

IN THE NAME OF GOD



ANAPHYLAXIS

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WHY DOES ANAPHYLAXIS MATTER?

Potentially life threatening

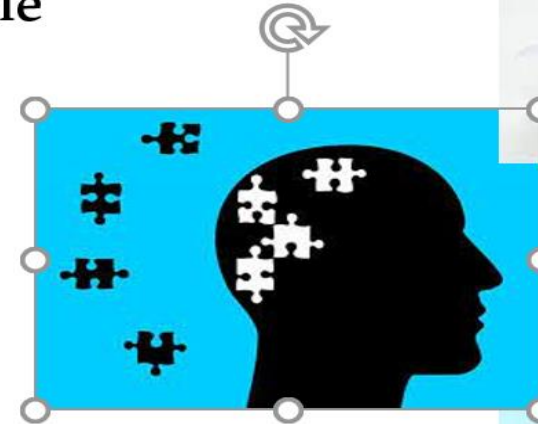
Effective and safe treatment is available

Should always be kept in mind

Timely treatment is lifesaving

Many cases are iatrogenic

Under diagnosed and under treated





DEFINITION OF ANAPHYLAXIS

- An acute
- potentially life threatening
- multisystem syndrome
- caused by sudden release of mast cell mediators into the systemic circulation



EPIDEMIOLOGY

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

- significant underreporting

- the true incidence is significantly higher than formally reported

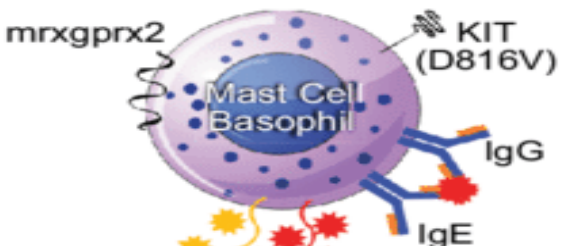

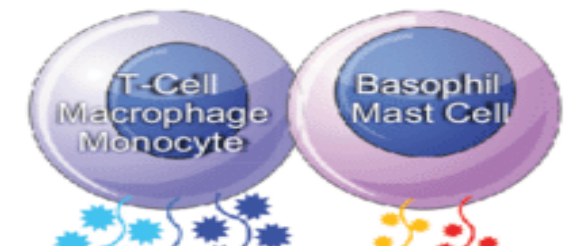





- **Foods** are probably the **most common triggers**

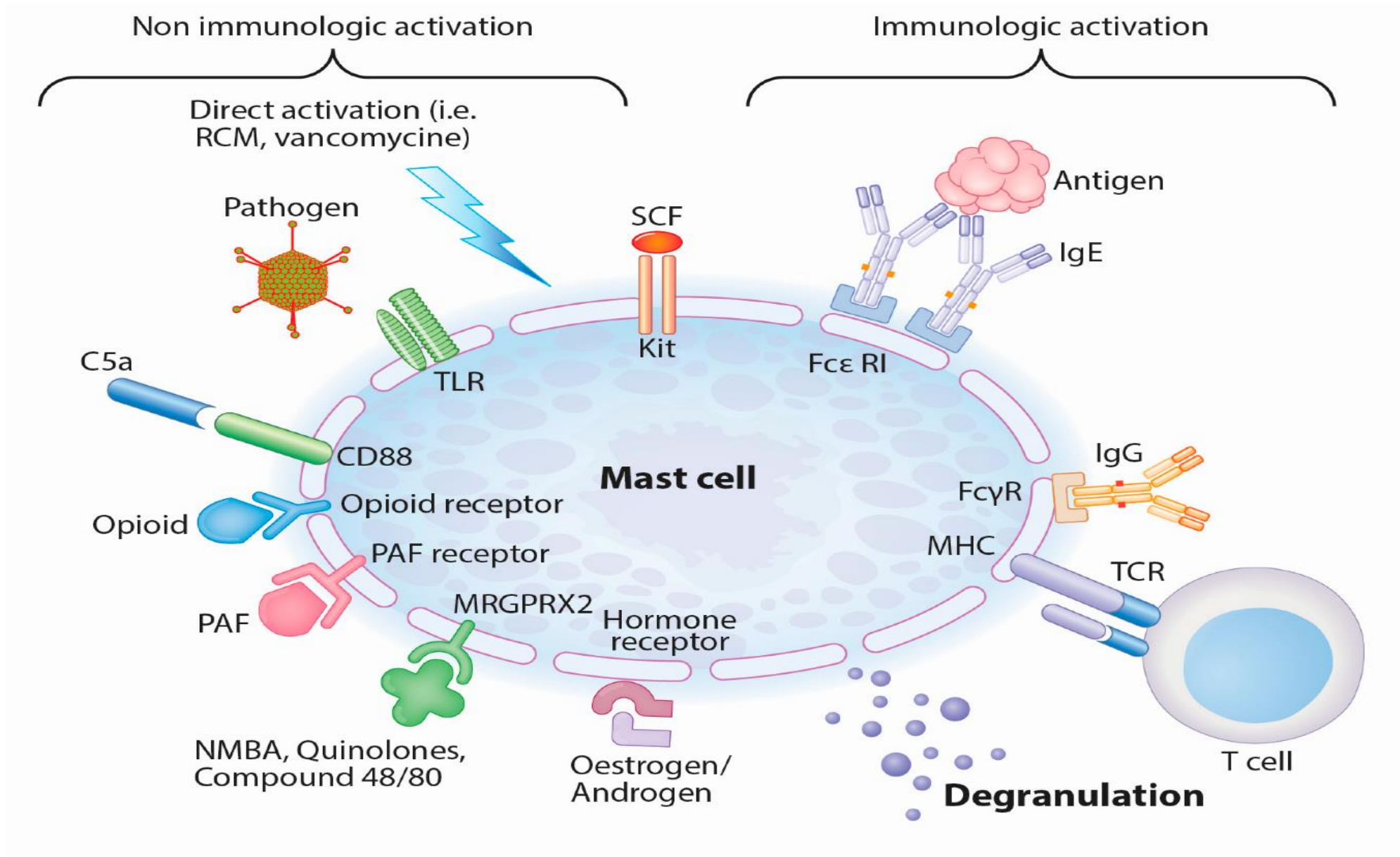
- followed by **drugs** (nonsteroidal antiinflammatory drugs and antibiotics)

