



King Saud University
College of Medicine
1st Year, 3rd Block

Drugs Used in Anaphylaxis

5



RESPIRATORY BLOCK

Objectives :

- 1 Perceive the differences between Anaphylactic shock and other types of shocks.
- 2 Recognize its nature, causes, and 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.

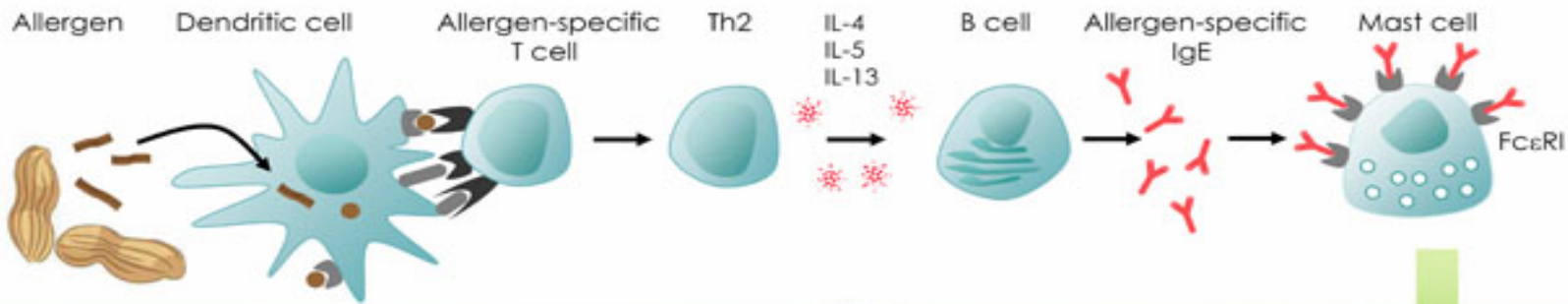
Remember That :

The adverse reactions of drugs (Type A, B, C, D) Type B(Bizarre) happens usually due to the patient's genetic defect or immunological response, and this Anaphylactic shock is an example for the immunological response of adverse effect of drugs. But it's not only due to drugs.





Sensitisation



Allergic reaction



Local symptoms

Swelling
Itching
Nausea
Vomiting
Diarrhoea

Systemic symptoms

Airway obstruction
Hives
Blood pressure drop
Arrhythmia



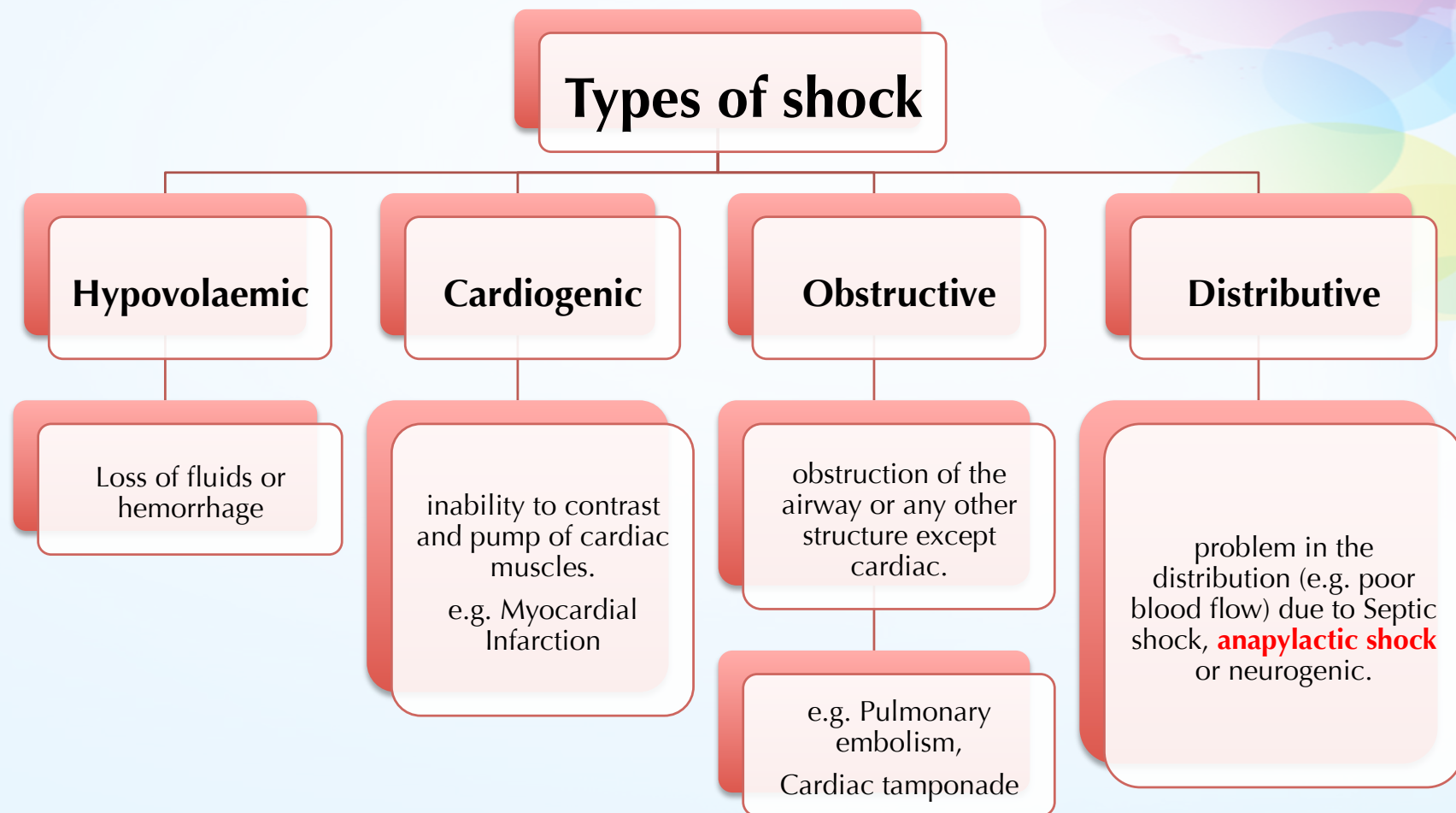
Remember:

