

IN THE NAME OF GOD



ANAPHYLAXIS

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WHY DOES ANAPHYLAXIS MATTER?

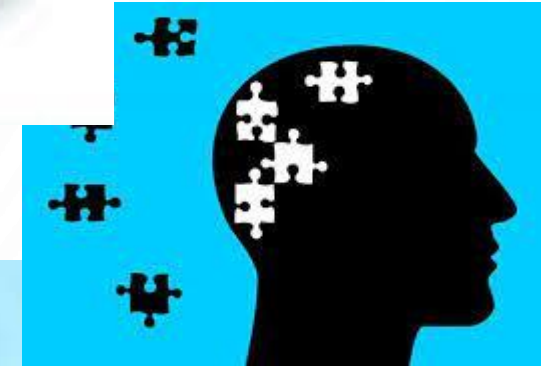
Potentially life threatening

Effective and safe treatment is available

Should always be kept in mind

Timely treatment is lifesaving

Many cases are iatrogenic



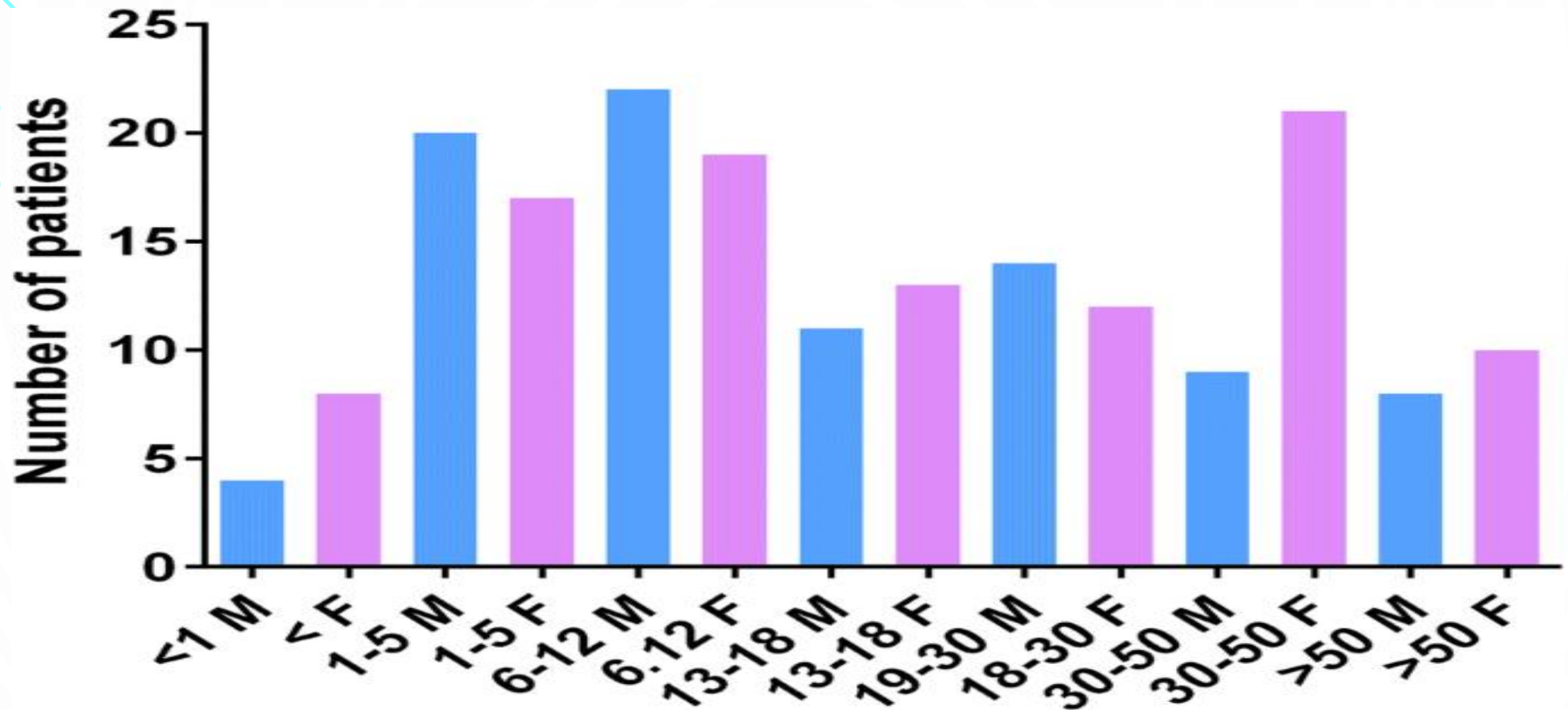
DEFINITION OF ANAPHYLAXIS

An acute serious
generalized (systemic)
hypersensitivity reaction
can be life-threatening or fatal




EPIDEMIOLOGY

- lifetime prevalence of 0.5% to 2%
- case fatality : less than 0.001% to 2%
- 1500 deaths annually



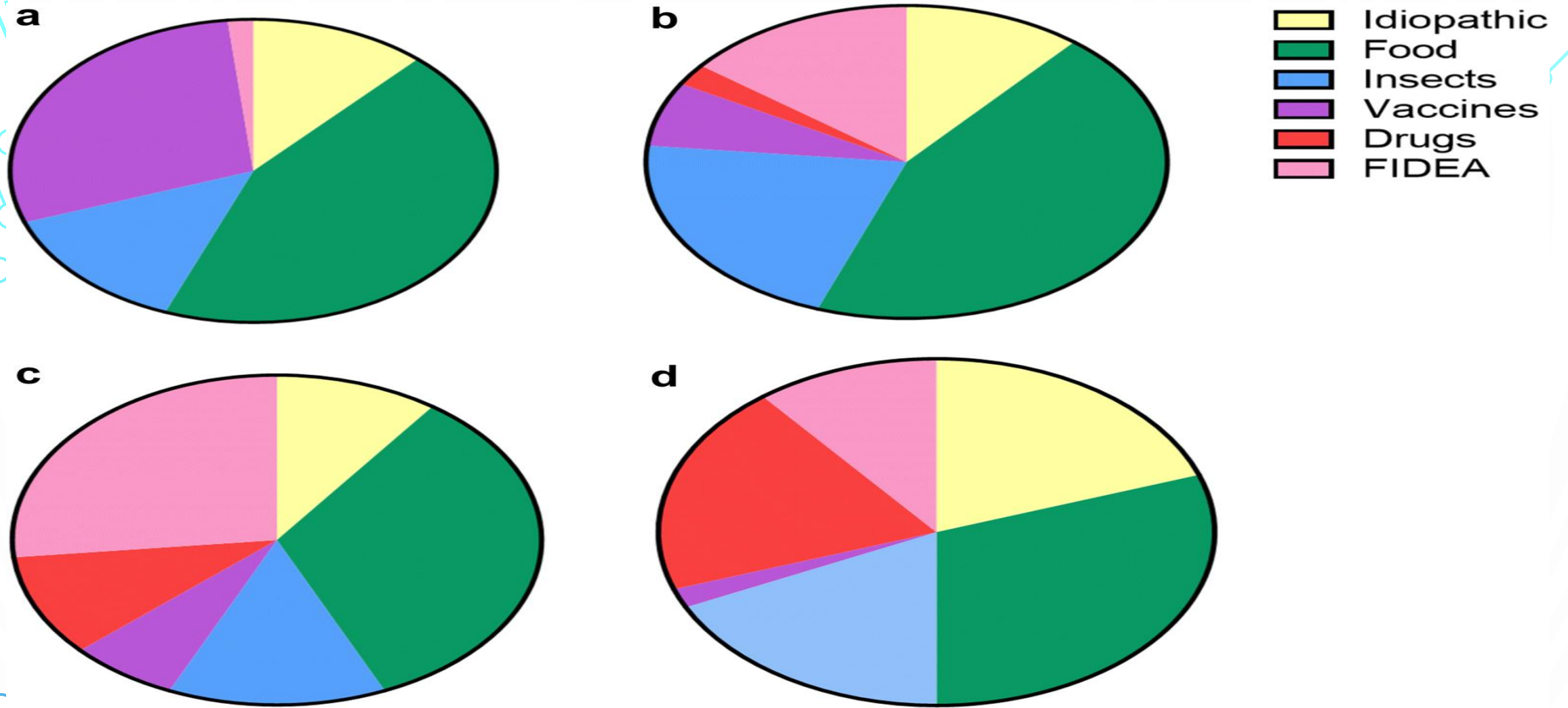
Aetiology of anaphylaxis in patients referred to an immunology clinic in Colombo, Sri Lanka