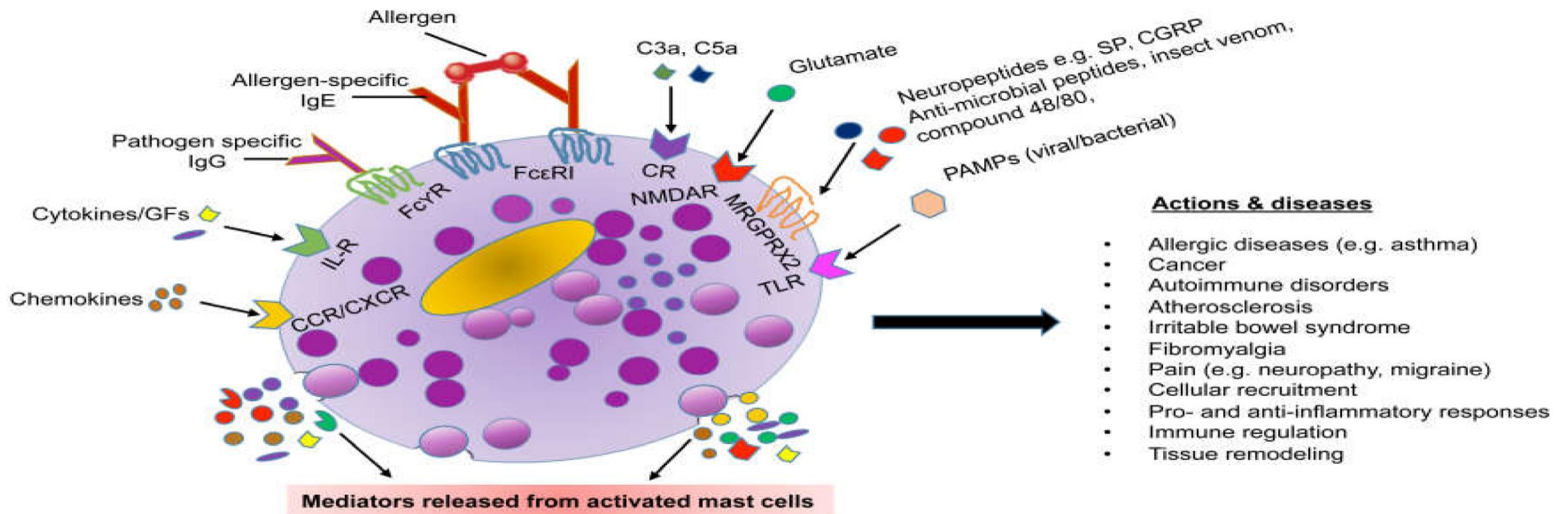
FACTORS AFFECTING INCIDENCE AND SEVERITY

- 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
- Mast cell–related diseases
- Medications delivered by the oral route are less likely
- Gaps in administration may predispose to reactions
- Time since last reaction (Particularly for antibiotics) the longer the interval, the less likely

Pathways of anaphylaxis

Triggers	<div> <div>Environmental Allergens</div> <div>Food Allergens</div> <div>Antibiotics</div> <div>Chemotherapy</div> <div>Monoclonal Antibodies</div> <div>Other Drugs</div> <div>Hymenoptera Venom</div> </div> <div> <div>Chemotherapy</div> <div>Monoclonal Antibodies</div> </div> <div> <div>Chemotherapy</div> <div>Monoclonal Antibodies</div> </div> <div> <div>Contrast Dyes</div> <div>Oversulfated chondroitin sulfate</div> <div>Glycosaminoglycans</div> <div>Dyalisis Membranes</div> </div>			
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	<div> Flushing, Pruritis, Urticaria, Throat Tightness Shortness of Breath, Back Pain, Nausea, Vomiting, Diarrhea, Cardio Vascular Collapse </div>	<div> Fever+Chills/Rigors, Nausea, Pain, Headache, Hypotension, Oxygen desaturation </div>	<div> Fever+Chills/Rigors, Nausea, Pain, Headache, Flushing, Pruritis, Rash, Urticaria, Throat Tightness, Shortness of Breath, Nausea, Vomiting, Diarrhea, Cardio Vascular Collapse </div>	<div> Hypotension Oxygen desaturation </div>
Treatment	<div>Epinephrine</div>			
Desensitization	<div>  Yes </div>	<div>  Selected cases </div>	<div>  Selected cases </div>	<div>  No </div>





Preformed mediators

- Lysosomal hydrolases: e.g. β -hexosaminidase
- Mast cell-restricted proteases: tryptase, chymase, carboxypeptidase A3
- Biogenic amines: e.g. histamine, serotonin
- Proteoglycans: serglycin
- Cytokines/Chemokines: e.g. TNF, IL-4, CCL5
- Growth factors: e.g. SCF, VEGF, NGF, TGF- β

De novo-synthesized mediators

- Lipid mediators: e.g. PGD2, PGE2, LTB4, LTC4, PAF
- Cytokines: e.g. TNF, IFN γ , IL-1, -2, -3, -4, -6, -9, -10, -13, -33
- Chemokines: e.g. CCL1, 2, 3, 4, 5, 7, 11, 17, 20, 22; CXCL2, 8, 10
- Growth factors: e.g. VEGF, NGF, SCF, FGF, TGF- β , PDGF, GM-CSF

SUMMARY OF INCIDENCE FOR COMMON TRIGGERS

- Foods (more common in children)
- Drugs & venom (more common in adult)
- Latex
- Radiocontrast media
- Allergen specific immunotherapy
- Physical triggers



