



Lecture 3

Drugs used in anaphylaxis.

Objectives :

1. Perceive the differences between anaphylactic shock and other types of shock
 2. Recognize its nature, causes & characteristics.
 3. Specify its diagnostic features
 4. Identify its standard emergency management protocol
 5. Justify the mechanism of action and method of administration of each of the different used drugs to limit its morbid outcomes
- Additional Notes
 - Important
 - Explanation –Extra-

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com

Anaphylaxis: Is a sudden, severe allergic reaction affecting the whole body.

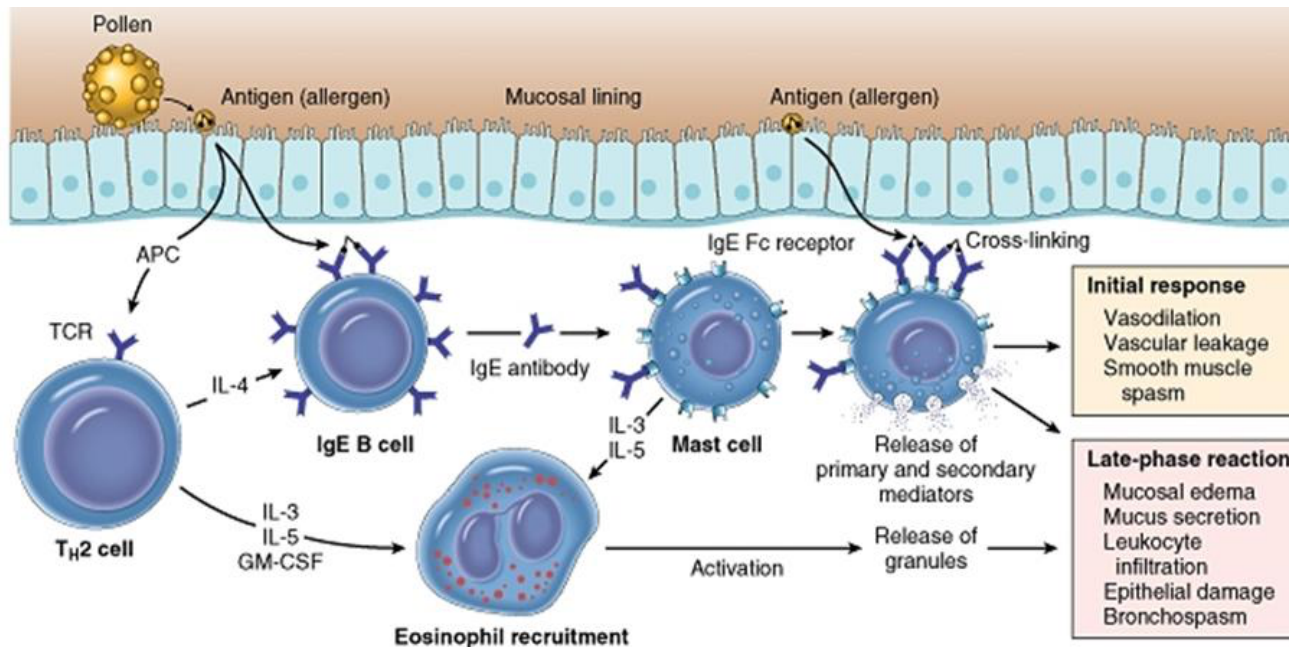
Symptoms: Rash, Mucosal swelling (laryngeal edema → Suffocation → Death), Difficulty breathing, Reduced blood pressure.

Shock

1. Generalized circulatory derangement causing multiple organ **HYPOPERFUSION** [Inadequate oxygen delivery to meet metabolic demands] & strong sympathetic activation. (The blood goes from organs to subcutaneous tissues in response to vasodilation caused by Histamine).
2. Severe, life-threatening, generalized or systemic hypersensitivity reaction in response to allergen. When the shock intense or sustained enough, irreversible derangements sets → permanent functional deficit or death.