[Nilhan Rajiva de Silva](#) , [W. M. D. K. Dasanayake](#), [Chandima Karunatilake](#), [Geethani Devika Wickramasingha](#), [B. D. De Silva](#) & [Gathsauri Neelika Malavige](#)

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EPIDEMIOLOGY

- significant underreporting
- the true incidence is significantly higher
- **Foods** are probably the **most common triggers**
- followed by **drugs** (NSAIDs and antibiotics)



- The etiology of anaphylaxis in different age groups (n = 238). **a** In children < 5 years of age (n = 59), **b** in children between 5 and 18 years of age (n = 90), **c** in individuals between 19 and 30 years of age (n = 30) and **d** in individuals > 30 years of age (n = 56)

Table 3. Causative factors in pediatric and adult anaphylaxis

Cause	Pediatric: n (%)	Adult: n (%)	Total: n (%)
Patient	72	(52.94%) 64	(47.05%) 136
Food	42 (58.33%)	27 (42.18%)	69 (50.73%)
Milk	17 (23.61%)	5 (7.81%)	22 (16.17%)
Egg	9 (12.5%)	6 (9.37%)	15 (11.02%)
Wheat	9 (12.5%)	2 (3.12%)	11 (8.08%)
Sesame	1 (1.38%)	6 (9.37%)	7 (5.14%)
Hazelnut	2 (2.77%)	3 (4.68%)	5 (3.67%)
Almond	1 (1.38%)	0 (0%)	1 (0.73%)
Peanut	2 (2.77%)	1 (1.56%)	3 (2.2%)
Peach	0 (0%)	2 (3.12%)	2 (1.47%)
Saffron	0 (0%)	2 (3.12%)	2 (1.47%)
Kiwi	1 (1.38%)	0 (0%)	1 (0.73%)
Drug	14 (19.44%)	20 (31.25%)	34 (25%)
Penicillin	3 (4.16%)	5 (7.81%)	8 (5.88%)
Ceftriaxone	0 (%)	2 (3.12%)	2 (1.47%)
Co-trimoxazol	2 (2.77%)	1 (1.56%)	3 (2.2%)
NSAIDs	0 (0%)	14 (21.87%)	14 (19.04%)
Phenobarbital	3 (4.16%)	1 (1.56%)	4 (2.94%)
Lamotrigine	2 (2.77%)	0 (0%)	2 (1.47%)
Losartan	0(0%)	1 (1.56%)	1 (0.73%)
Idiopathic	3 (4.16%)	13 (20.31%)	16 (11.76%)
*Exercise	1 (1.38%)	5 (7.81%)	6 (4.41%)
Venom sting	3 (4.16%)	4 (6.25%)	7 (5.14%)
**Vaccine	3 (4.16%)	0 (0%)	3 (2.2%)
Latex	0 (0%)	1 (1.56%)	1 (0.73%)

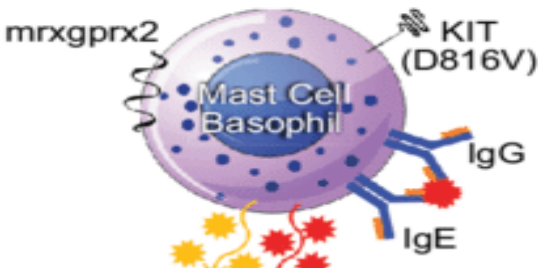

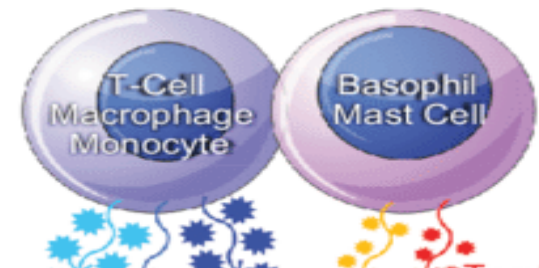
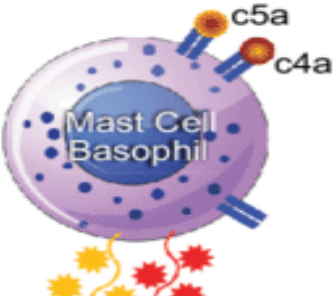




*3 of them were food dependent exercise induced anaphylaxis (one pediatric and two adult)