What is a shock ?

It is a generalized circulatory derangement, causing :

- Multiple organ **Hypo-perfusion** (inadequate oxygen delivery to meet metabolic demands),
- Strong sympathetic activation.

*When intense or sustained enough → irreversible derangements sets causing permanent functional deficit or death.

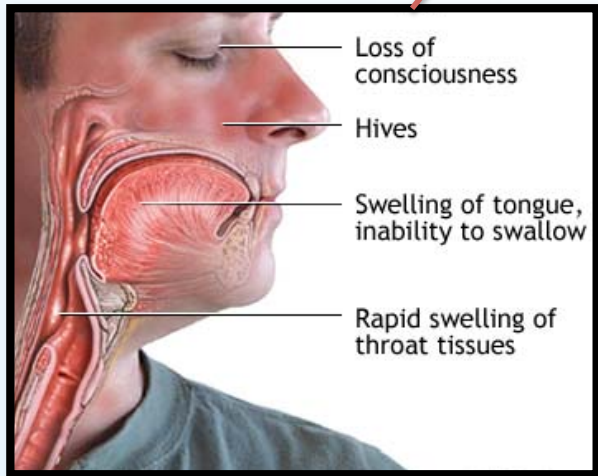


A sudden, severe allergic reaction affecting the **whole body (multisystem involvement)**.

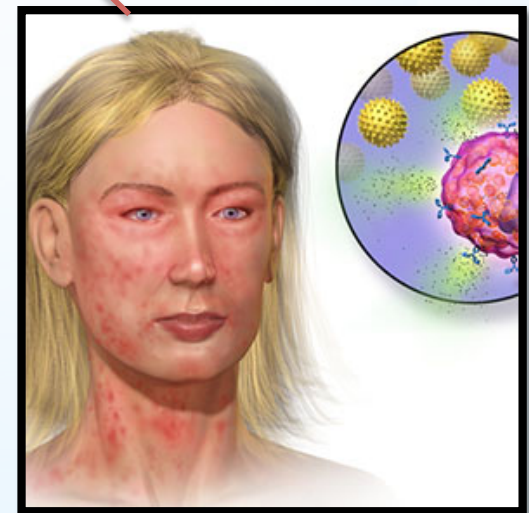
It is a distributive shock that causes Hypoperfusion and is life threatening. It needs immediate treatment to prevent death.

Symptoms:
Rash, mucosal swelling, difficulty in breathing, reduced blood pressure.

Anaphylactic shock



-It rapidly develops: 5-30 min.
-The mortality happens due to:
70% Respiratory
25% cardiovascular



Immunology of The Anaphylactic Shock

-Type I Hypersensitivity reaction (Anaphylaxis), its mechanism :

- 1- After exposure to a foreign substance (allergens/antigens), the antigen-specific IgE antibodies start to attack.
- 2- Once bound to the Antigen, it will be recognized by Mast cell and stimulate it.
- 3- Stimulation of mast cell degranulate mediators e.g.: Histamine, Leukotrienes, Prostaglandins....etc
- 4- Histamine is responsible for the hypersensitivity reaction.