Types of shock:

- 1-Hypovolemic: Hemorrhage / fluid loss (plasma, ECF)
- 2-Cardiogenic: Inability to contract & pump → myocardial infarction
- 3-Obstructive: Extra-cardiac obstruction → Pulmonary embolism, cardiac tamponade.
- 4-Distributive: Decreased PR → septic shock, neurogenic, **anaphylactic shock**.



Anaphylactic shock: A life-threatening allergic reaction that causes shock (hypo-perfusion) and airway swelling, it occurs after exposure to an allergen in a previously sensitized person (type 1 hypersensitivity – IgE mediated).

- Rapidly developing [5/30 min / can be hours].
- Severe, life-threatening.
- Multisystem involvement.
- Mortality: due to respiratory (70%) or cardiovascular (25%).

[exposure → mast cell degranulation → histamine , leukotriene production → systemic affects].

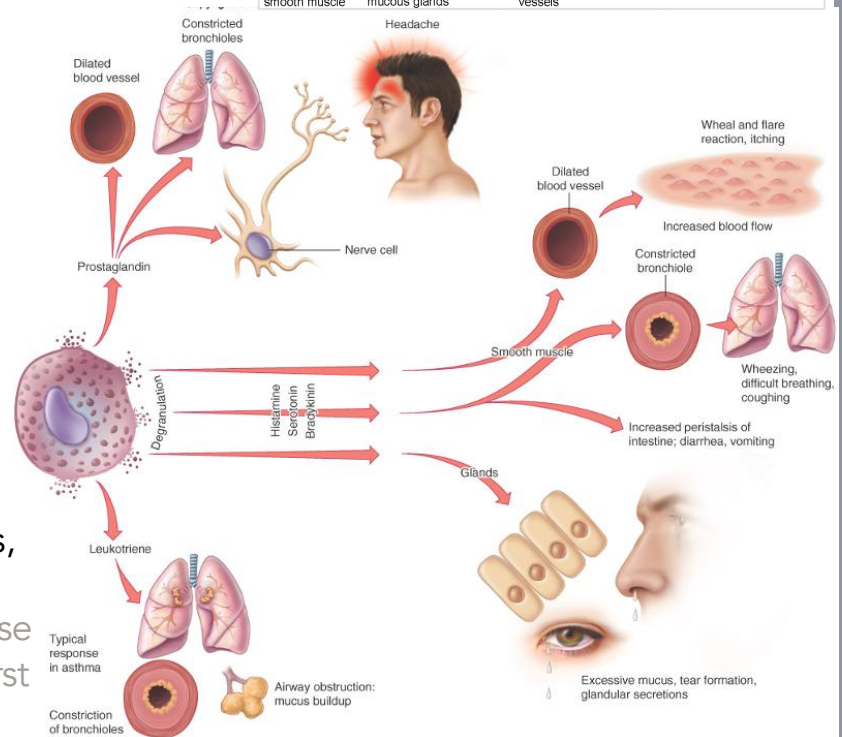
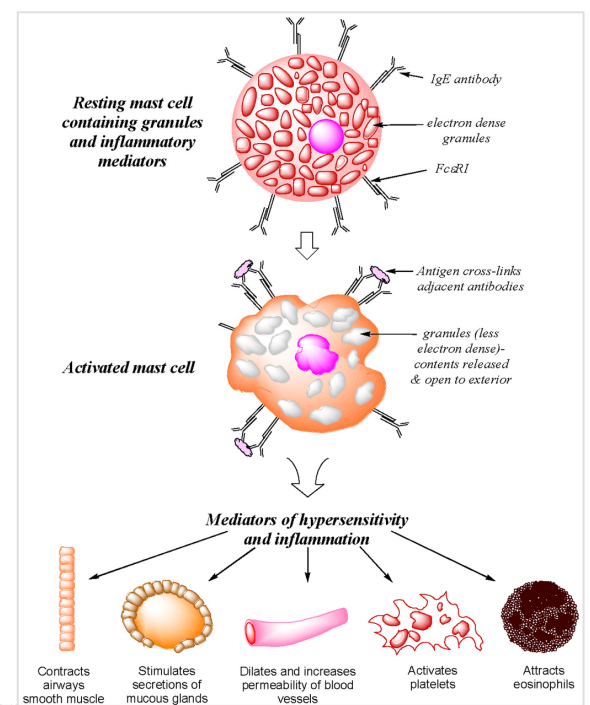
Characters:

- 1- skin (88%): edema / urticaria / pruritus .
- 2- Blood vessels : Hypoperfusion { vasodilatation / leakiness } → decreased BP.
- 3- lungs (47%) : bronchospasm / vasoconstriction.
- 4- heart (33%): circulatory collapse → decreased [cardiac output / coronary flow].
- 5- mucosa swelling :
 - Rhinitis 16%
 - Angioedema 88%
 - Airway 56%
 - GIT 30%

Non-Immunologic Anaphylaxis (ANAPHYLACTOID):

Exogenous substances directly degranulate mast cells .
Such as : Radiocontrast dye, Opiates, Depolarizing drugs, Dextran's.

Anaphylactoid reaction doesn't need first exposure to release histamine from mast cells while in Anaphylactic shock the first exposure should happen first before to form the IgE.



Treatment of Anaphylactic shock

It is a A medical emergency where immediate treatment is needed to prevent potential death.



- **Circulatory support:**
 - Lay down / legs up (Facilitate blood flow to brain) / fluid replacement .
- **Respiratory support:**
 - Open Airway / O2 inhalation.
- **Adrenaline:**
 - IM by auto injector [Disposable, prefilled devices → automatically administer a single dose of epinephrine in emergency] or a syringe .

Life support	Open airway / control breathing and circulation
1 st line	IM adrenaline / IV to be given only by an experienced specialist
2 nd line	Chlorphenamine, Hydrocortisone
Adjuvant to 2 nd line	1- Bronchodilators [Salbutamol nebulizer, Ipratropium nebulizer, Aminophylline IV] 2- glucagon [For patients taking b-blockers & with refractory hypotension → 1 mg IV q 5 minutes until hypotension resolves] 3- H2 blockers [Ranitidine 50 mg IV / No cimetidine in elderly, renal/hepatic failure, or if on b-blockers]

Objective of therapy:

- To support the respiratory & circulatory deficits.
- To halt the existing hyper-reaction.
- To prevent further hyper-reaction of immune system → Biphasic phenomenon:
 - 2nd release of mediators without re-exposure to antigen (in up to 20%).
 - Clinically evident 3-4h after the initial manifestations clear.
- It is very important to know the differences between 1st line & 2nd line.

Adrenaline (1st line)

Mechanism

- A sympathomimetic
- **Non selective** (α - β Adrenaline agonist)

Action

- **α agonist:**
 - Reverses peripheral vasodilation \rightarrow maintains BP/ directs blood flow to major organs.
 - α 1: vasoconstriction \gg \downarrow edema .
- **β agonist:**
 - β 2 :Dilates bronchial airways + \downarrow histamine & leukotriene release from mast cells .
 - β 1 : \uparrow force of myocardial contraction.
- IgE mediated reactions.

Indication

Drug of choice for **anaphylactic shock** and most of the allergic reactions, Status asthmatics.

Contraindications

- Patients with β blockers "adrenaline may antagonize their effects" \rightarrow give glucagon
- Old Man >40 cardiac patient (instead give glucagon) .

Side effect

Dysrhythmias if given IV.

Administration

- IM: * Easily accessible.
- * Greater margin of safety \rightarrow no dysrhythmias as with IV.
- * No need to wait for IV line \rightarrow if present \rightarrow given by physician under monitoring.

Notes

- Repeat every 5-10 min as needed
- Patient should be observed in fear of biphasic anaphylaxis
- If hypotension persist start **Dopamine** (To protect the kidney)
- If need to activate the heart for circulatory support \rightarrow give **glucagon** .

