow jackets, sawflies),\* jellyfish, kissing bug (*Triatoma*), rattlesnakes

### Antibiotics

Amphotericin B (Fungizone), cephalosporins, chloramphenicol (Chloroptic), ciprofloxacin (Cipro), nitrofurantoin (Furadantin), penicillins,\* streptomycin, tetracycline, vancomycin (Vancocin)

### Aspirin and nonsteroidal anti-inflammatory drugs\*

### Miscellaneous other medications

Allergy extracts, antilymphocyte and antithymocyte globulins, antitoxins, carboplatin (Paraplatin), corticotropin (H.P. Acthar), dextran, folic acid, insulin, iron dextran, mannitol (Osmitol), methotrexate, methylprednisolone (Depo-Medrol), opiates, parathormone, progesterone (Progestasert), protamine sulfate, streptokinase (Streptase), succinylcholine (Anectine), thiopental (Pentothal), trypsin, chymotrypsin, vaccines

### Latex rubber\*

### Radiographic contrast media\*

### Blood products

Cryoprecipitate, immune globulin, plasma, whole blood

### Seminal fluid

### Physical factors

Cold temperatures, exercise

### Idiopathic\*

# Food anaphylaxis

- Leading cause of anaphylaxis treated in the ED in the US
- Cumulative prevalence of 3-6%
- Cardiovascular system is less affected than other anaphylaxis
- Food-dependent exercise-induced anaphylaxis occurs within 2-6h of ingestion
  - Anaphylaxis does not occur in the absence of exercise

# Food anaphylaxis

- Patients with asthma and adolescents are at increased risk for severe food anaphylaxis
- Among reactions to food, most occurred in Asian restaurants, ice cream parlors and bakeries
- Death usually occur within 30 minutes of ingestion
  - Missing cutaneous reaction is a risk factor for death
  - Fatal reactions are associated with asphyxia

# Insect bite anaphylaxis

- Typically occur in children and adolescents
- However, fatalities are more common in middle-aged and older adults
- Fatal reactions are associated with **cardiovascular shock**



# Insect bite anaphylaxis

- 2 types of reactions
  - Local
    - Erythema, swelling, and pain confined to the tissues contiguous to the sting site
  - Systemic
    - Systemic manifestations of varying severity
    - Urticaria, angioedema, abdominal pain, diarrhea, airway obstruction, bronchospasm, shock

# Pitfalls in the ED

- Lack of
  - Epinephrine use
  - Prescription of auto-injectors
  - Follow-up by an allergist

# Differential Diagnosis

**Table 2. Differential diagnosis of anaphylaxis**

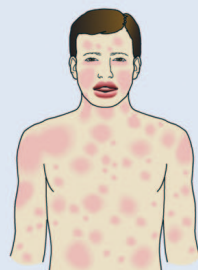
Urticaria	Asthma	Cardiogenic shock	Syncope	Acute coronary syndrome	Systemic mastocytosis
Angioedema	Inhalation of foreign body	Hypovolemic shock	Panic attack with hyperventilation	Arrhythmia	Mast cell leukemia
Epiglottitis	Pulmonary embolism		Cerebral vascular accident		
Scromboidosis	Acute respiratory distress				
Carcinoid syndrome					
Flushing disorders					
Vancomycin flushing					
Transfusion reaction					

# Clinical Diagnosis

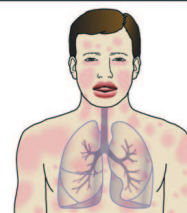
**Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:**

**1**

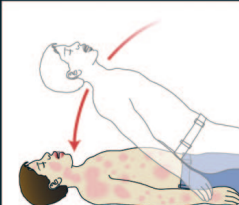
Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)



AND AT LEAST ONE OF THE FOLLOWING:



**Sudden respiratory symptoms and signs**  
(e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)



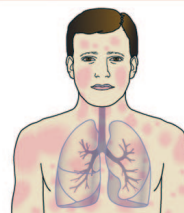
**Sudden reduced BP or symptoms of end-organ dysfunction** (e.g. hypotonia [collapse], incontinence)

**OR 2**

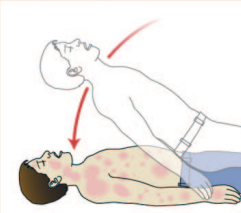
Two or more of the following that occur suddenly after exposure to a *likely allergen or other trigger\** for that patient (minutes to several hours):



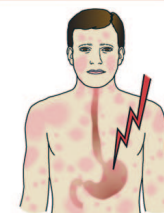
**Sudden skin or mucosal symptoms and signs**  
(e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)



**Sudden respiratory symptoms and signs**  
(e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)



**Sudden reduced BP or symptoms of end-organ dysfunction** (e.g. hypotonia [collapse], incontinence)



**Sudden gastrointestinal symptoms** (e.g. crampy abdominal pain, vomiting)

**OR 3**

Reduced blood pressure (BP) after exposure to a *known allergen\*\** for that patient (minutes to several hours):



**Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP\*\*\***



**Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline**

\* For example, immunologic but IgE-independent, or non-immunologic (direct mast cell activation)

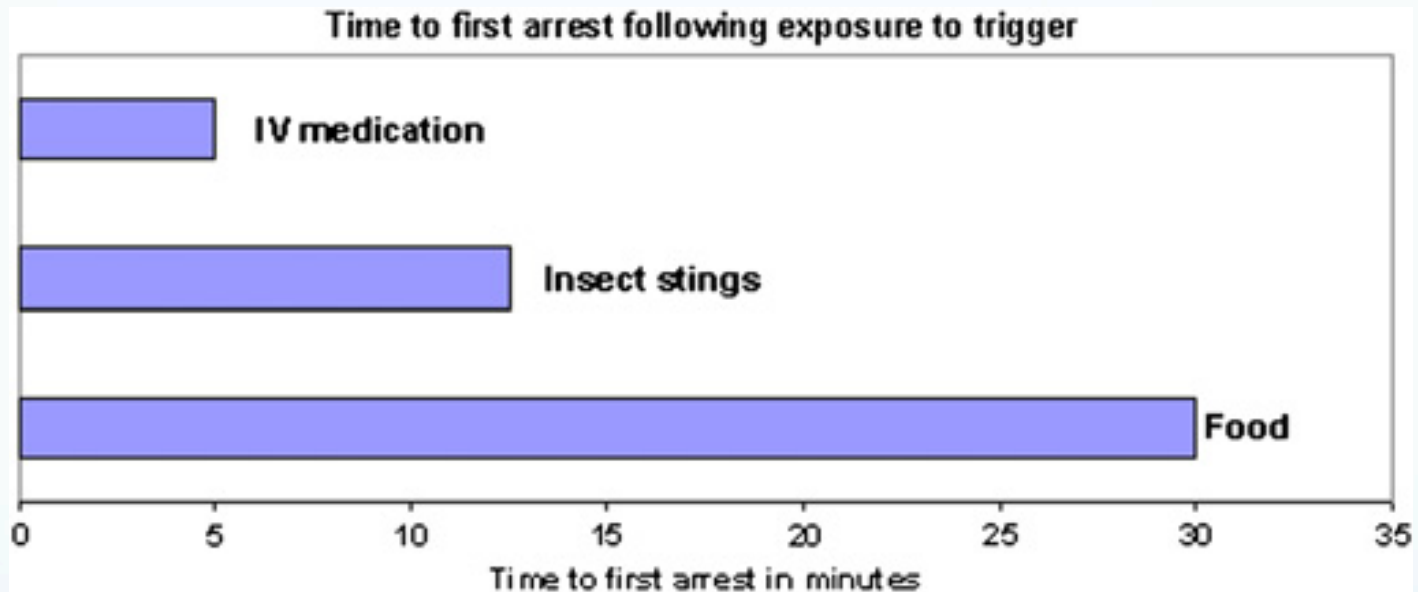
\*\* For example, after an insect sting, reduced blood pressure might be the only manifestation of anaphylaxis; or, after allergen immunotherapy, generalized hives might be the only initial manifestation of anaphylaxis.