Actions of chemical mediators on Different Organs



Central nervous system:

Dizziness, headaches, confusion



Skin:

Rash/hives, itching, swelling of the lips and/or tongue



Airway:

Trouble breathing, chest tightness, itchy throat



Gastrointestinal system:

Nausea, stomach pain

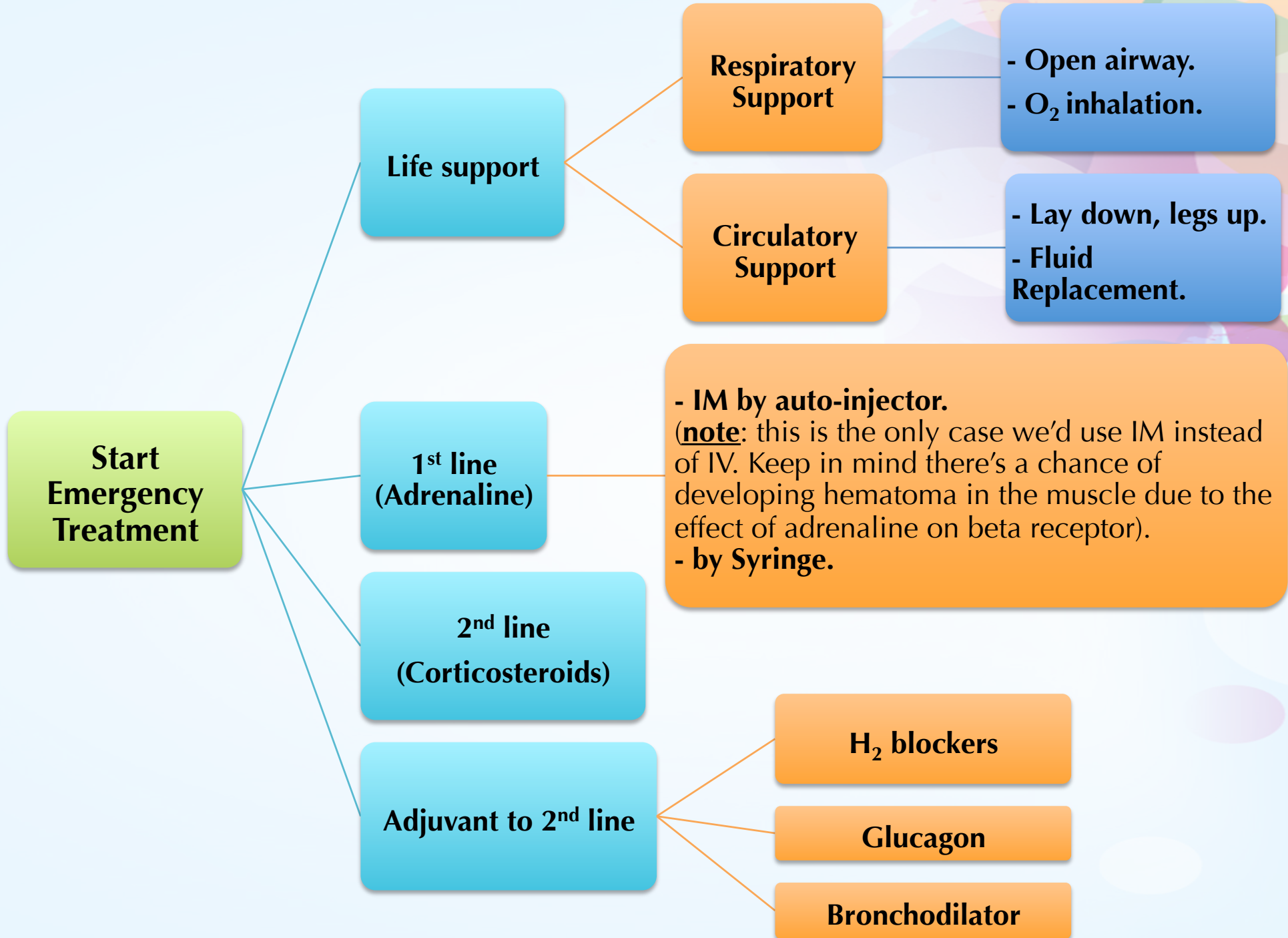


Cardiovascular system:

Chest pain, weak pulse, dizziness, fainting

Anaphylactoid

It is a non-immunomediated reaction occurs due to exposure of exogenous substances that directly degranulate mast cell. E.g. Radiocontrast dye, opiates, depolarizing drugs (succinylcholine), dextrans.