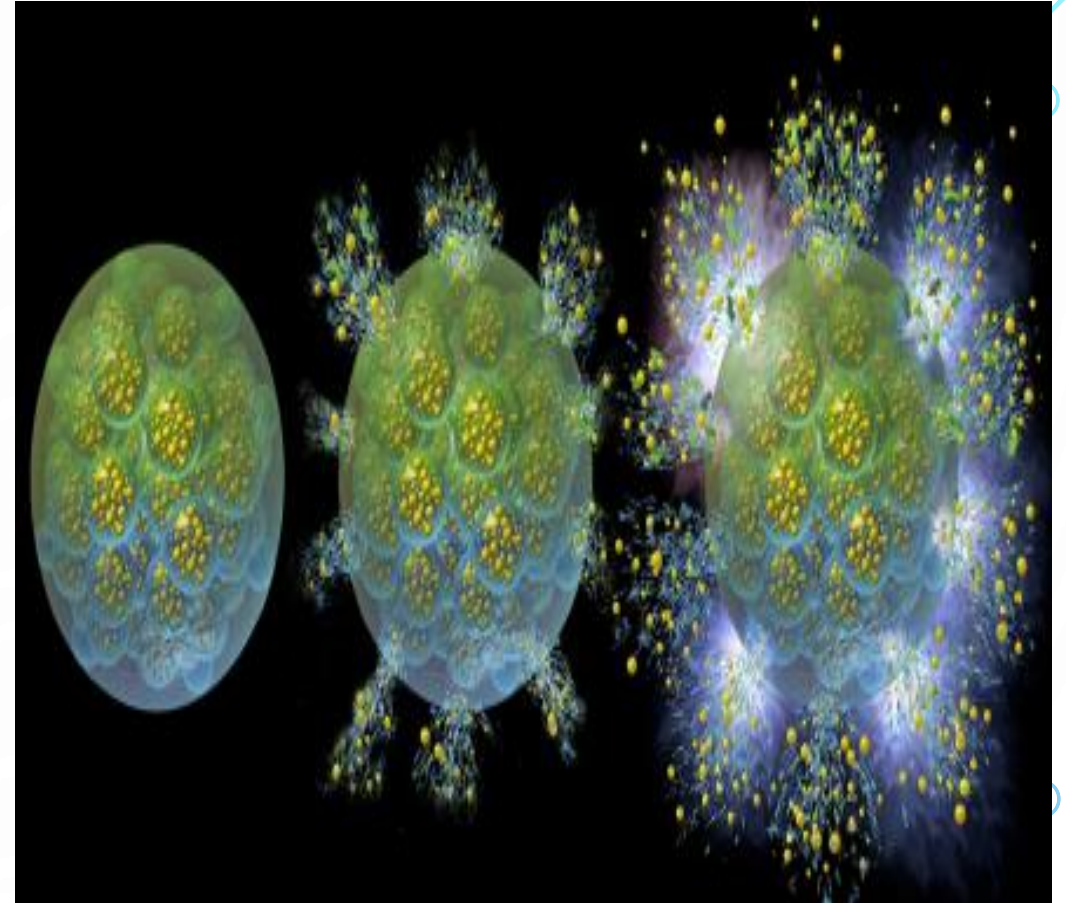
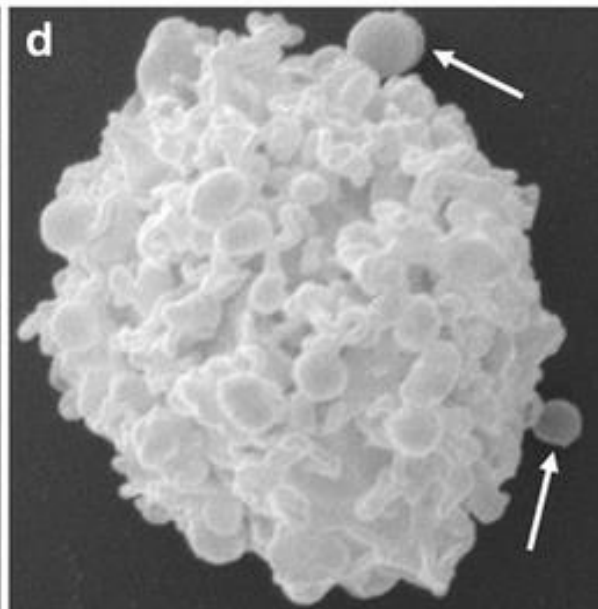
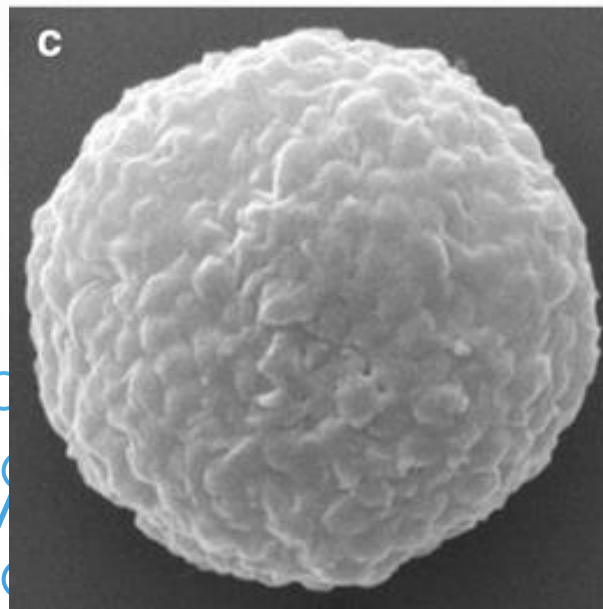
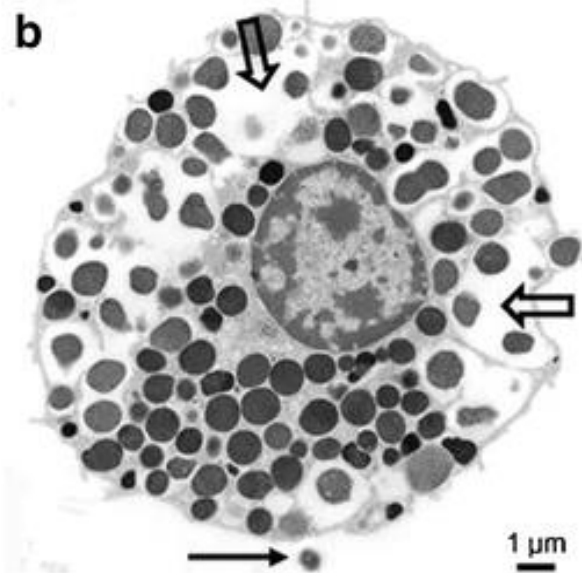
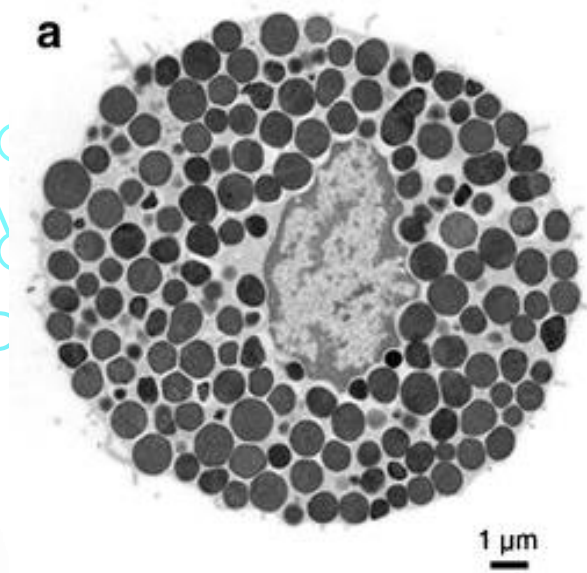
**all of them were due to MMR vaccine (mumps, measles and rubella)

Characteristics, Etiology and Treatment of Pediatric and Adult Anaphylaxis in Iran

FACTORS AFFECTING INCIDENCE AND SEVERITY

- more common in children (0 to 4 years), Diagnosis is more difficult in infants
- Atopy is a clear risk factor for food-induced anaphylaxis
- Poorly controlled asthma is a risk factor of an adverse outcome
- Gaps in administration may predispose to reactions
- Medications delivered by the oral route are less likely
- Time since last reaction (Particularly for antibiotics) the longer the interval, the less likely

Triggers	Environmental Allergens Food Allergens Antibiotics Chemotherapy Monoclonal Antibodies Other Drugs Hymenoptera Venom	Chemotherapy Monoclonal Antibodies	Chemotherapy Monoclonal Antibodies	Contrast Dyes Oversulfated chondroitin sulfate Glycosaminoglycans Dialysis Membranes
Phenotype	Type I IgE/non-IgE	Cytokine-release	Mixed	Complement
Endotypes				
Biomarkers	Histamine Tryptase	TNF-α IL-6 IL-1β	TNF-α IL-6 IL-1β Histamine Tryptase	Histamine Tryptase
Symptoms	Flushing, Pruritis, Urticaria, Throat Tightness Shortness of Breath, Back Pain, Nausea, Vomiting, Diarrhea, Cardio Vascular Collapse	Fever+Chills/Rigors, Nausea, Pain, Headache, Hypotension, Oxygen desaturation	Fever+Chills/Rigors, Nausea, Pain, Headache, Flushing, Pruritis, Rash, Urticaria, Throat Tightness, Shortness of Breath, Nausea, Vomiting, Diarrhea, Cardio Vascular Collapse	Hypotension Oxygen desaturation
Treatment	Epinephrine			
Desensitization	 Yes	 Selected cases	 Selected cases	 No



SUMMARY OF INCIDENCE FOR COMMON TRIGGERS

- **Drugs**
- **Foods**
- **Venom**
- **Latex**
- **Radiocontrast media**
- **Allergen specific immunotherapy**
- **Physical triggers**
- ...