\*\*\* Low systolic blood pressure for children is defined as less than 70 mm Hg from 1 month to 1 year, less than (70 mm Hg + [2 x age]) from 1 to 10 years, and less than 90 mm Hg from 11 to 17 years. Normal heart rate ranges from 80-140 beats/minute at age 1-2 years; from 80-120 beats/minute at age 3 years; and from 70-115 beats/minute after age 3 years. In infants and children, respiratory compromise is more likely than hypotension or shock, and shock is more likely to be manifest initially by tachycardia than by hypotension.

# Time is anaphylaxis

- Symptoms frequent occur within 5-30 minutes after the exposure to a trigger, but sometimes they may not occur for several hours
- Time between allergen contact and *death* can range from
  - 5 minutes (drug injection)
  - 10-15 minutes (insect bite)
  - 35 minutes (food allergies)

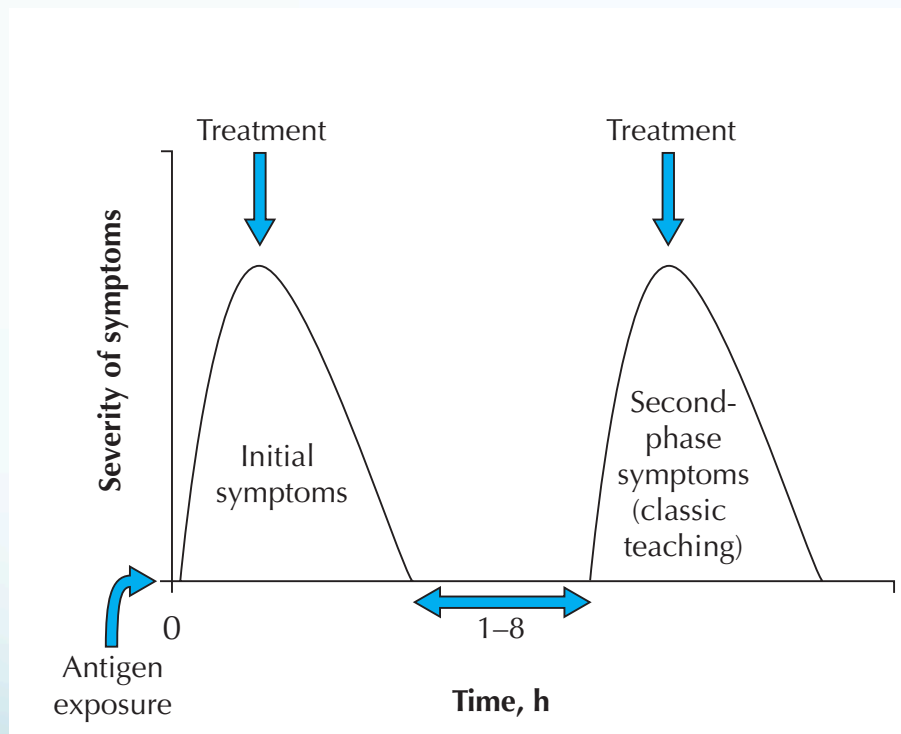
# Time is anaphylaxis



# Clinical features

- Presents with a range of clinical symptoms of varying severity
- Diagnosis is made by the typical pattern of clinical features with rapid progression of symptoms, often with a history of a preceding trigger

# Biphasic anaphylactic reaction



- Biphasic anaphylaxis (despite no further re-exposure to the allergen) has been reported to occur in up to 20% of adults
- Can occur as late as 24-38 hours later
- 1/3 can be more severe than the initial reaction



# Symptoms and Signs

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**TABLE 2.** Symptoms and Signs of Anaphylaxis

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Skin, subcutaneous tissue, and mucosa<sup>a,b,c</sup>

Flushing, itching, urticaria (hives), angioedema, morbilliform rash, pilor erection

Periorbital itching, erythema and edema, conjunctival erythema, tearing

Itching of lips, tongue, palate, and external auditory canals; and swelling of lips, tongue, and uvula

Itching of genitalia, palms, and soles

Respiratory<sup>a</sup>

Nasal itching, congestion, rhinorrhea, sneezing

Throat itching and tightness, dysphonia, hoarseness, stridor, dry staccato cough

Lower airways: increased respiratory rate, shortness of breath, chest tightness, deep cough, wheezing/bronchospasm, decreased peak expiratory flow

Cyanosis

Respiratory arrest

Gastrointestinal<sup>a</sup>

Abdominal pain, nausea, vomiting (stringy mucus), diarrhea, dysphagia

Cardiovascular system<sup>a</sup>

Chest pain

Tachycardia, bradycardia (less common), other arrhythmias, palpitations

Hypotension, feeling faint, urinary or fecal incontinence, shock

Cardiac arrest

Central nervous system<sup>a</sup>

Aura of impending doom, uneasiness (in infants and children, sudden behavioral change, eg. irritability, cessation of play, clinging to parent); throbbing headache (pre-epinephrine), altered mental status, dizziness, confusion, tunnel vision

Other<sup>a</sup>

Metallic taste in the mouth

Cramps and bleeding due to uterine contractions in females

# Symptoms

- “*Angor animi*” (sense of impending doom) is common
- Infrequently, seizures have been reported
- Death is usually due to
  - Respiratory obstruction
  - Cardiovascular collapse

# Symptom frequency

## Frequency of Signs and Symptoms

<i>Signs and symptoms</i>	<i>Frequency (%)</i>
Urticaria, angioedema	88
Dyspnea, wheeze	47
Dizziness, syncope, hypotension	33
Nausea, vomiting, diarrhea, cramping abdominal pain	30
Flush	46
Upper airway edema	56
Headache	15
Rhinitis	16
Substernal pain	6
Pruritus without rash	4.5
Seizure	1.5

# Special circumstances

- *In severe anaphylaxis, rapid cardiovascular compromise and shock can occur without preceding cutaneous features*
- Patients in the ICU or OR
  - Show atypical manifestations
  - Patients cannot voice their symptoms (sedated or intubated)
    - First symptom will be hypotension or shock

# Severe Anaphylaxis

- Risk factors
  - Asthma (5.2 times higher rate of shock)
  - Age < 5
  - Medications: B-Blockers, ACEI, NSAIDS
  - Chronic respiratory diseases
  - Mastocytosis
  - Alcohol
  - Vitamin D insufficiency (correlation with latitude and anaphylaxis)
  - Emotional stress
  - Fever
  - Exercise
  - Delay in Epinephrine administration (*80-87% of fatal cases*)

Clin Exp Allergy 2011; 41: 923-938

WAO J 2011; 4: 13-37

J Allergy Clin Immunol 2011; 125: S161-S181

Pediatr Allergy Immunol 2011; 22: 813-819


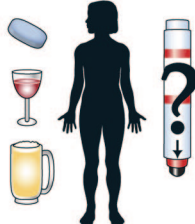

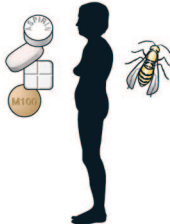


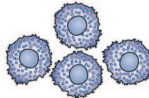








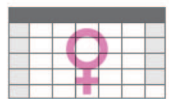
# Anaphylaxis and the heart

- May be complicated by MI and arrhythmia without any underlying cardiac pathology and in the absence of Epinephrine administration

Due to...