Adrenaline (1st line treatment)

Mechanism of action	Non-selective adrenergic agonists: Works on all the receptors (but β more than α)
Actions	On α : vasoconstriction(α_1) \rightarrow decrease edema.
	On β : Bronchodilation (β_2), Inotropic (β_1)
Indications	Drug of choice for anaphylactic shock and most of the allergic reactions, Status asthmatics.
Administration	<ul style="list-style-type: none">*Best route of administration in anaphylaxis is intramuscularly (IM) because:<ul style="list-style-type: none">1- Easily accessible2- More safety margin (dysrhythmias when given I.V)3- No need to wait for IV administration.*Repeated every 5-10 min. as needed.*Patients are observed for 4-6 hours to make sure they will not get a biphasic⁽¹⁾ anaphylaxis.
Side effects	Dysrhythmias
Some cases	<ul style="list-style-type: none">-If hypotension persists: give Dopamine "better than norepinephrine because Dopamine is beta-1 selective (increase inotropic with little chronotropic effect) and won't cause renal failure""-If heart/circulatory support is needed \rightarrow Glucagon⁽²⁾
Contraindications	Patients with B blockers "adrenaline may antagonize their effects" Cardiac patients 40 years or older. (we give them bronchodilator or Glucagon instead"

(1) 2nd release of mediators without re-exposure to antigen. Look at page #10

(2) An adjuvant to 2nd line drug page #12

Corticosteroids (2nd line treatment)

Pharmacokinetics

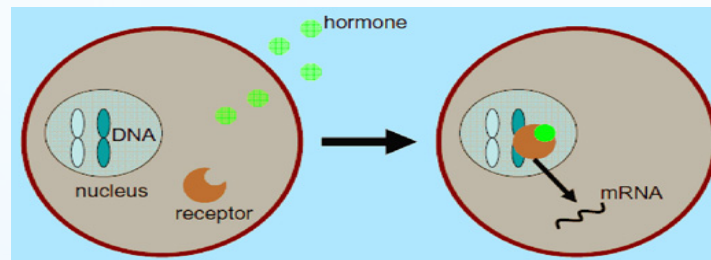
Administered slowly I.V or I.M

These are nuclear receptors "cytosolic receptors" which take long time (hours to days) to produce actions "Genomic actions".
But they also exert rapidly "non-genomic actions" by acting on "membrane bound receptors" modulating 2nd messengers levels within minutes. [That's why it is used in anaphylactic shock].

Pharmacodynamics

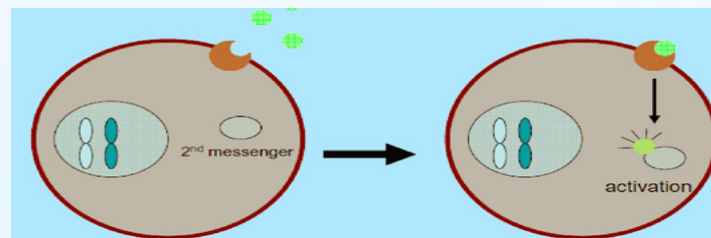
- Reverse hypotension
- Bronchoconstriction:
(It has anti-chemotactic and mast cell stabilizing effects [decrease the release of inflammatory mediators])
- Decrease mucosal swelling and skin reactions.
- May help to limit biphasic reactions by decreasing the allergic mediators.

Genomic action



- *Intracellular receptors (cytosol or nucleus)
- *Long onset of action

Non-genomic action



- *membrane bound receptors.
- *Rapid onset of action.

Adjuvant to 2nd line drugs

These drugs are prescribed in order to:

- 1- Support respiratory and circulatory deficits.
- 2- Prevent the existing of hyper-reactions.
- 3- **Prevent Biphasic Phenomenon** "further hyper-reaction of the immune system, when there is a 2nd release of mediators without re-exposure to antigen (in up to 20% patients) clinically evident 3-4h after the initial manifestations clear" (repeated symptoms).

e.g. **Bronchodilators, Glucagon, H2 blocker,**

H1 Blockers (Histamine receptor blocker)

- Cannot be used alone.
- Given slowly I.V or I.M.
- Though mast cells have already de-granulated, yet these drugs can still help to counter act histamine-mediated vasodilation and bronchoconstriction.
- **May help to limit biphasic reactions by preventing more release of Histamine.**

H2 Blockers (Histamine receptor blocker)

- Block the effects of released histamine at H₂ receptors.
- Ramifying the heart and some BV → help in Improving the hypotension.
- Responsible for glandular hyper-secretion → help in reducing bronchial & laryngeal manifestations.
- Adjuvant to H₁ blockers → additive benefits in treating anaphylaxis.