LATROGENIC ANAPHYLAXIS

DRUG ALLERGY



MOST COMMON DRUG TRIGGERS

Antibiotics

NSAIDs

muscle relaxants

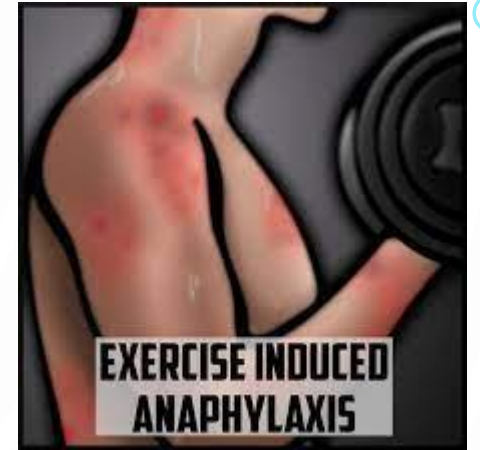
biologic agents

any other drug...



FOOD-DEPENDENT EXERCISE-INDUCED ANAPHYLAXIS

- more common in females
- late teens to mid-30's
- exercise 2-4 hours after ingesting offending food
- foods implicated: wheat, seafood, fruit, milk, celery, fish
- mechanism: two signals required

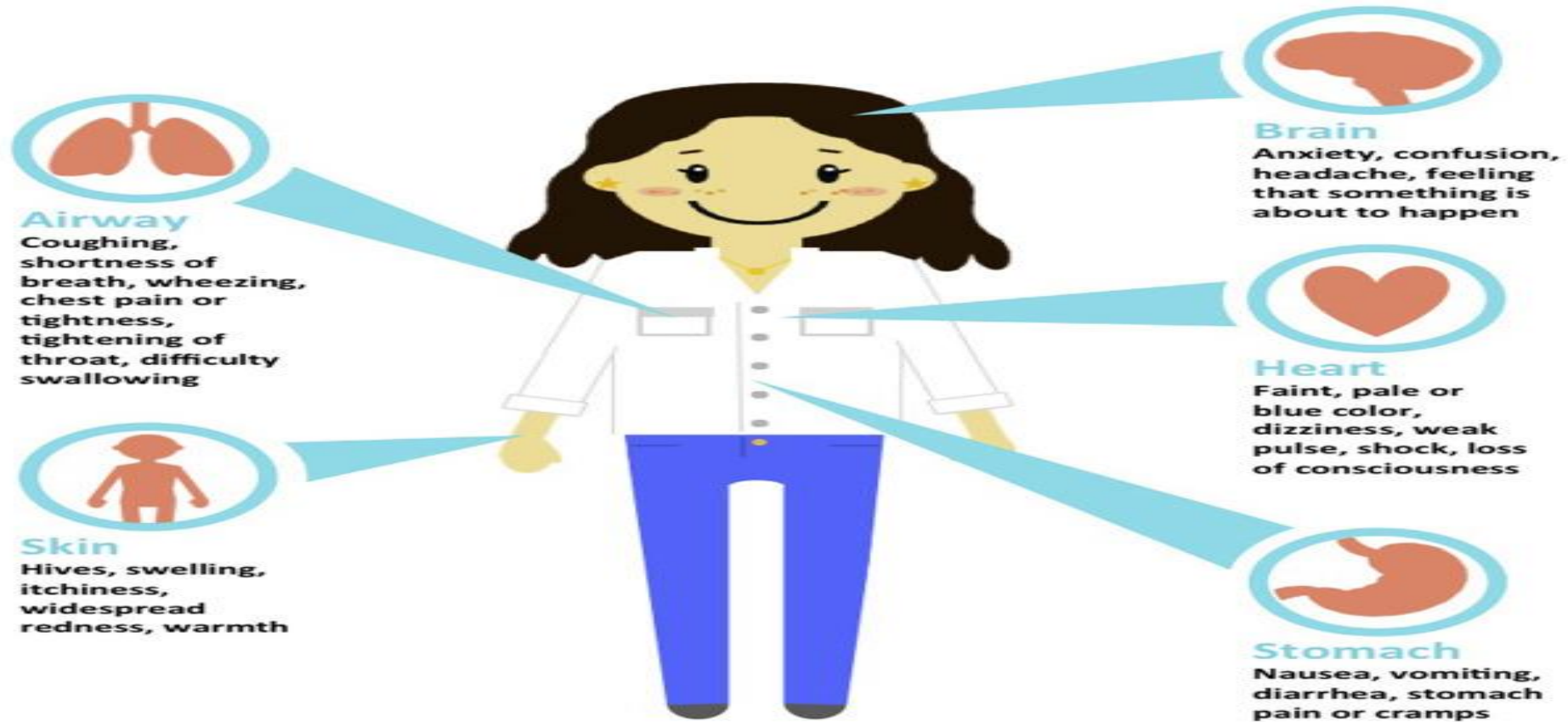


IDIOPATHIC ANAPHYLAXIS

- **common in adults** / uncommon in children
- **negative skin tests** / **negative** dietary **history**
- no associated diseases eg. mastocytosis
- **deaths rare**
- may **gradually improve** over time

SYMPTOMS OF ANAPHYLAXIS



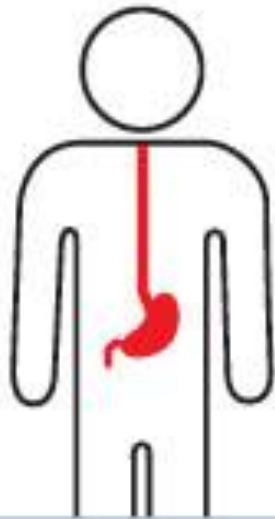

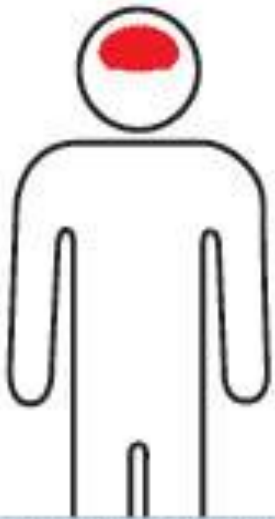
SIGNS and SYMPTOMS of ANAPHYLAXIS



GIVE
EPINEPHRINE

&

CALL
911

				
SKIN	RESPIRATORY	GASTROINTESTINAL	CARDIOVASCULAR	NEUROLOGICAL
hives, swelling, itching, warmth, redness	coughing, wheezing, shortness of breath, chest pain or tightness, throat tightness, trouble swallowing, hoarse voice, nasal congestion or hay fever-like symptoms, (sneezing or runny or itchy nose; red, itchy or watery eyes)	nausea, stomach pain or cramps, vomiting, diarrhea	dizziness/ lightheadedness, pale/blue colour, weak pulse, fainting, shock, loss of consciousness	anxiety, feeling of "impending doom" (feeling that something really bad is about to happen), headache
			hypotension	OTHER ²³
				uterine cramps