- Tachycardia
- Vasodilatation and relative volume depletion
  - Leading to empty vena cava syndrome
  - Coronary hypoperfusion
- PEA if severe refractory shock

## Patient Factors

AGE-RELATED FACTORS*				
				
<b>Infants</b> Cannot describe their symptoms	<b>Adolescents and young adults</b> Increased risk-taking behaviors	<b>Labor and delivery</b> Risk from medications (e.g. antibiotic to prevent neonatal group B strep infection)	<b>Elderly</b> Increased risk of fatality from medication or venom-triggered anaphylaxis	
CONCOMITANT DISEASES*				
				
<b>Asthma and other respiratory diseases</b>	<b>Cardiovascular diseases</b>	<b>Mastocytosis/clonal mast cell disorders</b>	<b>Allergic rhinitis and eczema**</b>	<b>Psychiatric illness</b> (e.g. depression)
CONCURRENT MEDICATIONS/ETHANOL/RECREATIONAL DRUG USE*				
				
<b><math>\beta</math>-adrenergic blockers and ACE inhibitors***</b>		<b>Ethanol/sedatives/hypnotics/antidepressants/recreational drugs</b> (potentially affect recognition of anaphylaxis triggers and symptoms)		
CO-FACTORS THAT AMPLIFY ANAPHYLAXIS*				
				
<b>Exercise</b>	<b>Acute infection</b> (e.g. a cold or fever)	<b>Emotional stress</b>	<b>Disruption of routine</b> (e.g. travel)	<b>Premenstrual status</b> (females)
<p>* Age-related factors, concomitant diseases, and concurrent medications potentially contribute to severe or fatal anaphylaxis. Co-factors potentially amplify anaphylaxis. Multiple factors and co-factors likely contribute to some anaphylactic episodes.</p> <p>** Atopic diseases are a risk factor for anaphylaxis triggered by food, exercise, and latex, but not for anaphylaxis triggered by insect stings.</p> <p>*** ACE, angiotensin-converting enzyme</p>				

# Lab tests

Assay	Timing	Comments
Total Tryptase	15min-3h from symptom onset	<ul style="list-style-type: none"><li>• Consider measuring levels in accurately timed serial blood samples during the anaphylactic episode</li><li>• Compare levels measured during the episode with baseline level</li><li>• Increased levels compared with basal levels confirms anaphylaxis</li><li>• Normal levels in the first sampling does not rule out anaphylaxis</li></ul>
Histamine	15min-1h of symptom onset	<ul style="list-style-type: none"><li>• Measure histamine and its metabolite N-Methylhistamine in a 24-h urine sample</li></ul>



# Serum Tryptase

- Useful when diagnosing anaphylaxis to objectively look for mast cell activation
- Peak at 1-2h after onset
- Elevation persists several hours
- First level should be measured immediately on arrival to the ED
- A second level should be measured 1-2h after the onset

# Serum Tryptase

- Elevated Tryptase is also found in:
  - Acute myelocytic leukemia
  - Myelodysplastic syndromes
  - End-stage renal disease with endogenous stem cell factor elevation
- *Lack of Tryptase elevation in food-induced anaphylaxis*

# Serum Histamine

- Short half-life
- Peaks at 5 minutes
- Remains elevated for 30-60 minutes
- Handling process is complicated and the samples require careful treatment
  - Not routinely available

# Practice gaps

REVIEW ARTICLE

# **Gaps in anaphylaxis management at the level of physicians, patients, and the community: a systematic review of the literature**

M. Kastner<sup>1</sup>, L. Harada<sup>2</sup> & S. Waserman<sup>3</sup>

<sup>1</sup>Department of Health Policy, Management and Evaluation, Faculty of Medicine, University of Toronto Ontario; Canada; <sup>2</sup>Anaphylaxis Canada, Toronto Ontario, Canada; <sup>3</sup>Department of Medicine, Clinical Immunology and Allergy, McMaster University, Hamilton, ON, Canada

# Gaps in anaphylaxis management

	Gaps	Setting
Lack of knowledge	<ul style="list-style-type: none"> <li>• Signs and symptoms or correctly diagnose</li> <li>• Auto-injectors                             <ul style="list-style-type: none"> <li>• How to use</li> <li>• Correct dose</li> <li>• Route of admin</li> <li>• Inadequate training to patients on how to use</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Army hospital</li> <li>• Pediatric allergy hospital</li> <li>• Tertiary pediatric hospitals</li> <li>• General hospitals</li> <li>• Community hospitals</li> </ul>
Anaphylaxis management	<ul style="list-style-type: none"> <li>• Infrequent treatment with Epinephrine</li> <li>• Delayed administration of Epinephrine</li> </ul>	<ul style="list-style-type: none"> <li>• Pediatric allergy clinic</li> <li>• Allergy clinic</li> <li>• Children's hospitals</li> </ul>
Follow-up care	<ul style="list-style-type: none"> <li>• Infrequent prescription of Epinephrine auto-injectors</li> <li>• No referral to an allergist after an acute episode</li> </ul>	<ul style="list-style-type: none"> <li>• EDs</li> <li>• Tertiary pediatric hospitals</li> <li>• Pediatric and general practices</li> </ul>

# Emergency Department Gaps

- ✓ **12% to 16% of patients received treatment with epinephrine at ED<sup>1,2</sup>**
- ✓ **16% to 27% of these patients received a prescription for self-injectable epinephrine<sup>1,2</sup>**



1. Clark S, et al: *J Allergy Clin Immunol* 2004; 113(2):347-52.

2. Clark S, et al: *J Allergy Clin Immunol* 2005; 116(3):643-9.

# Emergency Department Gaps



✓ **15% to 40%** of patients given instructions to avoid the offending **allergen**

✓ **12% to 20%** of patients had **documentation of referral** to an **allergist**

1. Clark S, et al: *J Allergy Clin Immunol* 2004; 113(2):347-52.

2. Clark S, et al: *J Allergy Clin Immunol* 2005; 116(3):643-9.



# Patient Gaps

- ✓ Lack of information of food allergen avoidance<sup>1</sup>
- ✓ No anaphylaxis management plan<sup>1,2</sup>
- ✓ Receive inadequate or no instruction or training on how to use auto-injectors<sup>1</sup>
- ✓ Do not carry, or unavailable at the time of reaction<sup>1,2</sup>
- ✓ Carry epinephrine but do not use it<sup>1</sup>



1. Kastner M, et al: *Allergy* 2010; 65(4):435-44.

2. Gold MS, et al: *J Allergy Clin Immunol* 2000; 106(1 Pt 1):171-6.

# Gaps in anaphylaxis management

- Insufficient knowledge of anaphylaxis and its management across all settings
- Insufficient knowledge on how to use an Epinephrine auto-injector
- Lack of clarity among physicians on how to manage a patient at risk of anaphylaxis

## POSITION PAPER

# Management of anaphylaxis in primary care: Canadian expert consensus recommendations

S. Wasserman<sup>1</sup>, Z. Chad<sup>2</sup>, M. J. Francoeur<sup>3</sup>, P. Small<sup>4</sup>, D. Stark<sup>5</sup>, T. K. Vander Leek<sup>6</sup>, A. Kaplan<sup>7</sup> & M. Kastner<sup>8</sup> [Correction added after online publication, 24 June 2010: First author's initial changed from 'D' to 'S'.]

