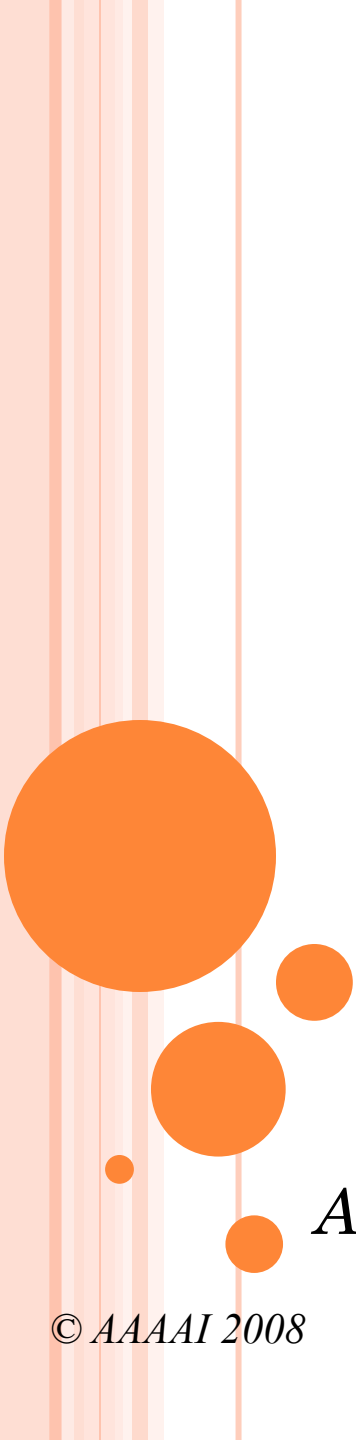




Anaphylaxis: Killer Allergy

Dr. H.Sadri

Allergist and clinical immunologist

DEFINITION

- Anaphylaxis is an **acute, life-threatening systemic reaction** with varied mechanisms, clinical presentations, and severity that results from the **sudden systemic release of mediators from mast cells and basophils**



CLINICAL CRITERIA

Any 1 of the following 3 criteria:

1- **Acute onset of an illness** with involvement of skin, mucosal tissue AND at least 1 of following:

- Respiratory compromise
- Reduced BP

2- Two or more that **occur rapidly after exposure**:

- Involvement of the skin–mucosal tissue
- Respiratory compromise
- Reduced BP
- Persistent gastrointestinal symptoms

3- Reduced BP after exposure to a known allergen for that patient



- *MANY DEATHS IN ANAPHYLAXIS, ESPECIALLY FROM FOOD ALLERGY, ARE DUE TO OBSTRUCTION TO AIRFLOW IN THE UPPER AND/OR LOWER RESPIRATORY TRACT THAT RESULT IN RESPIRATORY FAILURE.*

- *IF YOU WAIT FOR THE PATIENT TO DEVELOP SHOCK, YOU HAVE WAITED TOO LONG!*

- *TREAT LONG BEFORE SIGNS AND SYMPTOMS OF CARDIOVASCULAR COLLAPSE OCCUR!*



The most frequent manifestations of anaphylaxis are cutaneous, occurring in over 90% of reported series. The absence of cutaneous symptoms speaks against a diagnosis of anaphylaxis, but does not rule it out. **Severe episodes characterized by rapid cardiovascular collapse and shock can occur without cutaneous manifestations**

The incidence of cutaneous manifestations in children may be lower



Increased vascular permeability, a characteristic feature of anaphylaxis, allows transfer of as much as 35% of the intravascular fluid into the extravascular space within 10 min. As a result, hemodynamic collapse may occur rapidly with little or no cutaneous or respiratory manifestations.



TRIGGERS OF ANAPHYLAXIS



Table 149-2 Anaphylaxis Triggers in the Community***ALLERGEN TRIGGERS (IgE-DEPENDENT IMMUNOLOGIC MECHANISM)***

Foods (e.g., peanut, tree nuts, shellfish, fish, milk, egg, wheat, soy, sesame, meat [galactose- α -1,3-galactose])

Food additives (e.g., spices, colorants, vegetable gums, and contaminants)

Stinging insects: Hymenoptera species (e.g., bees, yellow jackets, wasps, hornets, and fire ants)

Medications (e.g., β -lactam antibiotics, ibuprofen)

Biologic agents (e.g., monoclonal antibodies [infliximab, omalizumab] and allergens [challenge tests, specific immunotherapy])

Natural rubber latex

Vaccines

Inhalants (rare) (e.g., horse or hamster dander, grass pollen)

Previously unrecognized allergens (foods, venoms, biting insect saliva, medications, biologic agents)

OTHER IMMUNE MECHANISMS (IGE INDEPENDENT)

IgG mediated (infliximab, high-molecular-weight dextrans)

Immune aggregates (IVIg)

Drugs (aspirin, NSAID, opiates, contrast material, ethylene oxide/dialysis tubing)