Airway obstruction



BIPHASIC AND PROTRACTED ANAPHYLAXIS

BIPHASIC ANAPHYLAXIS

- return of symptoms after resolution
- without exposure
- usually, within 6 hours

Up to 72 h

BIPHASIC ANAPHYLAXIS

- when the **inciting agent is unknown**
- if **hypotension** is present
- **Delayed administration** and **underdosing** of epinephrine
- Corticosteroids does not prevent biphasic anaphylaxis



PROTRACTED ANAPHYLAXIS

symptoms may be continuous for **several days**

early administration of epinephrine reduce the risk

but corticosteroids do not

AGE-RELATED FACTORS*

			
Infants Cannot describe their symptoms	Adolescents and young adults Increased risk-taking behaviors	Labor and delivery Risk from medications (e.g. antibiotic to prevent neonatal group B strep infection)	Elderly Increased risk of fatality from medication or venom-triggered anaphylaxis

CONCOMITANT DISEASES*

				
Asthma and other respiratory diseases	Cardiovascular diseases	Mastocytosis/clonal mast cell disorders	Allergic rhinitis and eczema**	Psychiatric illness (e.g. depression)

CONCURRENT MEDICATIONS/ETHANOL/RECREATIONAL DRUG USE*

	
β-adrenergic blockers and ACE inhibitors***	Ethanol/sedatives/hypnotics/antidepressants/recreational drugs (potentially affect recognition of anaphylaxis triggers and symptoms)

CO-FACTORS THAT AMPLIFY ANAPHYLAXIS*

				
Exercise	Acute infection (e.g. a cold or fever)	Emotional stress	Disruption of routine (e.g. travel)	Premenstrual status (females)

* 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.

** Atopic diseases are a risk factor for anaphylaxis triggered by food, exercise, and latex, but not for anaphylaxis triggered by insect stings.

*** ACE, angiotensin-converting enzyme

DIFFERENTIAL DIAGNOSIS OF ANAPHYLAXIS

Anaphylaxis

Anaphylaxis to exogenously administered agents

Physical factors

Exercise

Cold, heat, sunlight

Idiopathic

Vasodepressor (Vasovagal) Responses ✦

Flushing syndromes

Carcinoid, pheochromocytoma, medullary carcinoma of the thyroid

Menopause

Side effects of chlorpropamide, alcohol, calcium channel blockers

Autonomic epilepsy

Food-Associated Syndromes

Scrombroidosis ✦

Sulfites

Monosodium glutamate (MSG)

Other Forms of Shock

Cardiogenic

Septic

Vascular

Excess Endogenous Production of Histamine Syndromes

Mast cell activation syndrome

Systemic mastocytosis

Cutaneous mastocytosis

Mast cell leukemia

Acute promyelocytic leukemia

Nonorganic Disease

Panic attacks ✦

Munchausen stridor

Vocal cord dysfunction

Undifferentiated somatoform anaphylaxis

Miscellaneous

Acute urticaria with or without angioedema

Hereditary angioedema

Idiopathic angioedema

Neurologic (seizure, stroke)

Red man syndrome (vancomycin)

Capillary leak syndrome

DIAGNOSING ANAPHYLAXIS

The first step is to:

Just think about this...

Acute onset of an illness (minutes to several hours) with involvement of:

Skin and/Or Mucosa

Pruritus
Flushing
Hives
Angioedema

And either

Respiratory Compromise

Dyspnea
Wheeze-bronchospasm
↓ Peak expiratory flow
Stridor
Hypoxemia

Or

↓ BP Or end-organ Dysfunction

Collapse
Syncope
Incontinence

2 or more of the following that occur rapidly after exposure to a likely allergen for that patient:

Skin and/Or Mucosa

Pruritus
Flushing
Hives
Angioedema

Respiratory Compromise

Dyspnea
Wheeze-bronchospasm
↓ Peak expiratory flow
Stridor
Hypoxemia

↓ BP Or end-organ Dysfunction

Collapse
Syncope
Incontinence

Persistent GI Symptoms

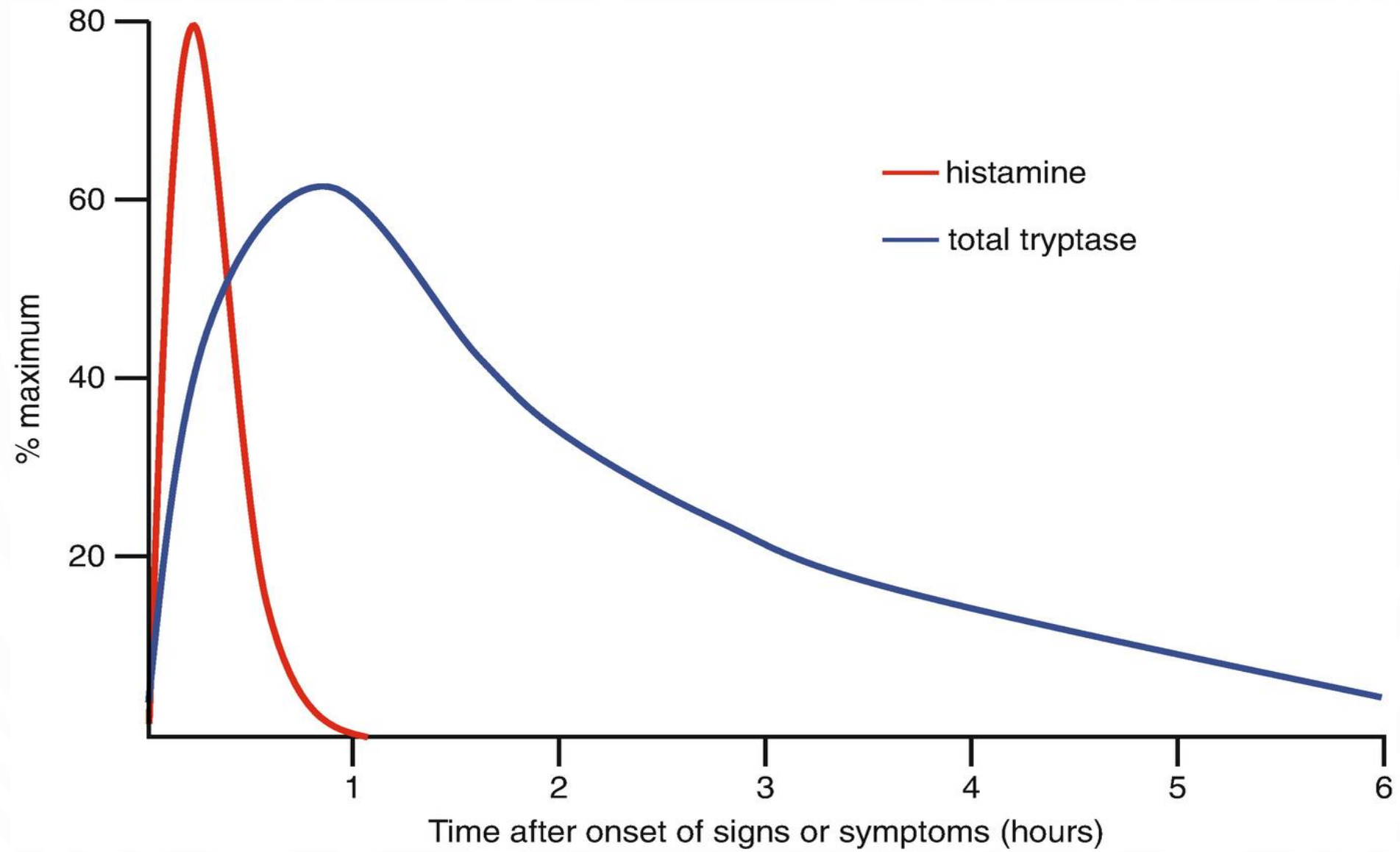
Vomiting
Crampy Abdominal Pain
Diarrhea

After exposure to known allergen for that patient (minutes to several hours):