<sup>1</sup>Department of Medicine, Clinical Immunology and Allergy, McMaster University, Hamilton, ON; <sup>2</sup>Department of Pediatrics, Allergy and Clinical Immunology, University of Ottawa, Ottawa, ON; <sup>3</sup>Médecin spécialiste en allergie pédiatrique, Spécialité en allergie et immunologie clinique pédiatrique, Hôpital de Montréal pour enfants, Université McGill, Montreal, QC; <sup>4</sup>Department of Medicine, Allergy and Clinical Immunology, McGill University, Montreal, QC; <sup>5</sup>Department of Medicine, Clinical Immunology and Allergy, University of British Columbia, Vancouver, BC; <sup>6</sup>Department of Pediatrics, Division Clinical Immunology and Allergy, University of Alberta, Edmonton, AB; <sup>7</sup>Department of Family Medicine, University of Toronto, Toronto, ON; <sup>8</sup>Department of Health Policy, Management and Evaluation, Faculty of Medicine, University of Toronto, Toronto, ON, Canada

# 30 Primary Care gaps

## Knowledge gaps

- Patients are not Dx accurately
- Patients are unsure when or how to use auto-injectors
- Parents of children with allergies have unmet information needs from their physicians
- Inadequate knowledge of anaphylaxis
- Few physicians know how to use auto-injectors
- Lack of knowledge on appropriate dosage of Epinephrine
- Confusion on appropriate route for Epinephrine
- Patients are not given action plans

## Practice Behavior gaps

- Few patients are being referred to a specialist after an allergic reaction
- Epi not given or administration was delayed
- Epi use was infrequent
- Patients receive no instruction on how to use the auto-injectors
- Epi auto-injectors prescription rate is low
- Few patients are given accurate information and advice by their GPs about managing anaphylaxis
- Lack of follow-up is common
- Few patients are given discharge instructions from the ED
- Physicians did not think that going to the hospital was necessary after taking Epinephrine

# Evidenced-based recommendations

**Table 4** Classification of levels of evidence and strength of recommendation\*

Category of evidence	Description	Strength of recommendation	Description
Ia	Evidence from meta-analysis or randomized controlled trials	A	Directly based on category I evidence
Ib	Evidence from at least one RCT	B	Directly based on category II evidence or extrapolated recommendation from category I evidence
IIa	Evidence from at least one controlled study without randomization		
IIb	Evidence from at least one other type of quasi-experimental study		
III	Evidence from nonexperimental descriptive studies, such as comparative studies	C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities or both	D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence

**Table 3** Evidence-based consensus recommendation statements

	Strength of recommendation*
<b>Anaphylaxis management</b>	
<u>How do I identify the signs and symptoms of anaphylaxis?</u>	C
Conduct a detailed history in all individuals who have had a known or suspected anaphylactic episode including (66)	
Nature of symptoms during event	
Agents encountered before reaction	
Ingestion of food or drugs	
Preceding bite or sting	
Complete sequence of events	
Activities preceding event such as exercise, sexual activity	
Prompt recognition of acute onset of systemic symptoms including (5, 64)	C
Mouth: Itching, swelling of lips/tongue	
Throat: Itching, tightness, closure, hoarseness	
Skin: Itching, hives, eczema, swelling, flushing	
Gut: Vomiting, diarrhea, abdominal pain	
Lung: Shortness of breath, cough, wheeze	
Heart: Hypotension, dizziness, syncope, tachycardia	
Neuro (or head): Lightheadedness	
Other: Feeling of impending doom, anxiety	
<u>How do I treat anaphylaxis?</u>	D
Epinephrine is the drug of choice for anaphylaxis (5, 58, 64, 66)	
Antihistamines should not be used as first-line treatment for anaphylactic reactions (5, 66)	
Prescribing epinephrine auto-injectors (5, 64, 66)	D
Prescribe epinephrine auto-injector to	
All patients who have experienced anaphylaxis previously (64, 66)	
Anybody who has ANY rapid onset systemic allergic reaction (GI, respiratory, cardiac) or diffuse hives to any food or stings (5, 64)	
Anybody who has ANY rapid onset (i.e., minutes to hours) reaction of any severity to highest risk foods such as peanut, tree nuts, fish, shellfish, sesame (5, 64)	
Additional high risk factors which support the need for epinephrine (64)	
Previous need for epinephrine or hospitalization	
Repeated reactions to the suspected food	
Symptoms caused by minute quantities of allergenic foods	
Age (teens and young adults)	
Allergic reaction with exercise	
Significant medical conditions (e.g., asthma, cardiovascular disease)	
Acute treatment with epinephrine (5, 58, 64, 66)	
ANY critically ill patient, treatment of anaphylaxis begins with rapid assessment of airway, breathing and circulation (5, 58, 64, 66)	C
Patient should receive epinephrine immediately (5, 58, 64, 66)	D
No contraindication to the use of epinephrine, if uncertain, err on the side of treatment (58, 64)	C
All patients receiving emergency epinephrine must be transported to hospital immediately for evaluation and observation (e.g. 911) (5, 58, 64, 66)	D
Additional epinephrine must be available during transport to hospital. A second dose may be administered 5–20 min after the first dose is given if symptoms have not improved (58, 66)	D
Patients with asthma (64)	
Asthmatics, especially those with poorly controlled asthma are at increased risk of a fatal allergic reaction	C
Anaphylaxis may be mistaken for asthma exacerbation and inappropriately treated solely with asthma inhalers	C–D
If there are ongoing asthma symptoms in an individual with known anaphylaxis, epinephrine should be given	D

**Table 3** (Continued)

	Strength of recommendation*
<b>Epinephrine use</b>	
<u>What is the correct dose?</u>	D
Acute care setting (5, 64, 66)	
Dosing of epinephrine is 0.01 mg/kg up to a maximum of 0.5 mg	
Administer intramuscularly for every 5–20 min as necessary	
Patient self-administration of auto-injectors (64)	D
>25 kg = 0.30 mg	
<25 kg = 0.15 mg	
<u>What is the correct route of administration and positioning?</u>	A
Intramuscular administration (5, 58, 66)	
A more rapid absorption and higher plasma epinephrine levels when epinephrine is administered intramuscularly in the anterior-lateral thigh with an auto-injector when compared with values after subcutaneous administration	
Positioning of the patient (5, 58, 66)	C
Patients in anaphylactic shock should be placed in a recumbent position with the lower extremities elevated unless precluded by shortness of breath or vomiting	
<b>Follow-up care</b>	
<u>What happens after an anaphylactic reaction?</u>	C
Observation (5)	
After treatment of an anaphylactic reaction, patients should be observed because the reaction might recur as the effect of epinephrine wears off and because of the risk of a biphasic reaction	
A biphasic reaction occurs in 1–20% of anaphylactic reactions ranging from 1 to 72 h	
Recommend observation periods be individualized on the basis of the severity of the initial reaction, reliability of the patient, and access to care (consider observing patients for 4–6 h postanaphylactic reaction; consider prolonged observation times or hospital admission for patients with severe or refractory symptoms)	
Referral to an Allergist (5, 66)	D
After acute anaphylaxis, patients should be assessed for future risk for anaphylaxis (5, 66)	
Anybody who has ANY rapid onset systemic allergic reaction (GI, respiratory, cardiac) or diffuse hives to any food or stings	
Anybody who has ANY rapid onset (i.e., minutes to hours) reaction of any severity to highest risk foods such as peanut, tree nuts, fish, shellfish, sesame	
If uncertain, refer patient to allergist for evaluation (66)	
<u>What do patients need to know about their anaphylaxis?</u>	C
All patients should receive information about how to avoid the precipitating allergen (if known) (5, 66)	
At prescription of an epinephrine auto-injector, healthcare providers must demonstrate to the patient how to and when to use the device (64)	D
Family physicians are encouraged to provide training on how to use an epinephrine auto-injector (66)	D
Patients require repeated follow-up education/demonstrations on how to use devices (66)	D
Suggest learning more about anaphylaxis through patient support groups (5, 64, 66)	D
Provide general information about food allergy and specific information about how to read food labels (especially about peanut, tree nuts, milk, egg, shellfish, fish, sesame, soy and wheat) (66)	C
A comprehensive anaphylaxis action plan should be prepared which defines roles and responsibilities and emergency protocol (5, 64, 66)	D

# Anaphylaxis Protocol

- ✓ **4-year** retrospective/prospective **study**
- ✓ **Anaphylaxis Protocol** based on **EAACI Position Paper**
- ✓ **Education provided** to Residents and ER team



# Anaphylaxis Protocol

## Improvements in:

- Epinephrine use – **27% vs. 57.5%**
- Epinephrine prescription – **6.7% vs. 57.5%**
- Length of stay – **2.5 vs. 9 hours**