	Corticosteroids (2 nd line) [anti- inflammatory] (Not rescue therapy)	H1 Blockers (adjuvant 2 nd line)	H2 Blockers (adjuvant 2 nd line)	Glucagon (adjuvant 2 nd line)
Mechanism	<p><u>Genomic action:</u></p> <p>* Intracellular receptors (cytosol or nucleus) (takes hours to days to be activated)</p> <ul style="list-style-type: none"> • Long onset of action. • But it has also <u>non-genomic actions</u> which occurs on Membrane bound receptors → modulate 2nd messengers levels. <p>Rapid onset of action → minutes. (That's why it is used in anaphylactic shock)</p> <p>[In anaphylactic shock it acts on the non genomic receptors]</p>	Block H1 receptors	Block H2 receptors	Act on glucagon receptors in heart
Action	<ul style="list-style-type: none"> - Reverse hypotension & bronchoconstriction → ↓ release of inflammatory and allergic mediators (anti-chemotactic & mast cell stabilizing effects). - ↓ mucosal swelling and skin reaction. - May help to limit biphasic reactions → ↓ allergic mediators 	<p>help to counteract histamine-mediated vasodilation & bronchoconstriction.</p> <p>May help to limit biphasic reactions by ↓ more histamine release</p>	<p>Improve hypotension → ramifying heart / BV</p> <p>Responsible for glandular hypersecretions Help in broncho & laryngeal manifestations</p> <p>So adjuvant to H1 blockers → additive benefits in treating anaphylaxis</p>	<p>↑ inotropic & chronotropic → effects → increase cardiac cyclic AMP</p> <p>It is independent of ADR → b2 blockade doesn't affect its action</p> <p>(Glucagon never does Bronchodilatation)</p>
Administration	Given slowly IV or IM		-	-
Notes	Not used alone → NOT LIFE SAVING		-	-

Bronchodilators (adjuvant 2nd line)

Salbutamol	Ipratropium	Aminophylline
Inhalation		Parenteral (IV)
B2 agonist	Anticholinergic	--
<p>Short acting</p> <p>Rapid onset of action</p> <p>Relaxation of bronchial smooth muscles</p> <p>↓ mediators released from mast cells</p> <p>↓ micro vascular leakage</p>	<p>Long acting</p> <p>Slower onset of action</p> <p>↓ secretions</p>	<p>IV → useful for anaphylactic shock</p> <p>But if inhaled → not effective in bronchodilatation and bronchospasm is persistent</p> <p>Given in hospital setting as levels of drug should be Therapeutically Monitored because it has a narrow therapeutic index</p>

★ Summary

	Adrenaline 1 st Line	Corticosteroid 2 nd Line	H1 blockers 2 nd adjuvant line	H2 Blockers adjuvant 2 nd line	Glucagon 2 nd adjuvant line
Indication	anaphylactic shock	↓ release of inflammatory and allergic mediators	↓ histamine release	Help in broncho & laryngeal manifestations	↑ inotropic & chronotropic → effects
Contra-indication	Patients with β blockers Cardiac patients	-	-	-	-
Side effects	Dysrhythmias (IV)	-	-	-	-
Admin.	IM	Given slowly I.V or I.M.		-	-
Notes	+ Dopamine in hypotension + Glucagon for heart support	Not used alone → NOT LIFE SAVING		So adjuvant to H1 blockers → additive benefits in treating anaphylaxis	-(Glucagon never does Bronchodilatation) -act on receptor in heart .



<https://www.youtube.com/watch?v=sX97LcDpgzo>

★ What does each drug look like?