FOOD-INDUCED ANAPHYLAXIS

- peanut
- tree nut
- seafood
- fin fish
- milk
- egg
- soy
- wheat



IATROGENIC ANAPHYLAXIS

DRUG ALLERGY



MOST COMMON DRUG TRIGGERS

- Antibiotics (the most common)
- NSAIDs
- Anesthetic drugs (particularly neuromuscular blocking agents)
- Biologics
- vaccines
- Any other drug or drug additives

LATEX-INDUCED ANAPHYLAXIS

Decreasing prevalence

highest among **healthcare workers**

latex gloves , injection vial covering, etc

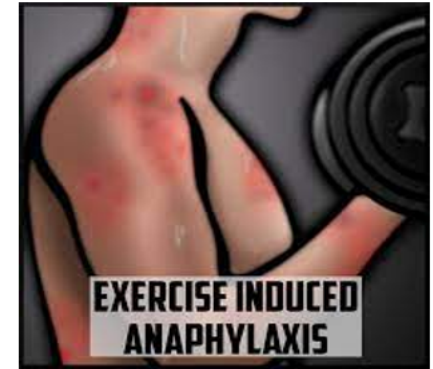
repeated exposure leads to higher risk

- **use of non-latex gloves**



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

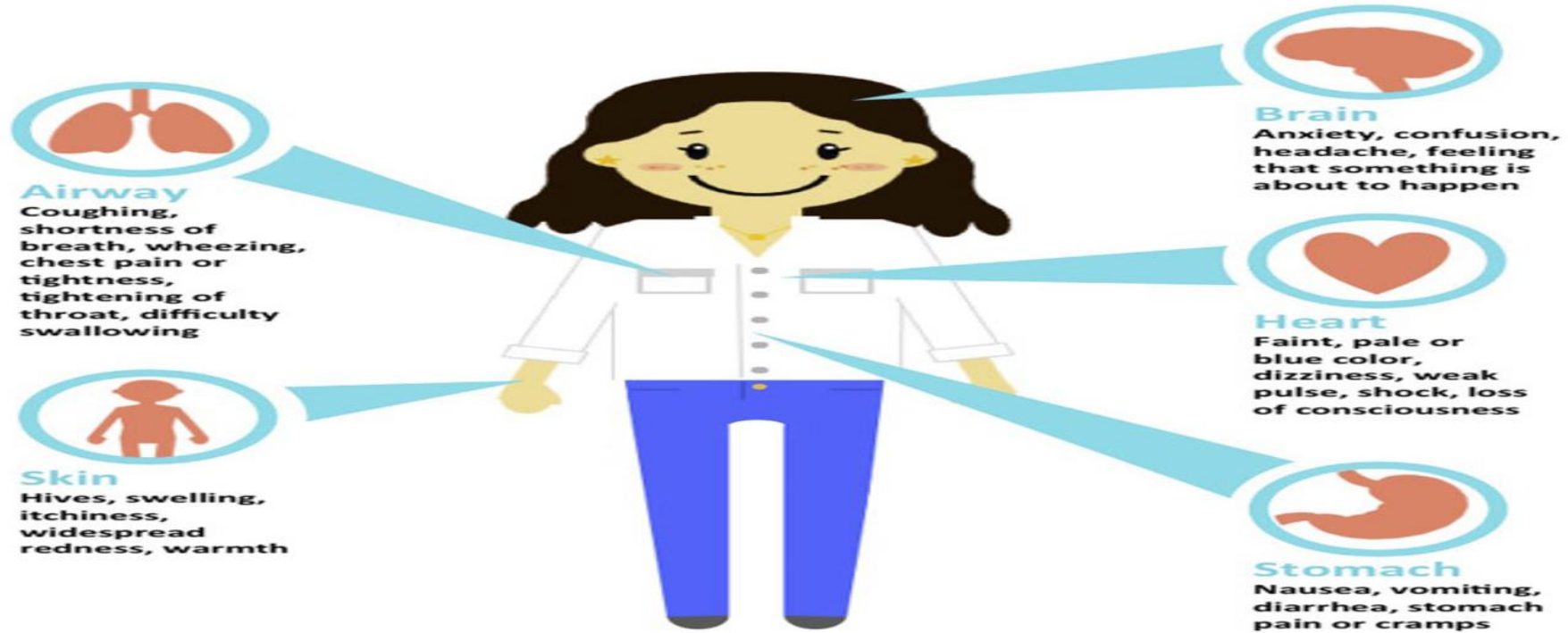


IDIOPATHIC ANAPHYLAXIS

- **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 

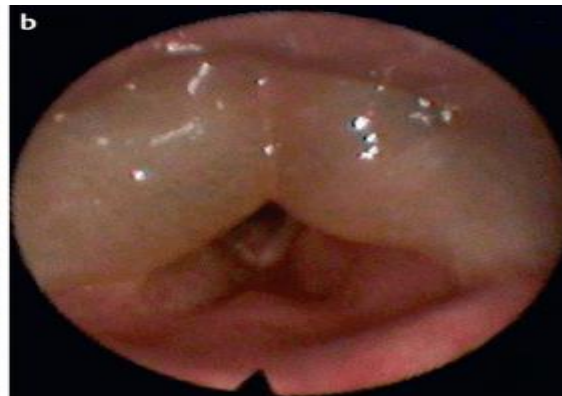
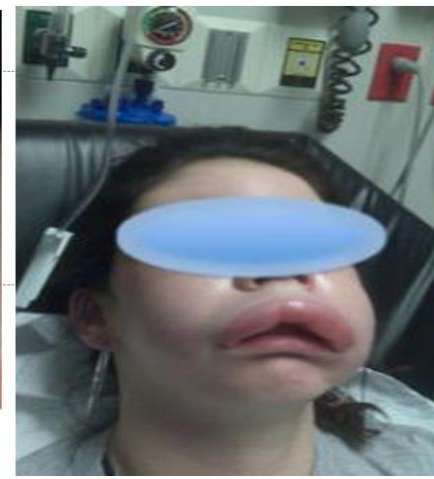
Skin: 80-90%

Flushing

itching

urticaria

angioedema



RESPIRATORY: 70%

Rhinorrhea

Shortness of breath

Congestion

Chest tightness

Stridor

Wheezing

Dysphonia

Cyanosis



Gastrointestinal: 45%

Nausea

Vomiting

Bloating

Cramping diarrhea



Cardiovascular: 45%

Chest pain

Hypotension

Tachycardia

Dysrhythmias

Bradycardia



Cardiac arrest







- Hypotension in infants and children :
- 1mo-1y: SBP < 70 mmHg
- 1y-10y: SBP < $70 + (2 \times \text{age})$ mmHg
- 11y-17y: SBP < 90 mmHg
- In adults:
- More than 30% decrease compared to baseline SBP or <90mmHg



central nervous system: 15%

- Sense of impending doom
 - Altered mental status
 - Dizziness
 - Confusion Headache
- 
- 



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





DIFFERENTIAL DIAGNOSIS OF ANAPHYLAXIS

Differential diagnosis for anaphylaxis and anaphylactic shock

Presentation

Differential Diagnosis

Hypotension



Septic shock
Vasovagal reaction
Cardiogenic shock (sudden asystole may be a sign of anaphylactic shock as well)
Hypovolemic shock

Respiratory distress with wheezing or stridor

Airway foreign body, especially in small children
Asthma and chronic obstructive pulmonary disease exacerbation

Postprandial syndromes

High monosodium glutamate ingestion
Sulfite ingestion
Scrombroid fish poisoning^a

Flush syndromes



Carcinoid syndrome
Postmenopausal hot flushes
Alcohol-induced flush
Red man syndrome (vancomycin injection)

Excess endogenous production of histamine syndromes

Systemic mastocytosis^a
Basophil leukemia^a
Acute promyelocytic leukemia (tretinoin treatment)^a



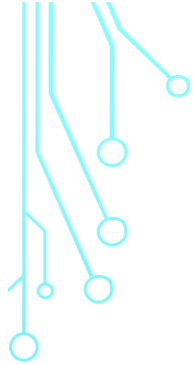
Nonorganic diseases



Panic attacks
Vocal cord dysfunction syndrome
Munchausen stridor

Miscellaneous

Cardiovascular (myocardial infarction)^a
Neurologic events (seizure, cerebrovascular event)



DIAGNOSING ANAPHYLAXIS

The first step is to:
Just think about this...