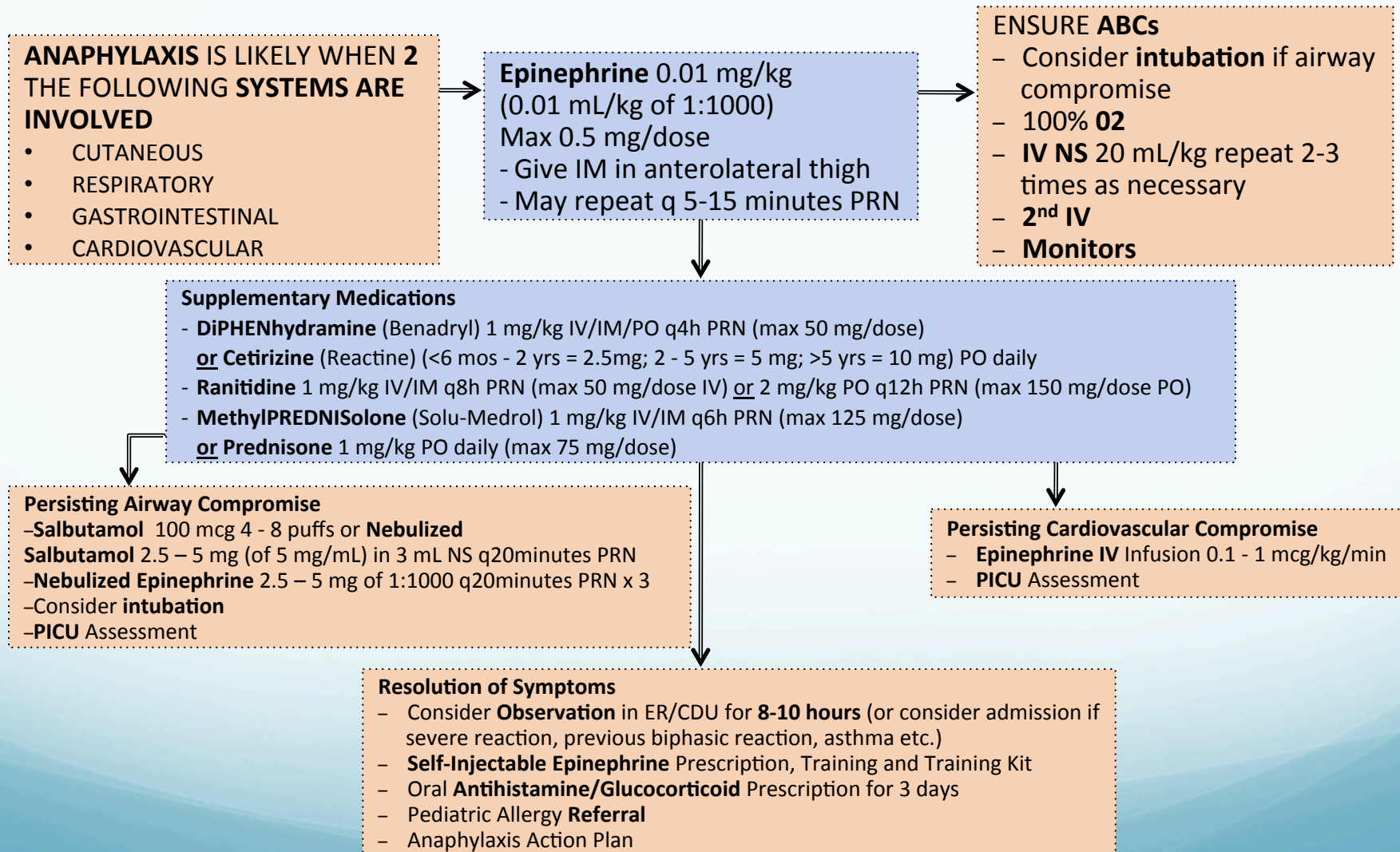
## Reduction in:

- Corticosteroid monotherapy – **29% vs. 3%**
- Patients discharged without follow-up with allergist – **69% vs. 22%**

# Anaphylaxis Protocol

*“The application of the anaphylaxis protocol substantially improved the physicians’ skills to manage this emergency in the Pediatric Emergency Unit”*

# McMaster Pediatric ER Anaphylaxis Treatment Plan



# McMaster Pediatric ER Anaphylaxis Treatment Plan

## ANAPHYLAXIS

THE FOLLOWING

INVOLVES

1. CUTANEOUS

2. RESPIRATORY

3. GASTROINTESTINAL

4. CARDIOVASCULAR

**Epinephrine 0.01 mg/kg**  
(0.01 mL/kg of 1:1000)

Max 0.5 mg/dose

-Give IM in anterolateral thigh

-May repeat q 5-15 minutes PRN

## Persistent Symptoms

- Salbutamol

Salbutamol 2.5 - 5 mg (of 5 mg/mL) in 3mL NS q20minutes PRN

- Nebulized Epinephrine 2.5 - 5 mg of 1:1000 q20minutes PRN x 3

- Consider intubation

- PICU Assessment

- Epinephrine IV Infusion 0.1-1 mcg/kg/min

- PICU Assessment

## Resolution of Symptoms

- Consider **Observation** in ER/CDU for **8-10 hours** (or consider admission if severe reaction, previous biphasic reaction, asthma etc.)

- **Self-Injectable Epinephrine** Prescription, Training and Training Kit

- Oral **Antihistamine/Glucocorticoid** Prescription for 3 days

- Pediatric Allergy **Referral**

- Anaphylaxis Action Plan

# McMaster Pediatric ER Anaphylaxis Treatment Plan

**ANAPHYLAXIS IS LIKELY WHEN 2  
THE FOLLOWING SYSTEMS ARE  
INVOLVED**  
1. CUTANEOUS

⇒ **Epinephrine** 0.01 mg/kg  
(0.01 mL/kg of 1:1000)  
Max 0.5 mg/dose  
- Give IM in anterolateral thigh

⇒ **ENSURE ABCs**  
- Consider **intubation** if airway  
compromise  
- 100% **O<sub>2</sub>**

## Supplementary Medications

- **DiPHENhydramine** (Benadryl) 1 mg/kg IV/IM/PO q4h PRN (max 50 mg/dose)  
or **Cetirizine** (Reactine) (<6 mos - 2 yrs = 2.5mg; 2 - 5 yrs = 5mg; >5 yrs = 10 mg) PO daily
- **Ranitidine** 1 mg/kg IV/IM q8h PRN (max 50 mg/dose IV) or 2 mg/kg PO q12h PRN (max 150 mg/dose PO)
- **MethylPREDNISolone** (Solu-Medrol) 1 mg/kg IV/IM q6h PRN (max 125mg/dose)  
or **Prednisone** 1 mg/kg PO daily (max 75 mg/dose)

- PICU Assessment

## Resolution of Symptoms

- **Observation** in ER/CDU for **8-10 hours** (or consider admission if severe reaction, previous biphasic reaction, asthma etc.)
- **Self-Injectable Epinephrine** Prescription, Training and Training Kit
- Oral **Antihistamine/Glucocorticoid** Prescription for 3 days
- Pediatric Allergy **Referral**
- Anaphylaxis Action Plan

# McMaster Pediatric ER Anaphylaxis Treatment Plan

**ANAPHYLAXIS** IS LIKELY WHEN 2  
THE FOLLOWING SYSTEMS ARE  
INVOLVED

1. CUTANEOUS
2. RESPIRATORY
3. GASTROINTESTINAL
4. CARDIOVASCULAR

**Epinephrine** 0.01 mg/kg  
(0.01 mL/kg of 1:1000)  
Max 0.5 mg/dose  
- Give IM in anterolateral thigh  
- May repeat q 5-15 minutes PRN

**ENSURE ABCs**

- Consider **intubation** if airway compromise
- 100% **02**
- **IV NS** 20 mL/kg repeat 2-3 times as necessary
- **2<sup>nd</sup> IV**
- **Monitors**