Complement activation

Physical factors (e.g., exercise[†], cold, heat, sunlight/ultraviolet radiation)

Ethanol

Idiopathic*

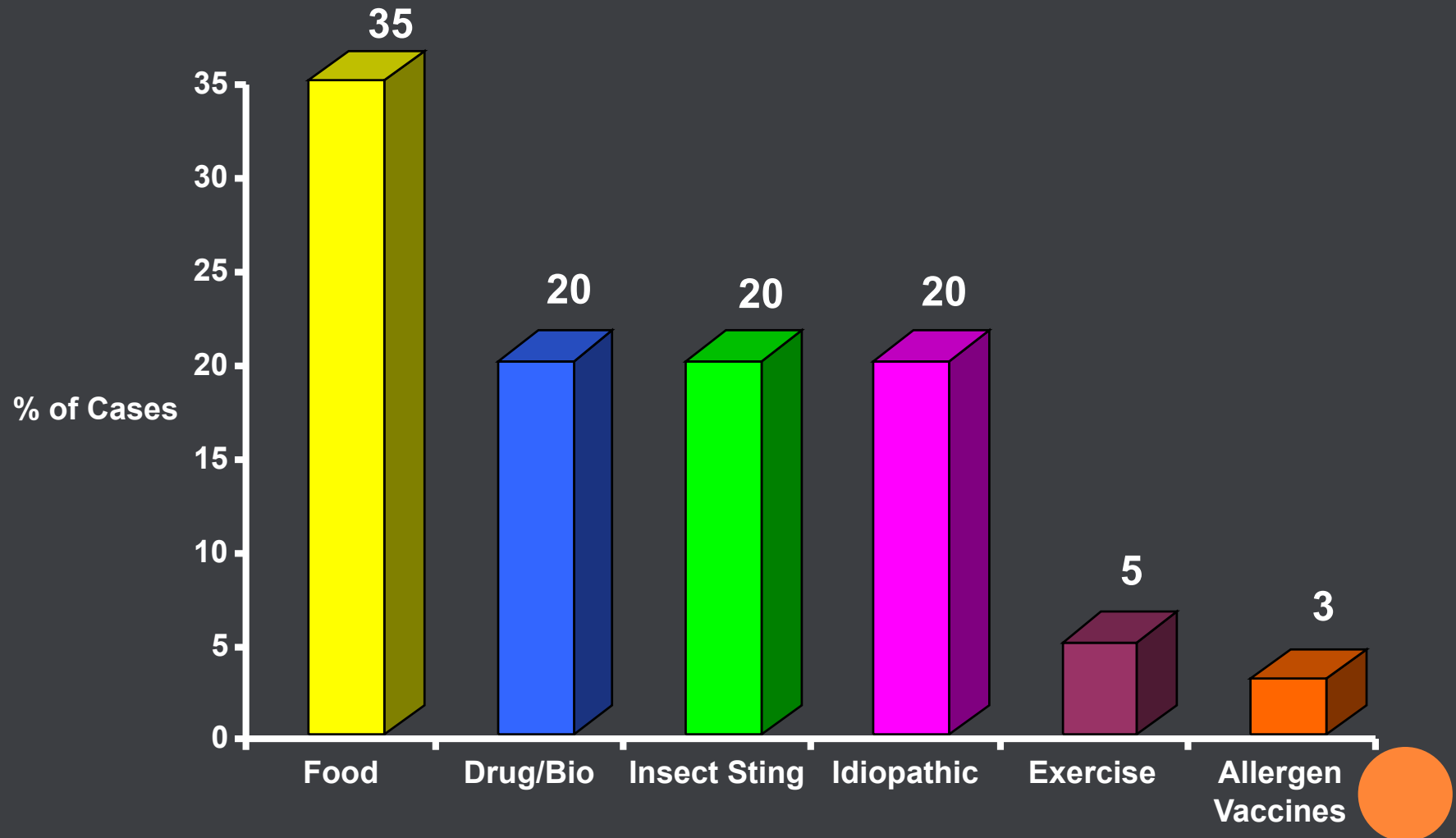
*In the pediatric population, some anaphylaxis triggers, such as hormones (progesterone), seminal fluid, and occupational allergens, are uncommon, as is idiopathic anaphylaxis.

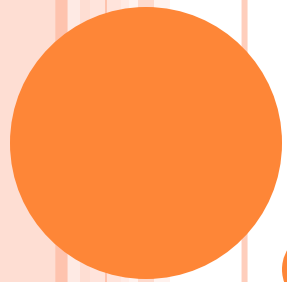
[†]Exercise with or without a cotrigger, such as a food or medication, cold air, or cold water.

IVIg, intravenous immunoglobulin; NSAID, nonsteroidal antiinflammatory drug.

Adapted from Leung DYM, Sampson HA, Geha RS, et al: Pediatric allergy principles and practice, New York, 2010, Elsevier, p. 652.