↓ BP

GRADING OF ANAPHYLACTIC REACTIONS

Grading	Muller	Ring & Messmer
I	Generalized urticaria, periorbital edema, itching, malaise, anxiety	Cutaneous manifestations (flushing, pruritus, urticaria, angioedema)
II	Angioedema or two or more of following: chest/throat tightness, nausea, vomiting	Mild respiratory, CV, GI (Rhinorrhea, hoarseness, dyspnea, tachycardia, BP change, arrhythmia)
III	Dyspnea, wheezing, or stridor or two or more of following: dysphagia, dysarthria, hoarseness, weakness, confusion, feeling of impending disaster	Severe multisystem involvement (Laryngeal edema, bronchospasm, anaphylaxis, cyanosis, shock, collapse)
IV	Hypotension, collapse, loss of consciousness, incontinence, cyanosis	Cardiac arrest



PHYSICIAN-SUPERVISED MANAGEMENT OF ANAPHYLAXIS

Act Fast

No One Can Survive Low Oxygen For Very Long

Remove Contact With Allergen, If Possible

Don't Panic

Follow The Sequence

Save A Life



8. Move To Hospital



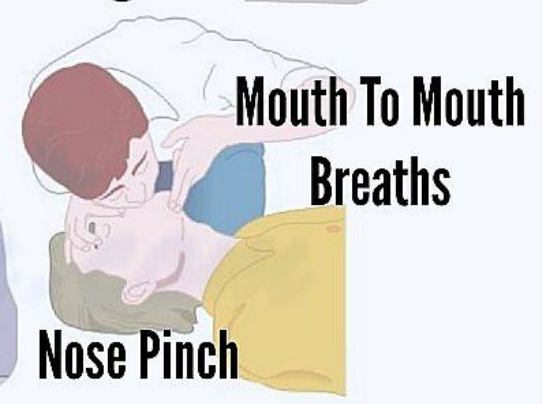
7. CPR

6. Support Breathing



Chin Pull

Head Tilt



Mouth To Mouth
Breaths

Nose Pinch

5. Adrenaline
Autoinjector



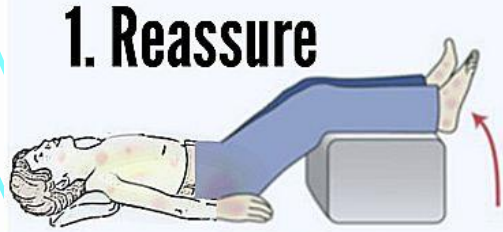
4. Call Help



3. Access



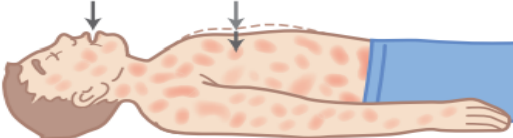
2. Position




1. Reassure

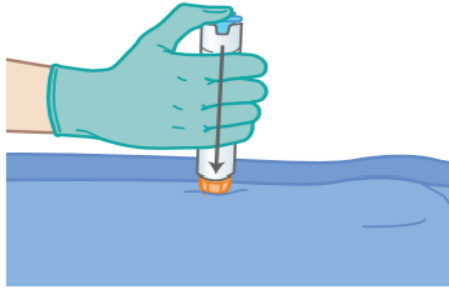
1 Have a written emergency protocol for recognition and treatment of anaphylaxis and rehearse it regularly. ★

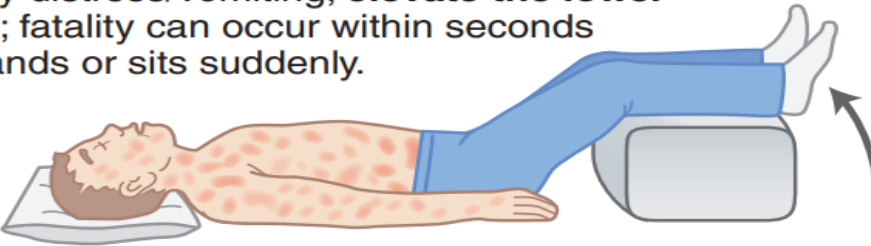
2 Remove exposure to the trigger if possible, e.g. discontinue an intravenous diagnostic or therapeutic agent that seems to be triggering symptoms. ★

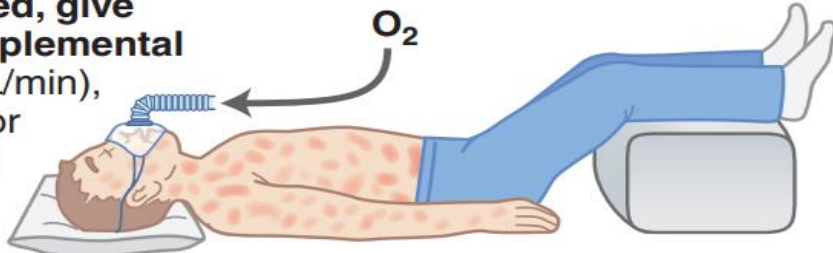
3 Assess the patient's circulation, airway, breathing, mental status, skin, and body weight (mass). 

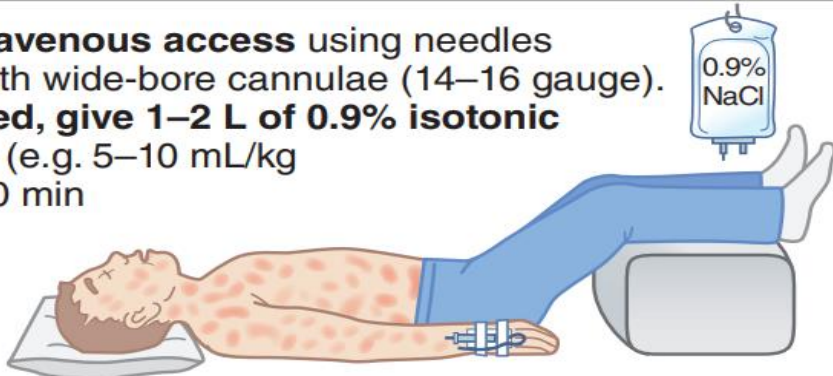
Promptly and simultaneously, perform steps 4, 5, and 6.

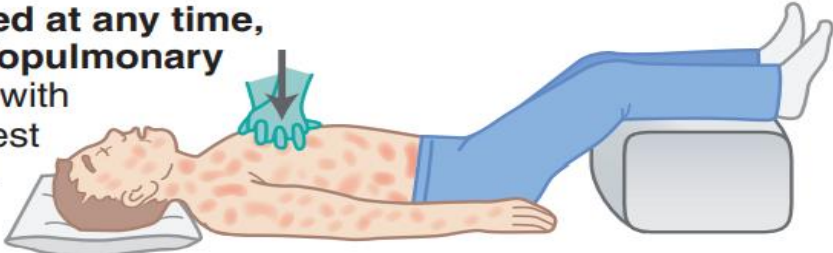
4 Call for help: resuscitation team (hospital) or emergency medical services (community) if available. ★ 

5 Inject epinephrine (adrenaline) intramuscularly in the mid-anterolateral aspect of the thigh, 0.01 mg/kg of a 1:1,000 (1mg/mL) solution, maximum of 0.5 mg (adult) or 0.3 mg (child); record the time of the dose and repeat in 5–15 minutes, if needed. Most patients respond to 1 or 2 doses. 