## Supplementary Medications

- **DiPHENhydramine** (Benadryl) 1 mg/kg IV/IM/PO q4h PRN (max 50mg/dose)  
    or **Cetirizine** (Reactine) (<6 mos – 2 yrs = 2.5mg; 2 - 5 yrs = 5mg; >5 yrs = 10 mg) PO daily
- **Ranitidine** 1 mg/kg IV/IM q8h PRN (max 50 mg/dose IV) or 2 mg/kg PO q12h PRN (max 150 mg/dose PO)
- **MethylPREDNISolone** (Solu-Medrol) 1 mg/kg IV/IM q6h PRN (max 125 mg/dose)  
    or **Prednisone** 1 mg/kg PO daily (max 75 mg/dose)

## Resolution of Symptoms

- Consider **Observation** in ER/CDU for **8-10 hours** (or consider admission if severe reaction, previous biphasic reaction, asthma etc.)
- **Self-Injectable Epinephrine** Prescription, Training and Training Kit
- Oral **Antihistamine/Glucocorticoid** Prescription for 3 days
- Pediatric Allergy **Referral**
- Anaphylaxis Action Plan

# Challenges in Management

- Guidelines are insufficiently applied (Arroabarren et al. 2011)
- Half of patients do not receive Epinephrine (Rudders et al. 2010)
  - When Epi was administered, it was subcutaneous
- Recommendations are based on expert opinion consensus
  - No randomized controlled trials for Epinephrine, Antihistamines, Corticosteroids
  - No randomized human study of epinephrine use

# What is the evidence?

**Table 1 Pharmacologic treatment of anaphylaxis: little high-quality evidence to be found**

	Epinephrine	H <sub>1</sub> -antihistamines	H <sub>2</sub> -antihistamines	Glucocorticoids
Systematic review or meta-analysis of randomized controlled trials in anaphylaxis <sup>a</sup>	No	No	No	No
Individual randomized controlled trials in anaphylaxis (without methodological problems) <sup>a</sup>	No	No	No	No
Observational studies in anaphylaxis (nonrandomized uncontrolled, cohort, or case control studies)	Yes	No	No	No
Retrospective analysis of fatalities <sup>b</sup>	Yes	No	No	No
Retrospective analysis of emergency department visits <sup>b</sup>	Yes	Yes	Yes	Yes
Retrospective population-based cohort studies <sup>b</sup>	Yes	Yes	Yes	Yes
Retrospective surveys <sup>b</sup>	Yes	Yes	Yes	Yes
Clinical experience (nonsystematic clinical observations, including case reports) <sup>b</sup>	Yes	Yes	Yes	Yes
Qualitative studies <sup>b</sup>	Yes	Yes	Yes	Yes
Expert opinion <sup>b</sup>	Yes	Yes	Yes	Yes
Clinical pharmacology studies <sup>c</sup> in patients with a history of anaphylaxis but not experiencing it at the time of study	Yes	No	No	No
Studies in animal models of anaphylaxis, <sup>c</sup> including blinded controlled studies	Yes	Yes	No	No
In vitro studies/molecular pharmacology studies <sup>c</sup>	Yes	Yes	Yes	Yes
References	[1 <sup>•</sup> ,7–13,14 <sup>•</sup> ,15–25]	[2,3,26,27]	[2,3,26,27]	[4,28–30]



# Approach to management

- ABC
- IV
- Oxygen
- Monitor
- Airway management
- Epinephrine

# Treatment of Anaphylaxis

## First line

- Epinephrine
- IV fluids
- Oxygen

## Second line

- H<sub>1</sub> antagonist
- H<sub>2</sub> antagonist
- Steroids
- Beta-agonist

# Medication

**TABLE 7.** Epinephrine (Adrenaline): First-Line Medication for Anaphylaxis Treatment

Strength of Recommendations <sup>a</sup>	B-C (As Defined in Footnote) <sup>a</sup>
Pharmacologic effects when given by injection <sup>b</sup>	<p>At alpha-1 adrenergic receptor</p> <p>Increases vasoconstriction and increases vascular resistance (in most body organ systems)<sup>c</sup></p> <p>Increases blood pressure</p> <p>Decreases mucosal edema in the airways</p> <p>At beta-1 adrenergic receptor</p> <p>Increases cardiac contraction force</p> <p>Increases heart rate</p> <p>At beta-2 adrenergic receptor</p> <p>Decreases mediator release</p> <p>Increases bronchodilation</p>
Clinical relevance	<p>Increases blood pressure and prevents and relieves hypotension and shock</p> <p>Decreases upper airway obstruction, eg. in larynx</p> <p>Decreases urticaria and angioedema</p> <p>Decreases wheezing</p>
Potential adverse effects after the usual epinephrine dose of 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution intramuscularly <sup>d</sup> (to a maximum of 0.5 mg [adult] or <b>0.3 mg [child]</b> )	<p>Pallor, tremor, anxiety, palpitations, dizziness, headache; these symptoms indicate that a pharmacologic dose has been injected</p>
Potential adverse effects after epinephrine overdose (eg. overly rapid intravenous infusion, intravenous bolus dose, or dosing error, eg. intravenous administration of an undiluted 1:1,000 (1 mg/mL) solution <sup>e</sup> )	<p>Ventricular arrhythmias, hypertension, pulmonary edema; note that the heart itself is a potential <b>target organ</b> in anaphylaxis; therefore, acute coronary syndromes (angina, myocardial infarction, arrhythmias) can also occur in untreated anaphylaxis in patients with known coronary artery disease, in those in whom subclinical coronary artery disease is unmasked, and even in patients (including children) without coronary artery disease in whom the symptoms are due to transient vasospasm</p>
Reasons why the intramuscular route is preferred over the subcutaneous route for initial treatment of anaphylaxis	<p>Epinephrine has a vasodilator effect in skeletal muscle<sup>c</sup>; skeletal muscle is well-vascularized; after intramuscular injection into the vastus lateralis (mid-anterolateral thigh), absorption is rapid and epinephrine reaches the central circulation rapidly; rapid absorption is important in anaphylaxis, in which the median times to cardiorespiratory arrest are reported as 5 minutes (iatrogenic, eg. injected medication), 15 minutes (stinging insect venom), 30 minutes (food)</p>
Reasons for apparent lack of response to epinephrine	<p>Error in diagnosis, patient suddenly stands or sits (or is placed in the upright position) after epinephrine injection; rapid anaphylaxis progression; patient taking a beta-adrenergic blocker or other medication that interferes with epinephrine effect; epinephrine injected too late; dose too low on mg/kg basis; dose too low because epinephrine is past expiry date<sup>f</sup>; not enough injection force used; route not optimal; injection site not optimal; other</p>

# Medication

**TABLE 8.** Second-Line Medications for Anaphylaxis Treatment

Medication	H <sub>1</sub> -Antihistamines <sup>a</sup> (eg. Intravenous Chlorpheniramine or Diphenhydramine; Oral Cetirizine)	Beta-2 Adrenergic Agonists <sup>a</sup> (eg. Salbutamol [Albuterol] by Inhalation)	Glucocorticoids <sup>a</sup> (eg. Intravenous Hydrocortisone or Methylprednisolone; Oral Prednisone or Prednisolone)
Strength of recommendation for use in anaphylaxis <sup>b</sup>	C	C	C
Pharmacologic effects	At H <sub>1</sub> -receptor, inverse agonist effect; stabilize receptors in inactive conformation; decrease skin and mucosal symptoms	At beta-2 receptor, increase bronchodilation	Switch off transcription of activated genes that encode pro-inflammatory proteins; decrease late phase allergic response
Clinical relevance	Decrease itch, flush, urticaria, sneezing, and rhinorrhea, but are not life-saving because they do not prevent or relieve obstruction to airflow or hypotension/shock	Decrease wheeze, cough and shortness of breath but are not life-saving because they do not prevent or relieve upper airway obstruction or hypotension/shock	Onset of action takes several hours; therefore, are not life-saving in initial hours of an anaphylactic episode; used to prevent and relieve protracted or biphasic anaphylaxis; however, these effects have not been proven
Potential adverse effects (usual dose)	First-generation drugs cause drowsiness, somnolence, and impaired cognitive function <sup>c</sup>	Tremor, tachycardia, dizziness, jitteriness	Unlikely during a short course
Potential adverse effects (overdose)	Extreme drowsiness, confusion, coma, respiratory depression, and paradoxical central nervous system stimulation, eg. seizures in infants and children	Headache, hypokalemia, vasodilation	Unlikely
Comment	From 0 to 14 different H <sub>1</sub> -antihistamines <sup>c</sup> and different dose regimens are listed as adjunctive medications in anaphylaxis guidelines; role not proven	Use in anaphylaxis is extrapolated from use in acute asthma; if given as adjunctive treatment for bronchospasm not relieved by epinephrine, should optimally be delivered by face mask and nebulization	From 0 to 3 different glucocorticoids <sup>d</sup> and different dose regimens <sup>d</sup> are listed as adjunctive medications in anaphylaxis guidelines; role not proven