1

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

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

3

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

↓ BP

LAB TESTS Almost always unnecessary

Anaphylaxis is CLINICAL DIAGNOSIS

Blood tests can be used to support, but negative test cannot refute clinical diagnosis

Need to draw soon after symptom onset

- **Serum or Plasma total tryptase (15 minutes to 3 hours)**
 - Insect stings, medications, hypotension more reliable
 - If still elevated 24 or more hours later: REFER allergist ?systemic mastocytosis
- **Plasma histamine (15 minutes to 60 minutes) – not as practical**
- **Potential Future Tests**
 - GOAL: rapid, sensitive, specific lab test or panel of tests that helps clinicians to confirm the diagnosis of anaphylaxis in real time





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

1. Reassure



2. Position



3. Access



4. Call Help



5. Adrenaline Autoinjector



6. Support Breathing

Chin Pull

Head Tilt



Mouth To Mouth Breaths

Nose Pinch



8. Move To Hospital

7. CPR



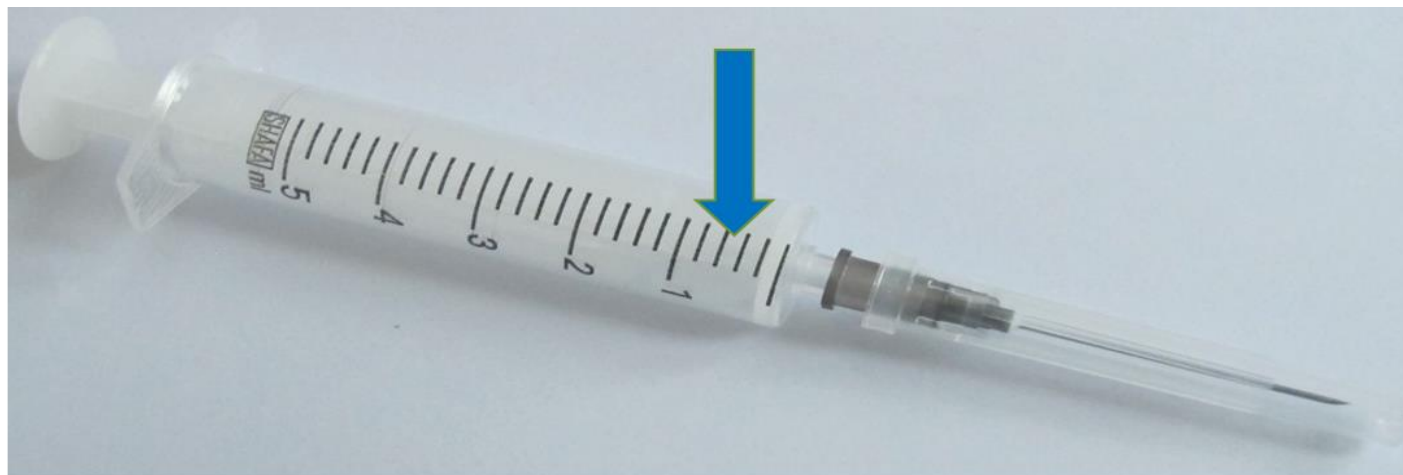
Adult: 0.3-0.5 mL / IM lateral thigh

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








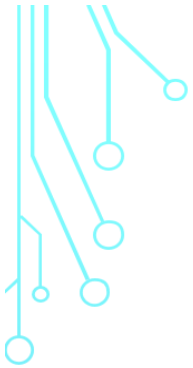
Drug	Dose/Route of Administration	Comment