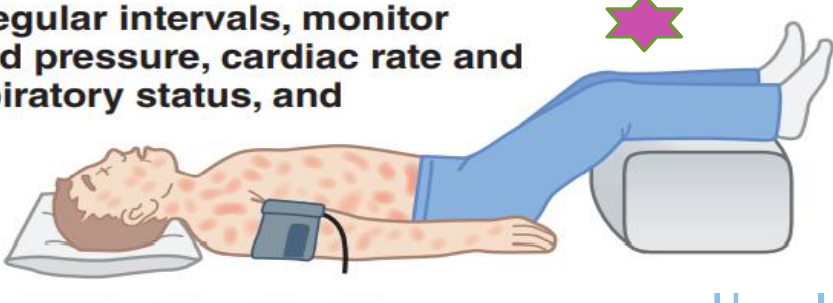
6 Place patient on the back or in a position of comfort if there is respiratory distress/vomiting; elevate the lower extremities; fatality can occur within seconds if patient stands or sits suddenly. ★ 

7 When indicated, give high-flow supplemental oxygen (6–8 L/min), by face mask or oropharyngeal airway. 

8 Establish intravenous access using needles or catheters with wide-bore cannulae (14–16 gauge). When indicated, give 1–2 L of 0.9% isotonic saline rapidly (e.g. 5–10 mL/kg in the first 5–10 min to an adult; 10 mL/kg to a child). 

9 When indicated at any time, perform cardiopulmonary resuscitation with continuous chest compressions. 

In addition,

10 At frequent, regular intervals, monitor patient's blood pressure, cardiac rate and function, respiratory status, and oxygenation (monitor continuously, if possible). ★ 

Adult: 0.3-0.5 mL / IM lateral thigh

of 1 : 1000 (1 mg/mL) solution

Child: 0.01 mg/kg of 1 : 1000 (1 mg/mL) solution
(maximum of 0.3 mL) / IM lateral thigh

May repeat every 5 to 15 min





Drug	Dose/Route of Administration	Comment
Epinephrine	Adult: 0.3-0.5 mL of 1 : 1000 (1 mg/mL) solution, IM lateral thigh Child: 0.01 mg/kg of 1 : 1000 (1 mg/mL) solution, to a maximum of 0.3 mL, IM lateral thigh	Initial drug of choice for all anaphylactic episodes; should be given immediately; may repeat every 5-15 minutes if needed
Antihistamines		
H ₁ antihistamine Diphenhydramine	Adult: 25-50 mg IM or IV Child: 1 mg/kg or 12.5-25 mg IM or IV	For relief of itching and urticaria
H ₂ antihistamine Ranitidine	Adult: 50 mg IV or 1 mg/kg IV Child: 1 mg/kg IV	
Drugs for Resistant Bronchospasm		
Aerosolized β_2 -agonist Albuterol	Adult: 2.5 mg/3 mL or 5 mg/3 mL given by nebulizer and face mask Child: 2.5 mg/3 mL given by nebulizer and face mask	Useful for bronchospasm not responding to epinephrine
Corticosteroids		
Hydrocortisone	Adult: 200 mg IV or IM Child: maximum 100 mg IV or IM	Exact dose not established
Methylprednisolone	Adult: 50-100 mg IV Child: 1 mg/kg, maximum 50 mg IV	
Volume Expanders		
Isotonic (0.9%) saline	Adult: 1000-2000 mL rapidly (i.e. 5-10 mL/kg in first 5-10 min) Child: 10-20 mL/kg in first 5-10 min	Rate titrated to BP response for IV volume expander After initial infusion, further administration requires tertiary care monitoring; larger amounts may be needed in β -blocked patients
Drugs in β-Blocked Patients		
Glucagon	Initial dose of 1-5 mg IV, followed by infusion of 5-15 μ g/min titrated to BP response	Glucagon probably drug of choice
Atropine sulfate	Adult: 0.3-0.5 mg IV; may repeat every 10 minutes to maximum 2 mg	Atropine probably useful only for bradycardia
Ipratropium	0.5 mg via nebulizer and face mask	As alternative or added to inhaled β -blockers for wheezing

NEW GRADING SYSTEM AND PROPOSED MEASURES

		SYSTEMS & Sx	SKIN/MUCOSAL	GASTRO- INTESTINAL	UPPER RESPIRATORY	LOWER RESPIRATORY	NEUROLOGICAL	CARDIOVASCULAR
		GRADE †						
DETAILED CLINICAL JUDGMENT IS CRUCIAL FOR THE DECISION	EPINEPHRINE AVAILABLE *	IF NON-PROGRESSING Sx & ONLY 1 SYSTEM INVOLVED PREPARE * EPINEPHRINE	SYSTEMIC ALLERGIC REACTION	<ul style="list-style-type: none"> • urticaria • pruritus (e.g., skin, lips, eyes, nose) • flushing • angioedema (not laryngeal) 	<ul style="list-style-type: none"> • oral/palatal pruritus • oral/palatal tingling • nausea • drooling 	<ul style="list-style-type: none"> • nasal symptoms • throat pruritus 		
	EPINEPHRINE YES	IF RAPIDLY PROGRESSING Sx OR > 1 SYSTEM INVOLVED GIVE EPINEPHRINE	I ANAPHYLAXIS					
		GIVE EPINEPHRINE	II ANAPHYLAXIS	<ul style="list-style-type: none"> • crampy abdominal pain • sudden and/or recurrent vomiting • diarrhea 	<ul style="list-style-type: none"> • feeling of difficult breathing • hoarseness 	<ul style="list-style-type: none"> • sudden repetitive cough • chest tightness • mild to moderate bronchospasm 	<ul style="list-style-type: none"> • sudden change in behavior or activity level • presyncope e.g. dizziness, weakness 	
		GIVE EPINEPHRINE	III ANAPHYLAXIS		<ul style="list-style-type: none"> • upper airway angioedema e.g. tongue swelling, throat tightness, difficulty swallowing, odynophagia • stridor 	<ul style="list-style-type: none"> • severe bronchospasm (not responding or worsening despite treatment) 	<ul style="list-style-type: none"> • confusion • somnolence • feeling of impending doom 	<ul style="list-style-type: none"> • sudden relevant hypotension ‡ • pale & floppy child • short episode of collapse • syncope
		GIVE EPINEPHRINE	IV ANAPHYLAXIS			<ul style="list-style-type: none"> • respiratory failure 	<ul style="list-style-type: none"> • loss of consciousness (non-transient) 	<ul style="list-style-type: none"> • cardiovascular failure • cardiac arrest

MEASURES TO REDUCE THE INCIDENCE OF DRUG-INDUCED ANAPHYLAXIS

MEASURES TO REDUCE THE INCIDENCE OF **DRUG-INDUCED ANAPHYLAXIS**

- Treatment:
- Intramuscular injection of **epinephrine at early** signs
of an anaphylactic reaction