Bronchodilators

	Inhalation		Parenteral
Drug	Salbutamol	Ipratropium	Aminophylline
Classification of drug	Short duration selective β_2 agonist.	Anti-muscarinic Anti-cholinergic	Xanthine preparation
Pharmacokinetics	<ul style="list-style-type: none"> -Short action -Rapid relief onset of action. 	<ul style="list-style-type: none"> -Longer duration of action than Salbutamol. -Less rapid in action of decreasing the mucous secretion. 	<ul style="list-style-type: none"> -Used when inhaled bronchodilators are no effective, and when bronchospasm is persistent - Has narrow therapeutic index so it is only given in hospital setting and the levels of it should be therapeutically monitored.
Pharmacodynamics	<ul style="list-style-type: none"> -Relaxation of bronchial smooth muscles. -Decrease mediators' release from mast cells and basophils. -Inhibit airway micro-vascular leakage. 		

Glucagon

Drug of choice for severe anaphylaxis in patients taking β -blockers.

- [-There are no glucagon receptors in the Bronchi.
- But there are in the heart.
- These patients take β blockers: β_1 in the heart, β_2 in the lungs. So the actions of β receptors are not working.
- So any other drug they take that work on β receptors, will not effect these two organs.
- Since there is a Glucagon receptor in the heart, This drug will produce its action without interrupting the β_1 receptor.]
- In the heart → exerts positive inotropic & chronotropic effects → increase cardiac cAMP → an effect entirely independent of Adrenoceptors. That is why effective in spite of beta-adrenergic blockade.
- No glucagon receptors in bronchi no evident bronchodilation.

SUMMARY

- *Perceive the differences between Anaphylactic shock and other types of shocks.
- *Recognize its nature, causes, and characteristics.

- Anaphylactic shock is a **Distributive shock**.

-Nature:

Belong to TYPE I HYPERSENSITIVITY REACTION

-Causes:

Occurs after exposure to foreign substances (antigen): food, insect or animal venom, drugs, blood products..etc.

Characters:

Rapidly developing
Severe, life-threatening
Multisystem involvement.

- *Identify its standard emergency management protocol.

1- Life support: respiratory by opening the airways, circulatory by fluid replacement.

2- 1st line treatment: Adrenaline. Drug of choice in anaphylactic shock.

Drugs	Characteristics
H2 blockers	Block the effects of released histamine
Bronchodilators	-Salbutamol & Ipratropium : given by inhalation. -Aminophylline: given parentally.
Glucagon	Drug of choice in patients taking β -blockers

MCQs

1. A man had a car accident and he lost too much blood (hemorrhage) what type of shocks he is developing ?

- A. Distributive
- B. Obstructive
- C. Hypovolemic
- D. Cardiogenic

2. Anaphylactic shock is a :

- A. Distributive shock
- B. Hypovolemic shock
- C. Obstructive shock
- D. Cardiogenic shock

3. The first line drug in case of anaphylactic shock is :

- A. Salbutamol
- B. Noradrenalin
- C. Adrenaline
- D. Dopamine

4. If hypotension persist with anaphylactic shock, what should we prescribe :

- A. Adrenaline
- B. Dopamine
- C. Glucagon
- D. Atropine

5. A drug which is not life saving but can help to limit the biphasic reaction :

- A. H1 blocker
- B. H2 blocker
- C. Salbutamol
- D. Ipratropium

6. The only drug can be given IV in hospital setting as a bronchodilator is :

- A. Salbutamol
- B. Ipratropium
- C. Aminophylline
- D. Tropicamide

7. If a patient has a severe anaphylactic shock and he is taking a B-blocker, what is the proper drug in this case ?

- A. Corticosteroid
- B. Glucagon
- C. Salbutamol
- D. Oxybutynin

8. The glucagon is not used as a bronchodilator, WHY?

- A. It is weak drug
- B. There is no glucagon receptors in bronchi
- C. Not used clinically
- D. Has a severe side effects

8-B

7-B

6-C

5-A

4-B

3-C

2-A

1-C



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Anaphylaxix

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**We hope that we made this lecture easier for you
Good Luck !**