OVERVIEW OF ANAPHYLACTIC TRIGGERS





SIGNS AND SYMPTOMS

Preview File Edit View Go Tools Window Help Nelson Textbook of Pediatrics 2Volume Set 20th Edition 2016.pdf (page 1,565 of 5,316) — Edited

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Table 149-1 Symptoms and Signs of Anaphylaxis in Infants

ANAPHYLAXIS SYMPTOMS THAT INFANTS CANNOT DESCRIBE	ANAPHYLAXIS SIGNS THAT MAY BE DIFFICULT TO INTERPRET/UNHELPFUL IN INFANTS, AND WHY	ANAPHYLAXIS SIGNS IN INFANTS
GENERAL Feeling of warmth, weakness, anxiety, apprehension, impending doom	Nonspecific behavioral changes such as persistent crying, fussing, irritability, fright, suddenly becoming quiet	
SKIN/MUCUS MEMBRANES Itching of lips, tongue, palate, uvula, ears, throat, nose, eyes, etc.; mouth-tingling or metallic taste	Flushing (may also occur with fever, hyperthermia, or crying spells)	Rapid onset of hives (potentially difficult to discern in infants with acute atopic dermatitis; scratching and excoriations will be absent in young infants); angioedema (face, tongue, oropharynx)
RESPIRATORY Nasal congestion, throat tightness; chest tightness; shortness of breath	Hoarseness, dysphonia (common after a crying spell); drooling or increased secretions (common in infants)	Rapid onset of coughing, choking, stridor, wheezing, dyspnea, apnea, cyanosis
GASTROINTESTINAL Dysphagia, nausea, abdominal pain/cramping	Spitting up/regurgitation (common after feeds), loose stools (normal in infants, especially if breastfed); colicky abdominal pain	Sudden, profuse vomiting
CARDIOVASCULAR Feeling faint, presyncope, dizziness, confusion, blurred vision, difficulty in hearing	Hypotension (need appropriate-size blood pressure cuff; low systolic blood pressure for children is defined as $<70 \text{ mm Hg}$ from 1 mo to 1 yr, and less than $(70 \text{ mm Hg} + [2 \times \text{age in yr}])$ from 1-10 yr; tachycardia, defined as $>140 \text{ beats/min}$ from 3 mo to 2 yr, inclusive; loss of bowel and bladder control (ubiquitous in infants)	Weak pulse, arrhythmia, diaphoresis/sweating, collapse/unconsciousness

reference

Mac OS X dock with various application icons.

MOST FREQUENT SIGNS AND SYMPTOMS OF ANAPHYLAXIS

Manifestation

Urticaria/angioedema

88

Upper airway edema

56

Dyspnea/wheeze

47

Flush

46

Hypotension

10-33

Gastrointestinal

30



- The median time from onset to cardiac arrest was faster for injected than for ingested antigen: 30 minutes for foods, 15 minutes for venom, and 5 minutes for iatrogenic reactions caused by injections