MEASURES TO REDUCE THE INCIDENCE OF **DRUG-INDUCED** ANAPHYLAXIS

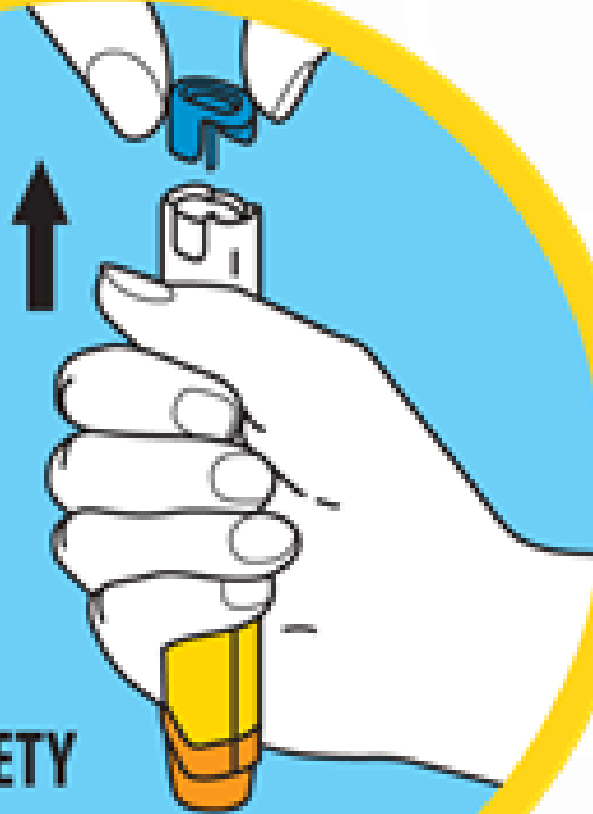
General measures:

- Obtain thorough **history** for drug allergy
- **Avoid cross-reactive** drugs
- Administer drugs **orally** rather than parenterally
- Check all drugs for **proper labeling**
- Keep patients in the office **30 minutes after injections**
- Follow guideline after specific drugs(omalizumab, ecallantide)



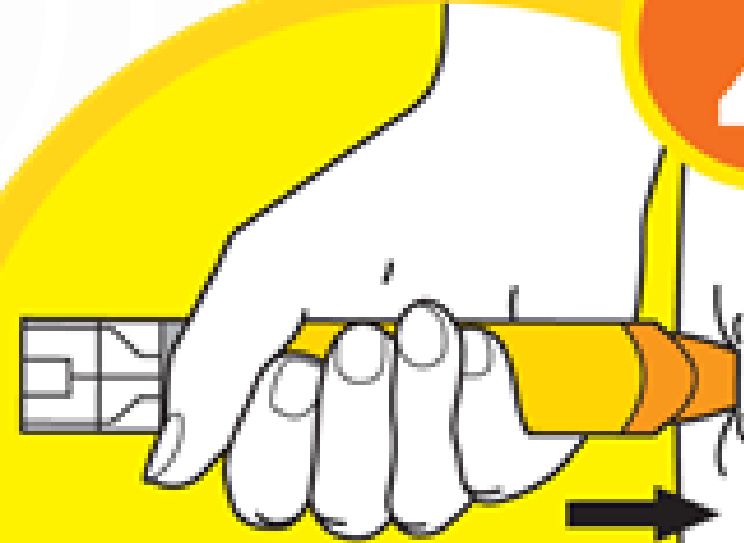
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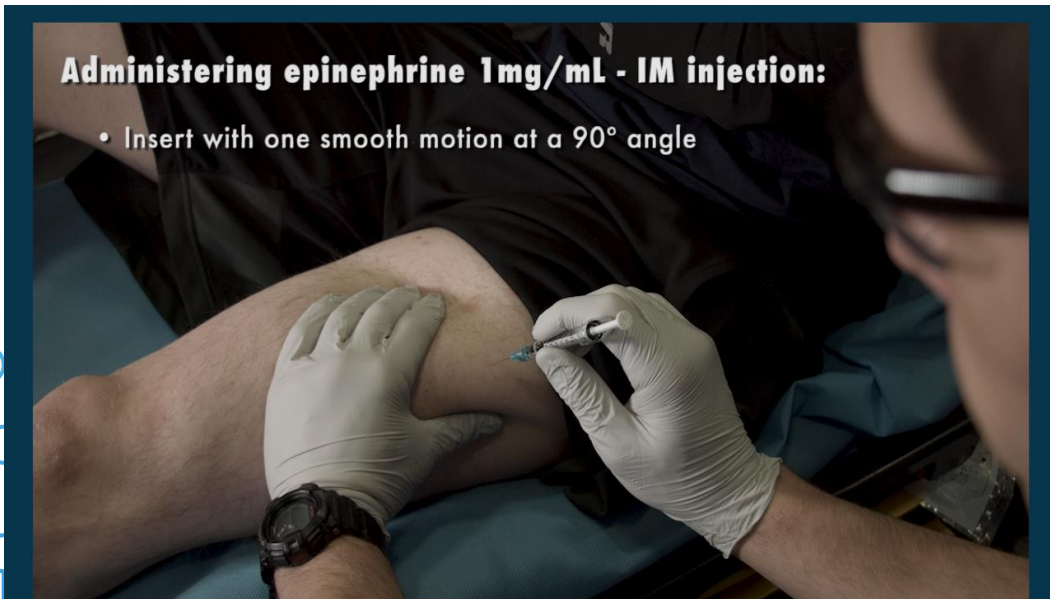
**Form FIST
around
EpiPen® and
PULL OFF
BLUE SAFETY
RELEASE**



2

**Place orange end HARD
into outer thigh so it
'CLICKS' and HOLD
for 10 seconds.**





CONTRAINDICATIONS

- No contraindications for epinephrine in anaphylaxis

**Yes!
It's
always
yes!**

OBSERVATION PERIOD

- 4 hours with relatively mild anaphylaxis
- 6 to 8 hours for those with respiratory compromise
- patients with hypotension for 8 to 24 h after resolution of symptoms

PREVENTION OF ANAPHYLACTIC REACTIONS TO RADIOCONTRAST MEDIA (RCM)

- Prednisone: 20-50 mg orally (12, 7, and 1 hours before)
- H₁ antihistamine (1 hour before)
- H₂ antihistamine (1hour before)

SPECIFIC ADVICE FOR **FOOD-INDUCED** ANAPHYLAXIS

- complete avoidance of a food is difficult
- **written Anaphylaxis Action Plan**
- **self-injectable epinephrine**
- **Medic Alert**-type identification



SPECIFIC ADVICE FOR **VENOM-INDUCED** REACTIONS

- Venom **immunotherapy**
- Avoidance of : eating, using perfumes, wearing light colored or short sleeved cloths in open areas

MEASURES TO REDUCE THE INCIDENCE OF DRUG-INDUCED ANAPHYLAXIS

- Measures for Patients at Risk:
- wear and carry **warning identification tags**
- Teach **self-injection of epinephrine**
- advise patients to carry an epinephrine autoinjector
- **repeat** instructions each year
- **Discontinue** β -blockers, ACE inhibitors, TCAs, MAO inhibitors
- **preventive techniques** (pretreatment, challenge, desensitization)

REFERRAL TO ALLERGIST

- risk assessment
- patient education
- medication review
- self-administered epinephrine
- new therapies



- Immunotherapy
- Premedication

POSTMORTEM

- **serum tryptase and antigen-specific IgE levels** up to 5 days after death
- **serum tryptase most useful to distinguish anaphylactic deaths from acute cardiac deaths**
- **normal serum tryptase value is 43 ng/mL (compared with 11 ng/mL for premortem samples)**

THANKS FOR YOUR ATTENTION