# What is the evidence?

**Table 3 Pharmacologic treatment of anaphylaxis: recommendations versus reality**

	Epinephrine	H <sub>1</sub> -antihistamines	H <sub>2</sub> -antihistamines	Glucocorticoids
<b>Recommendations</b>				
Cochrane systematic reviews [32•,33,34•]	First-line	Second-line	No Cochrane review	Second-line
What anaphylaxis guidelines recommend [35–39]	First-line	Second-line	Second-line	Second-line
World Health Organization – list of essential medications for anaphylaxis (www.who.int)	Yes	No	No	No
World Allergy Organization survey: availability for anaphylaxis, % of countries [43•]	100	77 (IV formulations); 86 (oral formulations)	70	89
<b>Reality</b>				
Actual prescriptions for anaphylaxis in US emergency departments showing trends from 1993 to 2004, expressed as % of visits for anaphylaxis [44]	19→7	59→62	7→18	22→50

# Medication

**Table 1: Initial pharmacologic management of acute anaphylaxis**

Drug and route of administration	Frequency of administration	Dose (adult)	Dose (child)
Epinephrine 1:1000, IM	Immediately, then every 5–15 min as needed*	0.3–0.5 mL	0.01 mL/kg (up to 0.3 mL)
Diphenhydramine, IV, IM or PO	Once patient's condition is stabilized with epinephrine and fluids, then every 4–6 h as needed	25–50 mg	1.25 mg/kg
Ranitidine, IV or PO	Once patient's condition is stabilized with epinephrine and fluids, then every 8 h as needed	50 mg IV or 150 mg PO	1.25 mg/kg IV or 2 mg/kg PO
Steroids: methylprednisolone, IV, or prednisone, PO	Once patient's condition is stabilized with epinephrine and fluids, then every 6 h as needed	125 mg IV or 50 mg PO	1 mg/kg IV or 1 mg/kg PO

# Epinephrine

- Parenteral Epinephrine is the cornerstone of management
- IM route has been proven more effective than SC route (Lee et al. 2011)
- Injection site should be the mid-anterolateral of the thigh
- Injection should be repeated after 5-15 min later if necessary
- IV may be needed in the case of refractory shock
  - A patient on *beta-blockers* may not respond well to Epi
    - *Glucagon* will be needed (1mg IV, may be repeated after 5min, then infusion of 1-5mg/h)
    - Max benefit within 5-15 minutes

# Epinephrine and its evidence

- All anaphylaxis guidelines recommend epinephrine as the first line treatment
- However, there are no randomized controlled trials
- Recommendations are based on
  - Century of clinical use
  - Fatality studies
  - Epidemiologic studies
  - Prospective observational studies



# Epinephrine

- 1:1000 solution
- 0.01mg/Kg
- Max dose
  - Adult: 0.5mg
  - Children: 0.3mg
- Can be repeated after 5-15 min later
- IV Epi (1:10 000) should be administered in severe anaphylaxis or shock

# Epinephrine

## Adult

- 0.5mg IM

## Children

< 6 years old

0.15mg IM

6-12 years old

0.3mg IM

12 years old

0.5mg IM

# Corticosteroids

- Used to reduce the risk of *biphasic reactions*
- Anti-inflammatory action
- Benefit is not realized for 6-12 hours after administration
- Used as a second line treatment
- Methylprednisolone 1mg/kg for 3-4 days
- Hydrocortisone 200mg
- Prednisone 50mg po

# H<sub>1</sub> Anti-Histamine

- Has effect on urticaria and rhinorrhea
- No effect on hypotension, shock, or airway obstruction
- Diphenhydramine 25-50mg IV

# H<sub>2</sub> Anti-Histamine

- No place in the treatment of anaphylaxis
- Ranitidine 50mg IV
- Famotidine 20mg IV

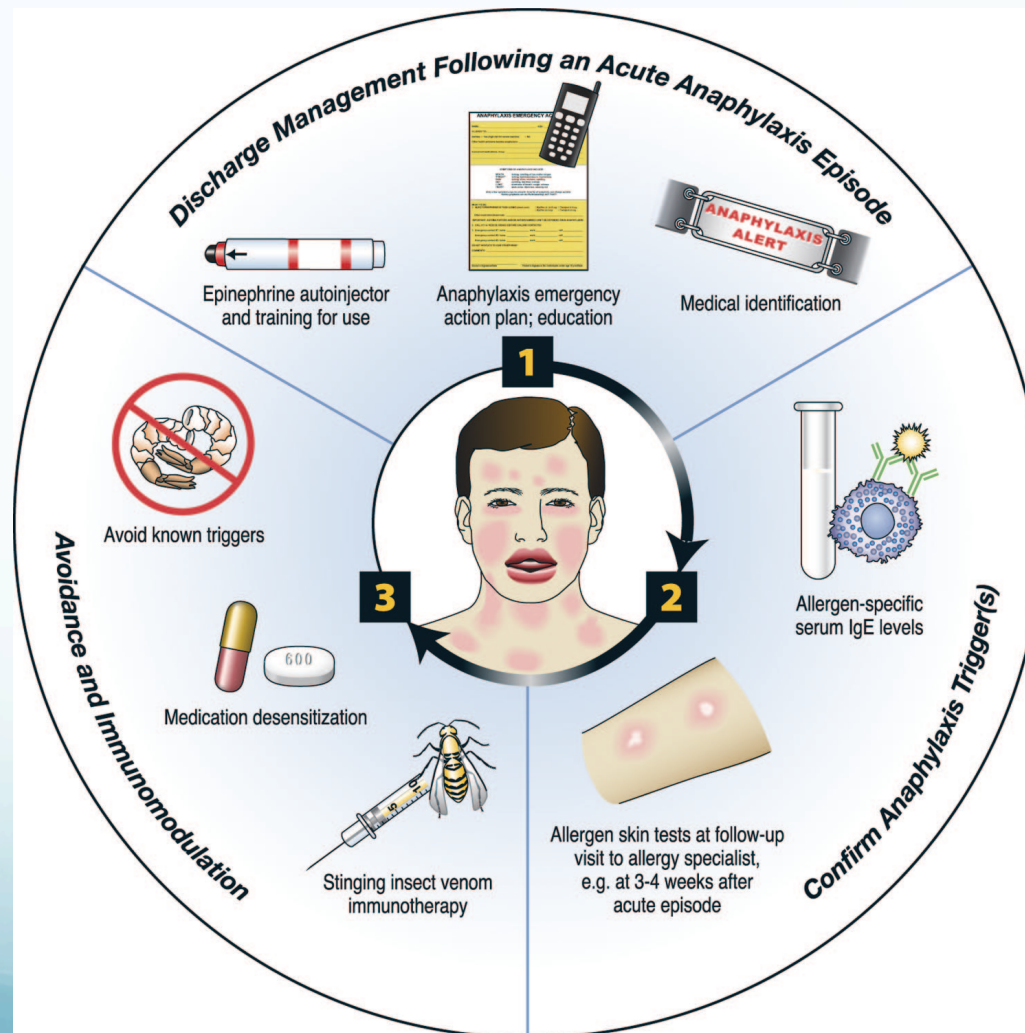
# B<sub>2</sub> Agonist

- Will not reduce airway swelling
- Act on smooth smooth muscle
- Used with conjunction with Epinephrine, never alone, in situations of severe bronchospasm