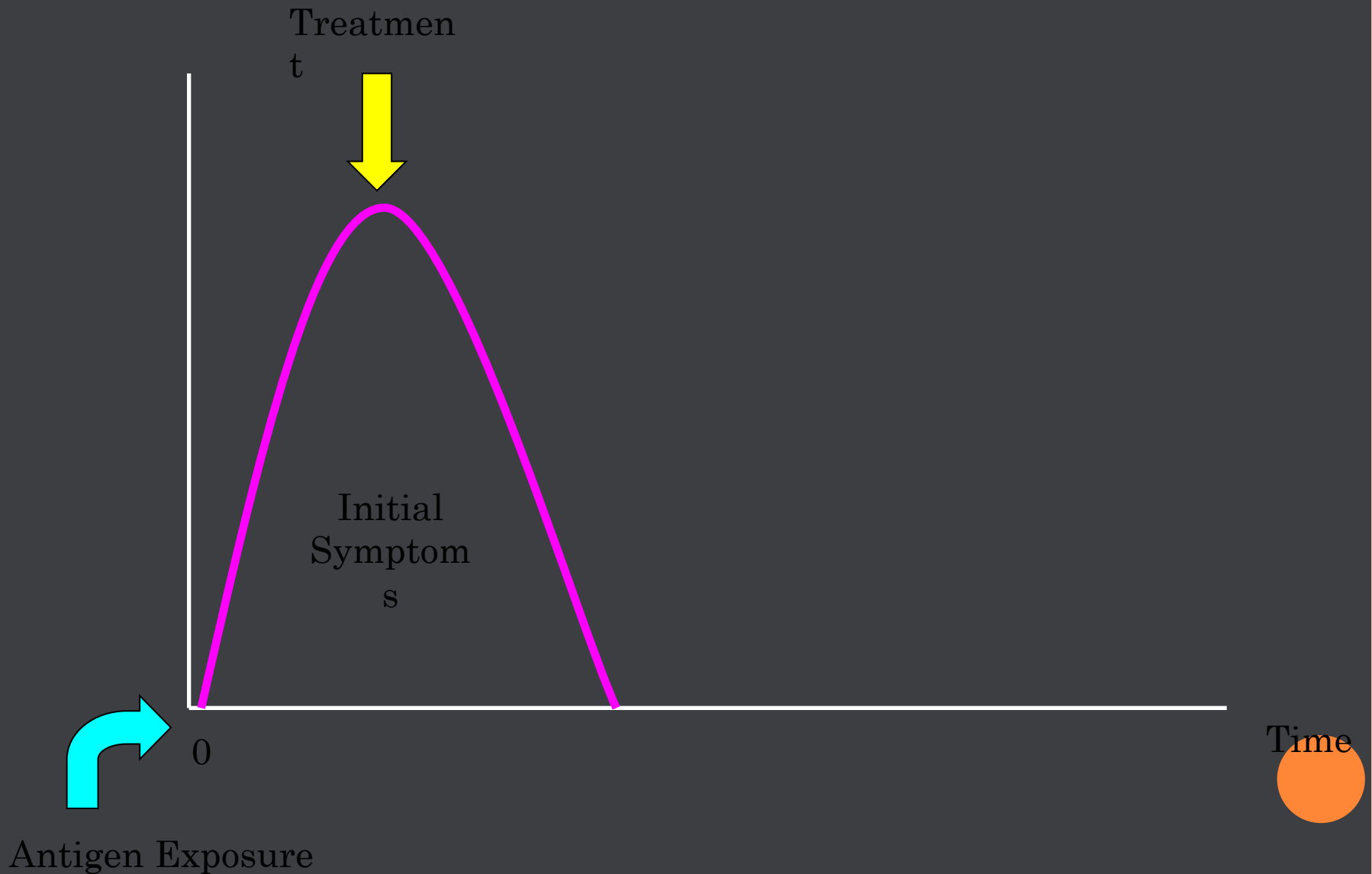


ANAPHYLAXIS -TEMPORAL PATTERN

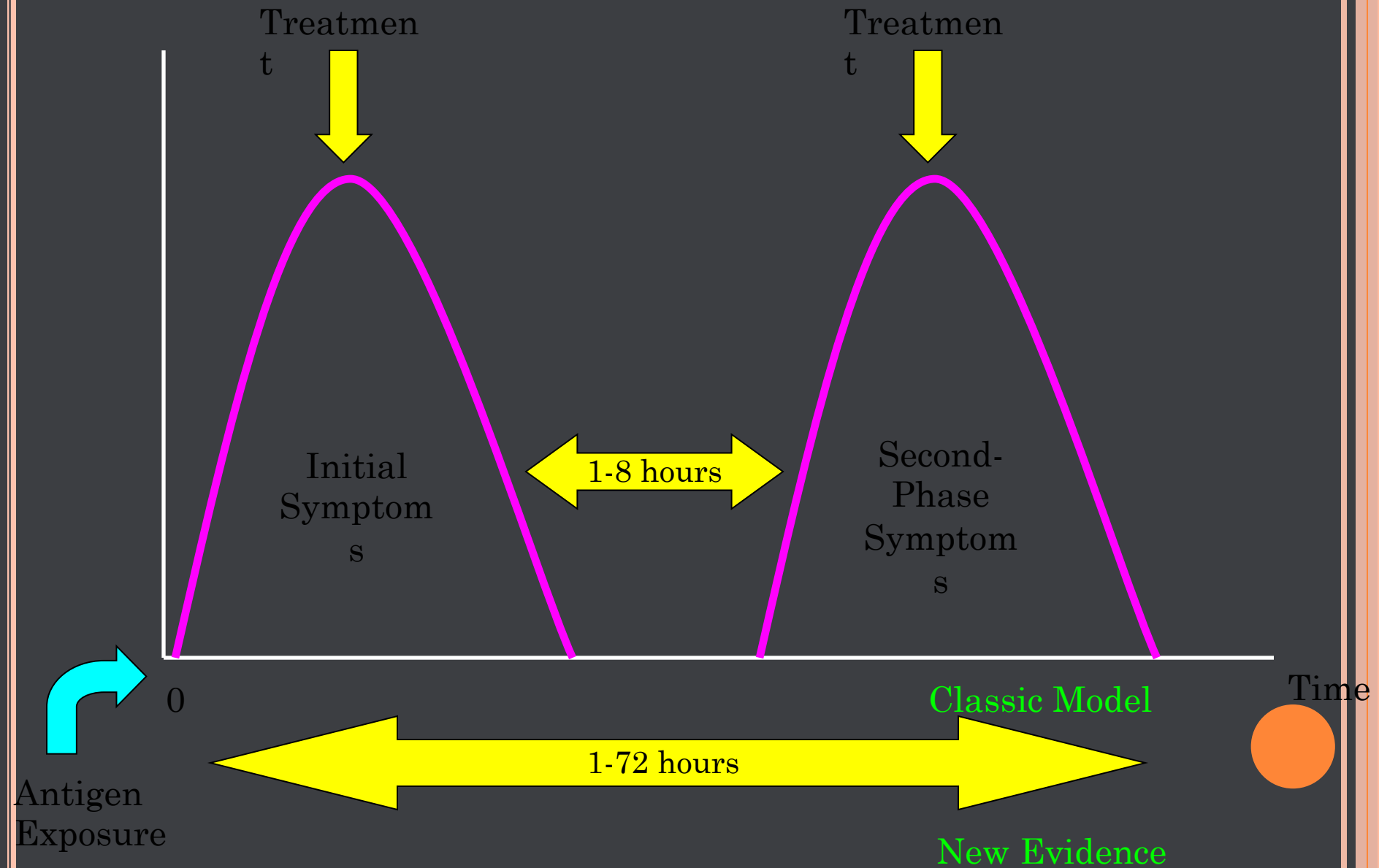
- Uniphasic
- Biphasic: without further exposure to the trigger, anaphylaxis symptoms recur up to 8 hours later and rarely much later (occurs in 1-20%)
- Protracted