Epinephrine	Adult: 0.3-0.5 mL of 1 : 1000 (1 mg/mL) solution, IM lateral thigh Child: 0.01 mg/kg of 1 : 1000 (1 mg/mL) solution, to a maximum of 0.3 mL, IM lateral thigh	Initial drug of choice for all anaphylactic episodes; should be given immediately; may repeat 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 GRADE ↑	SKIN/MUCOSAL	GASTRO- INTESTINAL	UPPER RESPIRATORY	LOWER RESPIRATORY	NEUROLOGICAL	CARDIOVASCULAR
DETAILED CLINICAL JUDGMENT IS CRUCIAL FOR THE DECISION	EPINEPHRINE AVAILABLE *	IF NON-PROGRESSING Sx & ONLY 1 SYSTEM INVOLVED PREPARE * EPINEPHRINE						
	EPINEPHRINE YES	IF RAPIDLY PROGRESSING Sx OR > 1 SYSTEM INVOLVED GIVE EPINEPHRINE	<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 			
		GIVE EPINEPHRINE						
		GIVE EPINEPHRINE						
		GIVE EPINEPHRINE & RESUSCITATION						
				<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 	
					<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
						<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



ALWAYS
OVER DIAGNOSE
AND
OVER TREAT



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:

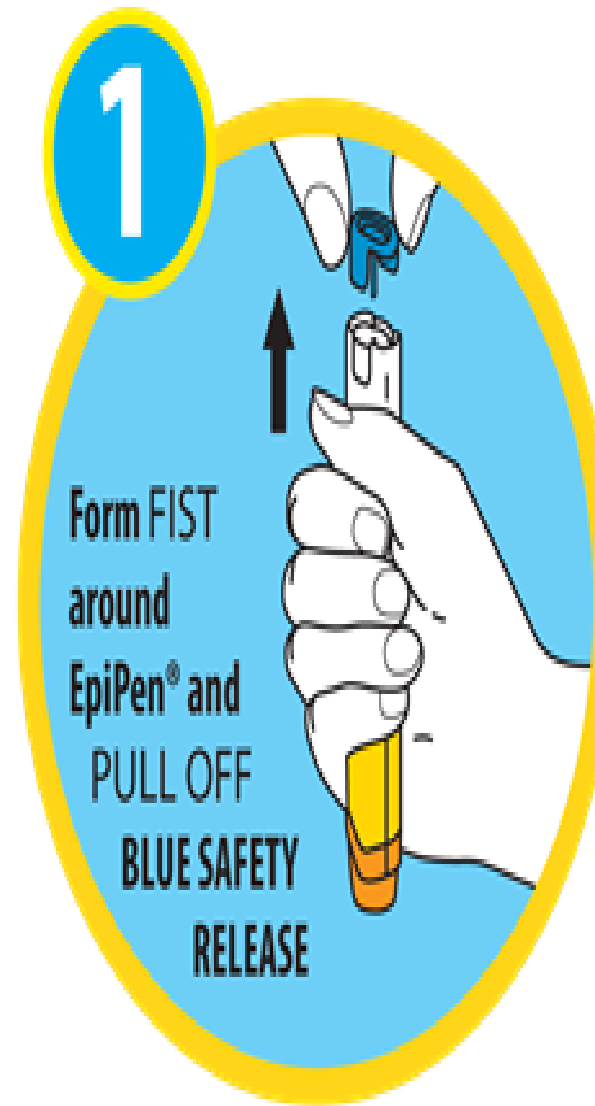
- Obtain thorough **history** for drug allergy
- **Avoid cross-reactive** drugs
- Administer drugs **orally** rather than parenterally
- Check all drugs for **proper labeling**
- Keep patients in the office **30 minutes after injections**
- Follow guideline after specific drugs(omalizumab, ecallantide)

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)







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
- 
- 



REFERRAL TO ALLERGY/IMMUNOLOGY SPECIALIST

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

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)