# Monitoring

- Patients should be monitored for 6-12 hours if signs were moderate
- Up to 24h if shock or severe reaction

# Discharge management





# Discharge management

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**TABLE 9.** Recommendations at Time of Discharge From the Healthcare Setting

---

Medication

Epinephrine/adrenaline auto-injector<sup>a</sup>

Epinephrine from an ampule/syringe<sup>b</sup> or prefilled syringe<sup>c</sup> (alternative but not preferred formulations)

Other aspects of discharge management

Anaphylaxis emergency action plan (personalized, written)

Medical identification (eg, bracelet, wallet card)

Medical record electronic flag (or chart sticker)

Emphasize the importance of follow-up, preferably with an allergy/immunology specialist

Assessment of sensitization to allergen

Before discharge, consider assessing sensitization to allergens suggested in the history of the acute episode, by measuring serum IgE levels to relevant allergen(s), if the test is available<sup>d</sup>

3-4 weeks after the episode, confirm allergen sensitization using skin tests<sup>e</sup>

Challenge/provocation tests might be needed in some patients, for example, with food or medication allergy, in order to assess risk of future anaphylactic episodes further<sup>f</sup>

Long-term risk reduction: avoidance and/or immunomodulation

Food-triggered anaphylaxis: avoidance of relevant food(s)

Stinging insect-triggered anaphylaxis: avoidance of stinging insects; subcutaneous venom immunotherapy (protects up to 80–90% of adults and 98% of children)

Medication-triggered anaphylaxis: avoidance of relevant medications; if indicated, medically supervised desensitization in a healthcare setting according to published protocols

Idiopathic anaphylaxis: for frequent episodes, consider glucocorticoid and H<sub>1</sub>-antihistamine prophylaxis for 2-3 months

Optimal management of asthma and other concomitant diseases

# Auto-injectors

- Should be discharged with auto-injectors
- Family members and caregivers of children should be trained on administering Epi
- Written instructions should be given
- Instructed to seek medical attention regardless of response
- Medical alerts bracelet
- Adults
  - 1:1000
  - 0.3ml
- Children
  - 1:2000
  - 0.3ml

# Follow-up

- Biphasic anaphylaxis (despite no further re-exposure to the allergen) has been reported to occur in up to 20% of adults
- Symptoms tend to occur within 1-72 hours
  - Usually 8-10 hours after the initial reaction has resolved
- Clear instructions to return to the hospital if symptoms recur should be provided
- 1-3 days of steroids may prevent the delayed reaction

# Role of the allergist

## Box 1 Role of allergy specialist in management of anaphylaxis

### Role of allergy specialist

1. Detailed history and elucidation of triggers and co-factors (eg, food dependent, exercise induced anaphylaxis)
2. Skin tests, blood tests including relevant specific IgE
3. Graded challenge and/or provocation if unclear or to identify alternative medication, for example, non-steroidal anti-inflammatory drug, antibiotic
4. Individualised avoidance plan
5. Written emergency treatment plan
6. Optimisation of asthma treatment
7. Immunotherapy (eg, for insect venom, etc)
8. Desensitisation to a drug if immediately required *and* no alternative available
9. Education (verbal, written; online resources)
10. Regular follow-up of patients with 'idiopathic anaphylaxis'

# Prevention

**Table 2: Strategies to prevent or manage exposure to known allergens**

Allergen	Strategy
<i>Hymenoptera</i>	Be alert when eating outdoors (wasps are attracted to food) Wear shoes and long pants when in fields Have nests or hives near to homes removed <sup>20</sup> Proven venom-sensitive patients should be offered specific immunotherapy <sup>21,22</sup>
Latex	Avoid contact with all latex products Surgical or dental procedures should be performed in latex-free areas <sup>23</sup> Foods with known crossreactivity to latex, such as kiwi, must be avoided
Penicillin	Desensitization protocols are available for penicillin-allergic patients who have serious infections requiring penicillin or a derivative <sup>24</sup> Avoid use of cephalosporins, due to cross-reactivity

# Prevention

## **Prevention and Early Treatment of Future Episodes of Anaphylaxis**

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Advise patient to wear or carry a medical alert bracelet, necklace, or keychain to warn emergency personnel of anaphylaxis risk.

Advise patient to keep epinephrine self-injection kit and oral diphenhydramine (Benadryl) for future exposures.

Avoid prescribing beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, monoamine oxidase inhibitors, and some tricyclic antidepressants.

Avoid administering cross-reactive agents.

Refer to allergist if causative agent or diagnosis is unclear, if in-depth patient education is needed, or if reactions are recurrent.

If re-exposure to an offending medicine is necessary, administer the questionable medicine orally and observe the patient for the following 20 to 30 minutes; consider pretreatment with steroids and antihistamines. Consider desensitization if available.

# Case revisited

# Case 1

- 19yo woman presents to your office because of a rash
- She ate a salad 30 minutes ago at a Thai restaurant
- She now complains of itchy palms and sensation of throat swelling
- She also complains of shortness of breath



# True or false?

- This patient is having an allergic reaction only

False

- At this point, she just needs Diphenhydramine

False

- Epinephrine is best given subcutaneously

False

# Case 2

- 65yo male presents in respiratory distress after eating shrimps in a restaurant
- On arrival, his BP was 90/50 and pulse was 120.
- His respiration rate is 28 and O2 saturation was 94% on RA
- He is very wheezy at the mouth
- He has a diffuse urticaria

# True or false?

- This patient is aware of his action plan should it recur

False

- He should be prescribed an Epinephrine auto-injector

True

# Summary

- Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death
- Allergen triggers precede the anaphylaxis and may be unrecognized
- Rapid initiation of treatment is crucial

# Summary

- Epinephrine is the cornerstone of management
- Epinephrine is best given intramuscular
- Discharge instructions and follow-up should be provided
- Auto-injectors should be prescribed with every patients at risk of anaphylaxis
- Prevention is possible and necessary
- Family doctors and pediatricians have a huge role in patient education around anaphylaxis

# References

- WAO J 2011; 4: 13-37
- Curr Opin Crit Care 2012; 18: 308-317
- Postgrad Med J 2012; 88: 458-464
- CMAJ Aug 19, 2003; 169 (4): 307-312
- Am Fam Physician 2003; 68: 1325-32
- Allergy 2010; 65: 435-444
- Allergy 2010; 65: 1082-1092
- Egypt J Pediatr Allergy Immunol 2007; 5 (2): 47-54

The background of the slide features a series of overlapping, wavy lines in various shades of blue and green, creating a sense of depth and movement. The colors transition from a light, almost white green at the top to a deeper blue at the bottom.

# Thank you

Vukiet.tran@rogers.com

# Clinical diagnosis

- Anaphylaxis is highly likely when any 1 of the following 3 criteria is fulfilled:
  - 1) Acute onset of illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both AND as least one of the following
    - a) Respiratory compromise
    - b) Reduced BP or associated symptoms of end-organ dysfunction
  - 2) Two or more of the following that occur rapidly after exposure to a likely allergen for that patient
    - a) Involvement of the skin-mucosal tissue
    - b) Respiratory compromise
    - c) Reduced BP or associated symptoms
    - d) Persistent GI symptoms
  - 3) Reduced BP after exposure to known allergen for that patient
    - a) Infants and children: Low SBP or > 30% decrease in systolic BP
    - b) Adults: SBP < 90mmHg or > 30% decrease from the patient's baseline