UNIPHASIC ANAPHYLAXIS



BIPHASIC ANAPHYLAXIS



Biphasic anaphylaxis occurs in 1% to 23% of episodes of anaphylaxis, and symptoms may recur hours (most within 10 hours) after apparent resolution of the initial phase. However, observation periods must be individualized since there are no reliable predictors of biphasic or protracted anaphylaxis based on initial clinical presentation



INDICATIONS FOR PROLONGED OBSERVATION OF ANAPHYLACTIC PATIENT

Moderate to severe reaction

Episode in asthmatic patient with wheezing

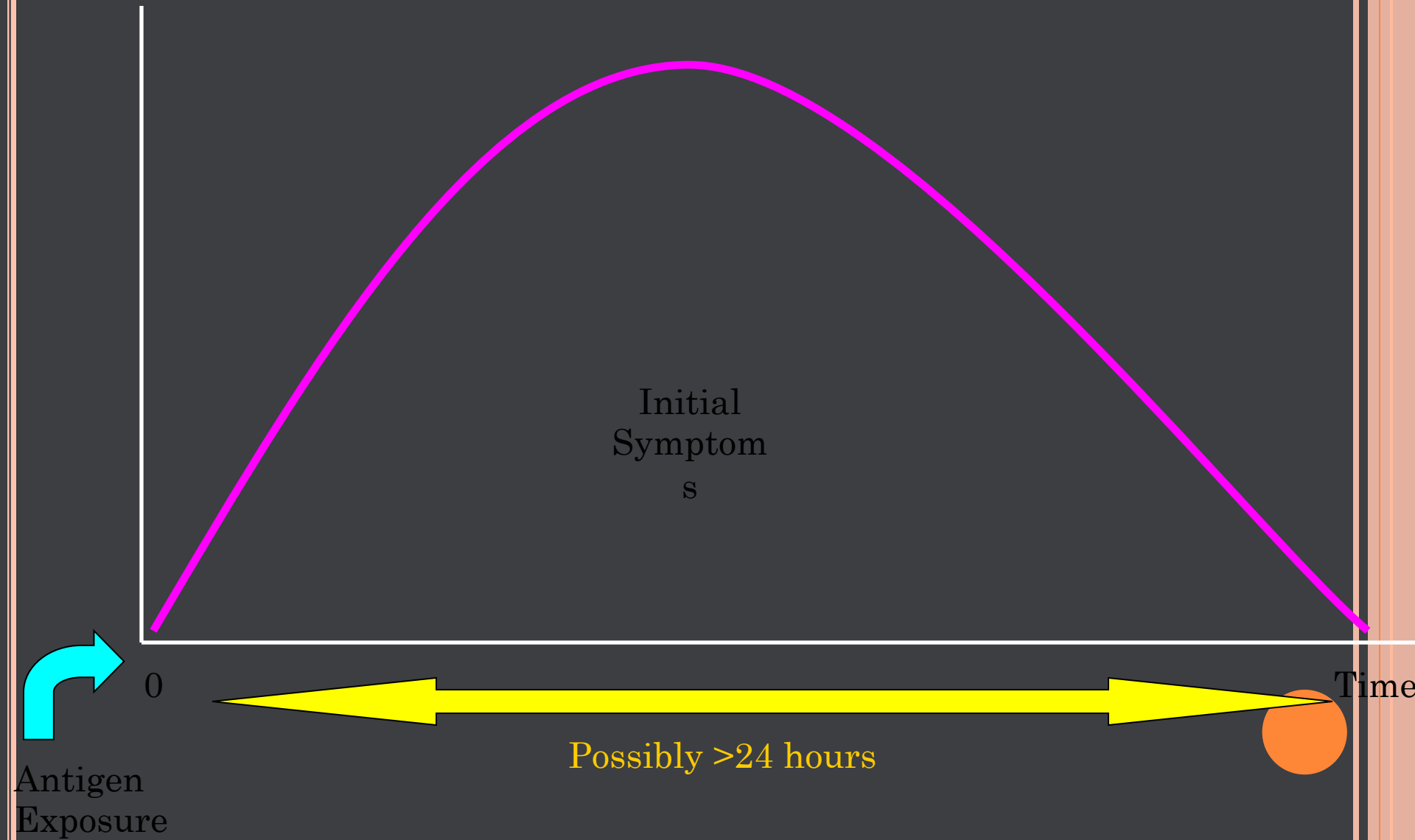
Ingested antigen with possibility of continued absorption

Previous history of biphasic response

- *8 to 24 hours after resolution of symptoms.