Adrenaline



Corticosteroid



Antihistamine
(H blockers)



Antihistamine (H1 blockers)



Antihistamine (H2 blockers)



Glucagon



Salbutamol



Ipratropium



Aminophylline

★ MCQs

Q1: Which of the following isn't considered as a first line therapy of anaphylactic shock :

- A. Open the airway
- B. Laying the patient down
- C. Glucocorticoids
- D. Adrenaline

Q2: In the sufficient hospitals the IV adrenaline injection isn't preferable because :

- A. Its local effect
- B. It may cause Hematoma
- C. It may cause muscular spasm
- D. It may cause dysrhythmias

Q3: Which of the following best describes adrenaline :

- A. $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$ antagonist
- B. $\alpha 1$ and $\alpha 2$ antagonist
- C. $\beta 1$ and $\beta 2$ agonist
- D. histamine antagonist

Q4: a 45 year old female with a history of chronic hypertension has come to the emergency department after having dinner in a seafood restaurant. she was unconscious and severely anaphylactic . what is the best therapy :

- A. adrenaline
- B. glucagon
- C. Glucocorticoids
- D. dopamine

Q5: an 32 year old male has taken an IM adrenaline injection because of his anaphylactic shock . 20 minutes later his blood pressure remained low . which of the following drugs is best for him :

- A. glucagon
- B. dopamine
- C. noradrenalin
- D. Glucocorticoids

Q6: to stop the inflammatory events in the case of anaphylaxis we use :

- A. NSAIDs
- B. DMARDs
- C. GCs
- D. H1 Blockers

Q7: In treating a patient with anaphylactic shock, you would:

- A. Transport to a medical facility immediately.
- B. Administer oxygen and wait for the reaction to subside.
- C. Place the victim in a supine position until the reaction clears.
- D. Place cold compresses on any swelling and give liquids.

Answers :
A
C
B
B
D
B
C

Good luck!

Done by Pharmacology team 434

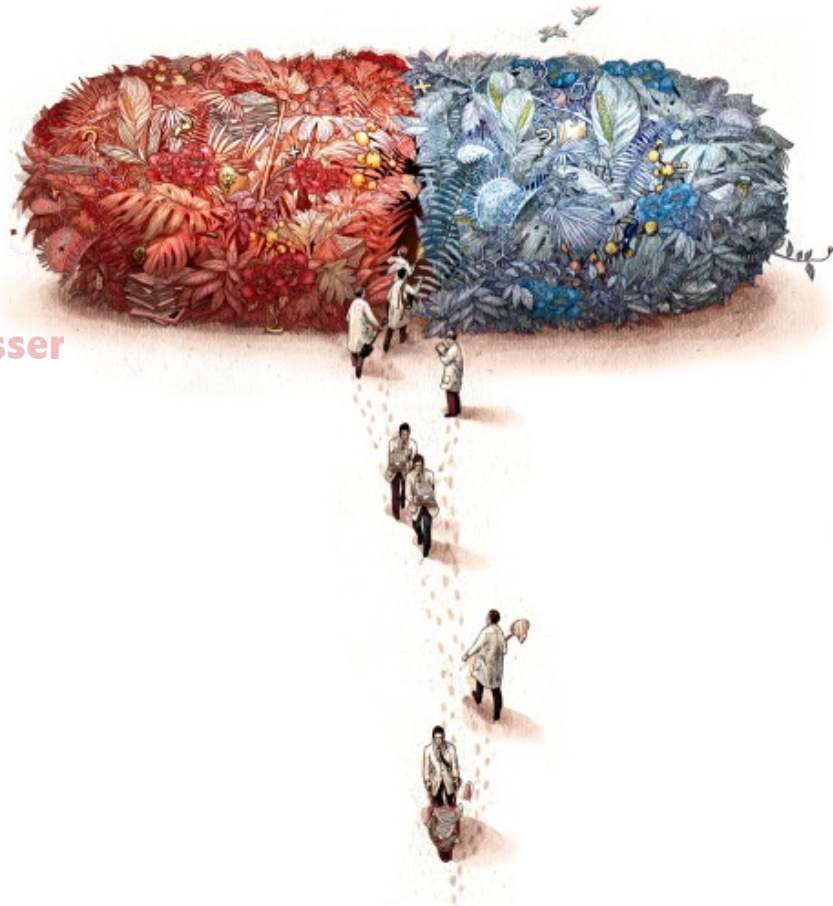
Moneera Al draihem

Maha Al-Rabiah

Reem Labani

Hanan Muhammad

Sara Muhammad Al Jasser



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