PROTRACTED ANAPHYLAXIS



D.DX

- (1) vasodepressor (vasovagal/neuro-cardiogenic)syncope
- (2) syndromes that can be associated with Flushing
(e.g., metastatic carcinoid)
- (3) postprandial syndromes(e.g., scombroid poisoning)
- (4) systemic mastocytosis;
- (5) psychiatric disorders that can mimic anaphylaxis
such as
panic attacks or vocal cord dysfunction syndrome
- (6) angioedema(e.g., hereditary angioedema)
- (7) other causes of shock(e.g., cardiogenic)
- (8) other cardiovascular or respiratory events



The vasodepressor (vaso-vagal) reaction probably is the condition most commonly confused with anaphylactic reactions. In vasodepressor reactions, however, **urticaria is absent**, the heart

rate is typically **bradycardic**, bronchospasm or other **breathing difficulty is generally absent**, the blood pressure is often decreased when accompanied by symptomatic bradycardia but it may be normal, and the **skin is typically cool and pale**



ANAPHYLAXIS: LAB DIAGNOSIS

Serum Tryptase

- Measured within 3 hours of the reaction.
- If positive helps to confirm the clinical diagnosis.
- If negative does not rule out anaphylaxis.



ANAPHYLAXIS: IN SEARCH OF THE CULPRIT!!

A detailed history of all potential causes should be obtained. This includes a list of **ingestants** consumed and/or medications taken **within six hours of the event**, any **sting** or bite occurring prior to the event, if the event occurred during **exercise**, **location of the event (e.g., work versus home)**, and whether or not the event was related to exposure to **heat, cold**, or occurred during **sexual activity**. The patient's **atopic status** should be noted since food-induced, seminal fluid, latex, exercise and idiopathic anaphylaxis are more common in atopic than non-atopic individuals. In women, the history should include any relationship between the attack and their **menstrual cycle**



ANAPHYLAXIS: IN SEARCH OF THE CULPRIT!!

Skin testing and measurement of allergen-specific

IgE in serum:

- Performed 2-4 weeks after the event
 - Foods
 - Insect venoms
 - Medications (some)
 - Latex

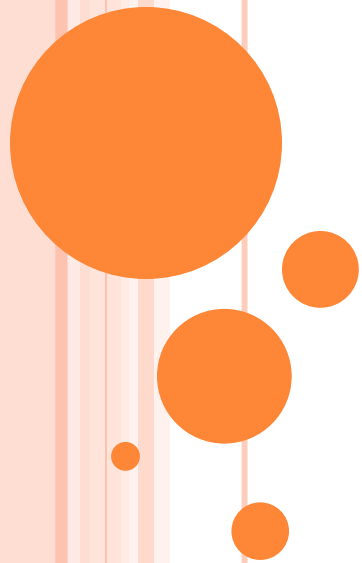


ANAPHYLAXIS: IN SEARCH OF THE CULPRIT!!

- Do not do random screening tests!
- Must correlate with history
- Refer to allergist



TREATMENT



ACCIDENTS ARE NEVER PLANNED

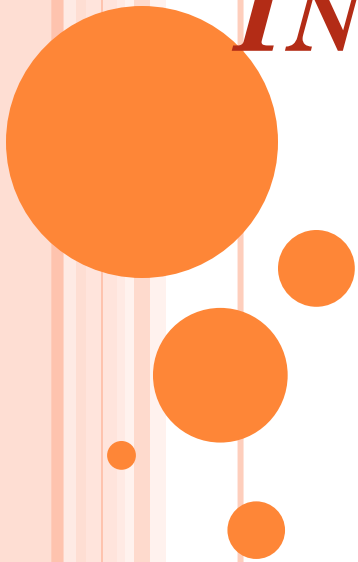
Emergency medications and a treatment plan must be immediately available and accessible at all times!



BE PREPARED!!!



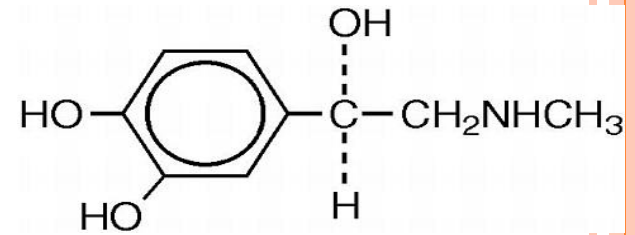
***WHEN IN DOUBT,
INJECT EPINEPHRINE!***



- The **more rapidly** anaphylaxis develops, the more likely the reaction is to be **severe** and potentially life-threatening.
- If there is any doubt, it is generally better to administer epinephrine



TREATMENT



- Epinephrine is the drug of choice for all anaphylactic episodes.
- Flexibility in dosing needed to treat effectively.
 - **Many patients(16% to 36%)require more than a single injection.**
 - Different doses for children and adults.
- Early and aggressive use to maintain airway, blood pressure, and cardiac output.



OUTDATED EPINEPHRINE LOSES EFFICACY

- As time passes, percent of labeled dose and epinephrine bioavailability are reduced.
- Improper storage and exposure to sunlight and heat increase degradation.
- Degradation often occurs without a color change in the epinephrine solution.



PHYSICIAN-SUPERVISED MANAGEMENT OF ANAPHYLAXIS

I. Speed is critical:

- a) assess airway, breathing, circulation, and mentation
- b) epinephrine, IM into the muscle of the anterolateral thigh;

**1:1000 dilution, 0.3 - 0.5 mL (0.01 mg/kg in children);
repeat, every 5-15 minutes as necessary.**



initial resuscitation dosage is 0.01 mg/kg (0.1 ml/kg of a 1:10,000 solution up to 1 mg/min rate of infusion), repeated every 3 to 5 min for ongoing arrest. Higher subsequent dosages (0.1-0.2 mg/kg; 0.1 ml/kg of a 1:1,000 solution) may be considered for unresponsive asystole or pulseless electrical activity (PEA)



- If severe hypotension is present, especially with cardiovascular collapse, and no response is obtained to IM administration, epinephrine can be administered intravenously.
- Numerous IV regimens are available but Animal models and human studies show **that continuous infusion is superior to IV bolus injection**
- Regardless of the dose and regimen used, special care should be taken and **the patient monitored for arrhythmias**



ALTERNATIVE ROUTES OF ADMINISTRATION

for example, **inhaled epinephrine in the presence of laryngeal edema** or sublingual administration if an intravenous route cannot be obtained. **Endotracheally administered**

Nebulized epinephrine, 5 mL of 1:1000 dilution (5 mg in 5 mL) has been recommended for the treatment of upper airway compromise in anaphylaxis and should be given in addition to parenteral (IM or IV) epinephrine



Review Article

Safety of epinephrine for anaphylaxis in the emergency setting

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BACKGROUND: While epinephrine is the recommended first-line therapy for the reversal of anaphylaxis symptoms, inappropriate use persists because of misunderstandings about proper dosing and administration or misconceptions about its safety. The objective of this review was to evaluate the safety of epinephrine for patients with anaphylaxis, including other emergent conditions, treated in emergency care settings.

METHODS: A MEDLINE search using PubMed was conducted to identify articles that discuss the dosing, administration, and safety of epinephrine in the emergency setting for anaphylaxis and other conditions.

RESULTS: Epinephrine is safe for anaphylaxis when given at the correct dose by intramuscular injection. The majority of dosing errors and cardiovascular adverse reactions occur when epinephrine is given intravenously or incorrectly dosed.

CONCLUSION: Epinephrine by intramuscular injection is a safe therapy for anaphylaxis but training may still be necessary in emergency care settings to minimize drug dosing and administration errors and to allay concerns about its safety.

KEY WORDS: Allergy; Anaphylaxis; Epinephrine; Safety; Cardiovascular side effects

Epinephrine administered to a patient taking a β -blocker can produce unopposed α -adrenergic and reflex vagotonic effects, possibly leading to hypertension and the risk of cerebral hemorrhage. In patients receiving β -blockers, increased propensity not only for **bronchospasm**, but also **decreased cardiac contractility** with perpetuation of hypotension and bradycardia might exist



If epinephrine is ineffective in treating anaphylaxis in patients taking β -blockers, both **glucagon** administration and isotonic volume expansion (in some circumstances, up to 7 L of crystalloid) may be necessary



There are no epidemiologic studies that indicate that anaphylaxis occurs more frequently in patients receiving b-blockers.

patients taking b –blockers may be more likely to **experience severe anaphylactic reactions characterized by paradoxical bradycardia, profound hypotension, and severe bronchospasm.**

These systemic effects have also been documented with use of ophthalmic b-blocker



GLUCAGON

Glucagon may reverse refractory bronchospasm and hypotension during anaphylaxis in patients on β -blockers **by activating adenyl cyclase directly and bypassing the β -adrenergic receptor**. The recommended dosage for glucagon is 1 to 5 mg (20-30 $\mu\text{g/kg}$ [max. 1 mg] in children) **administered intravenously over 5 min** and followed by an infusion, 5-15 $\mu\text{g/min}$, titrated to clinical response.

Protection of the airway is important since glucagon may cause emesis and risk aspiration in severely drowsy or obtunded patients. Placement in the lateral recumbent position may be sufficient airway protection for many of these patients.

- In addition, those taking β -adrenergic blockers may not respond optimally to epinephrine treatment and may need **glucagon**, a polypeptide with non–catecholamine-dependent inotropic and chronotropic cardiac effects, **atropine for persistent bradycardia**, or **ipratropium** for persistent bronchospasm.
- Cardiotonic effects are seen within 1 to 5 minutes and are maximal at 5 to 15 minutes after a single 5-mg bolus



Atropine if asystole or pulseless electrical activity (PEA) is present

Prolonged resuscitation is encouraged, if necessary, since a successful outcome is more likely in anaphylaxis



POSITIONING OF PATIENT

Patients who become hypotensive should remain recumbent until the cardiovascular system has been stabilized and they are completely asymptomatic. Deaths have occurred if the patient assumes the upright sitting position prematurely



Children should receive up to 30 ml/kg in the first hour. Adults receiving colloid solution should receive 500 ml rapidly, followed by slow infusion. Caution for volume overload is advised if the patient has a history of congestive heart failure



FLUID RESUSCITATION

Of available crystalloid solutions, **saline is generally preferred** in distributive shock (e.g., anaphylactic shock) because it stays in the intravascular space longer than dextrose and contains no lactate which may potentially exacerbate metabolic acidosis. Large volumes of fluid are often required, especially in patients taking a β -adrenergic blocking agent.



Consider diphenhydramine, 1-2 mg/kg or 25-50 mg/dose(parenterally). H1 antihistamines are considered secondline to epinephrine and should not be administered in lieu of epinephrine in the treatment of anaphylaxis

Cetirizine liquid—5 mg/5 mL 0.25 mg/kg up to 10 mg PO

Antihistamines have a vasodilating (α -blocking) effect and can trigger hypotension, particularly if given without epinephrine



Consider ranitidine, 50 mg in adults and 12.5-50 mg (1 mg/kg) in children, which may be diluted in 5% dextrose to a total volume of 20 ml and injected IV over 5 min. Cimetidine(4 mg/kg) may be administered IV to adults, but no pediatric dosage for the treatment of anaphylaxis has been established. In the management of anaphylaxis, a combination of diphenhydramine and ranitidine is superior todiphenhydramine alone.



Glucocorticosteroids should never be used in place of or prior to epinephrine and are not helpful acutely. However, they have the potential to prevent recurrent or protracted anaphylaxis.

- Methylprednisolone Solu-Medrol (IV) 1-2 mg/kg up to 125 mg IV
- Depo-Medrol (IM) 1 mg/kg up to 80 mg IM
- Prednisone 1 mg/kg up to 75 mg PO



Physician-supervised management of anaphylaxis

- nebulized albuterol (salbutamol) 2.5 - 5 mg in 3 ml normal saline for bronchospasm

for refractory hypotension

- glucagon, 1- 5 mg (20 - 30 $\mu\text{g}/\text{kg}$, max 1 mg in children), IV over 5 minutes followed with continuous IV infusion 5-15 $\mu\text{g}/\text{min}$
-



Anaphylaxis in the emergency department

chart review study in 21 North American Emergency Departments
random sample of 678 charts of patients presenting with food allergy
management:

- 72% received antihistamines
- 48% received systemic corticosteroids
- 16% received epinephrine (24% of those with severe reactions)

33% received respiratory medication (eg. inhaled albuterol)

only 16% received Rx for self-injectable epinephrine at discharge

only 12% referred to an allergist



PREVENTIVE TREATMENT

- Follow-up evaluation to determine/confirm etiology
- Immunotherapy for insect sting allergy
- Prescription for EpiPen and antihistamine
- Provide written plan outlining patient emergency management
- Patient Education
- Instruction on avoidance of causative agent
- Stress early treatment of allergic symptoms to avoid systemic anaphylaxis



EPIPEN



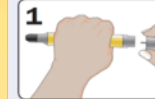
Hard flip-top
carry case

EpiPen® Adrenaline
Auto-Injector 0.3 mg



Easy-to-read,
illustrated instructions

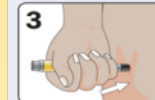
How to give EpiPen®
or EpiPen® Jr



Form fist around
EpiPen® and
PULL OFF GREY
SAFETY CAP.



PLACE BLACK
END against outer
mid-thigh (with or
without clothing).



PUSH DOWN
HARD until a
click is heard
or felt and hold
in place for 10
seconds.



REMOVE EpiPen®
and DO NOT
touch needle.
Massage
injection site for
10 seconds.

Oval shape
for easy grip



EPIPEN

- outdated epinephrine autoinjectors still contain some epinephrine, although the concentration and thus the dose are reduced. Therefore an outdated epinephrine autoinjector should be employed if it is the only therapy available.



Patients who have had anaphylactic reactions to food should be instructed on how to read food ingredient labels to identify foods that they should avoid

Patients with anaphylaxis to medications should be informed about all cross-reacting medications that should be avoided.



THANKS FOR YOUR ATTENTION

