# PHARMACOLOGY

## Anaphylactic shock

**OBJECTIVE:**

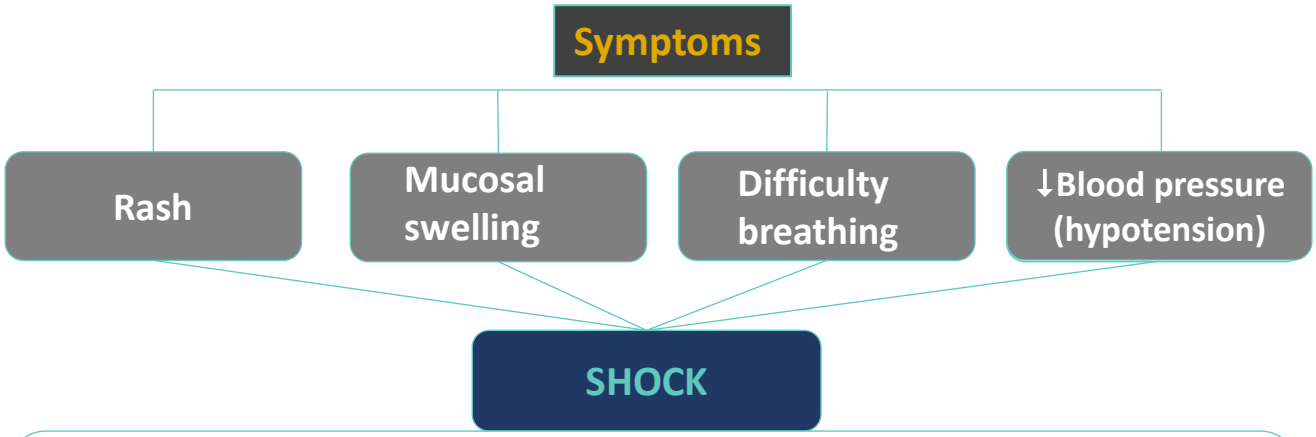
- Perceive the differences between anaphylactic shock and other types of shock
- Recognize its nature, causes & characteristics.
- Specify its diagnostic features
- Identify its standard emergency management protocol
- Justify the mechanism of action and method of administration of each of the different used drugs to limit its morbid outcomes

**Terminology:**

- **Chronotropic** = increase cardiac output
- **Inotropic** = increase cardiac force of contraction
- **Peripheral resistance** is the **resistance** of the arteries to blood flow. It increases s the arteries constrict, and decreases as the arteries dilate.

# ANAPHYLAXIS

**Anaphylaxis Is a sudden, severe hypersensitivity reaction affecting the whole body (generalized or systemic) in response to allergen.**




## ANAPHYLACTIC SHOCK :

**A life-threatening allergic reaction that causes shock (hypoperfusion) and airway swelling.** "Anaphylactic shock" is a term that specifically refers to an episode of anaphylaxis.

**SHOCK:** Generalized circulatory derangement causing multiple organ HYPOPERFUSION [Inadequate oxygen delivery to meet metabolic demands ] & strong sympathetic activation

- If the shock is intense or sustained enough, it will lead to irreversible derangements sets then to permanent functional deficit or death

## What type of shock is the anaphylactic shock?

Types of shock

| Hypovolemic | Cardiogenic | Obstructive | Distributive |
|---|---|---|---|
| • Hemorrhage<br>• fluid loss (plasma, ECF) e.g. Excessive vomiting | Inability to contract & pump. E.g.:<br>• myocardial infarction | Extra-cardiac obstruction:<br>• Pulmonary embolism<br>• Cardiac tamponade (pericardial effusion) | Decreased Peripheral Resistance → vasodilation → hypotension. As in:<br>• septic shock<br>• Neurogenic shock<br>• **Anaphylactic shock** |

YouTube Video : Types of shock (very good)

# ANAPHYLACTIC SHOCK

## Immunologic Anaphylaxis (known as ANAPHYLAXIS)

It belongs to type I hypersensitivity reaction (IgE)

Occurs after exposure to foreign substances [antigen] such as food, insect or animal venom, drugs, blood products.

The immune system will then develop antibodies for this antigen and it will remain in the body for a while.

After a 2nd exposure to the same antigen in previously sensitized persons (antigen-specific ige are present), IgE binds with mast cell causing its degranulation.

## Non-Immunologic Anaphylaxis (ANAPHYLACTOID)

Directly act on mast cells

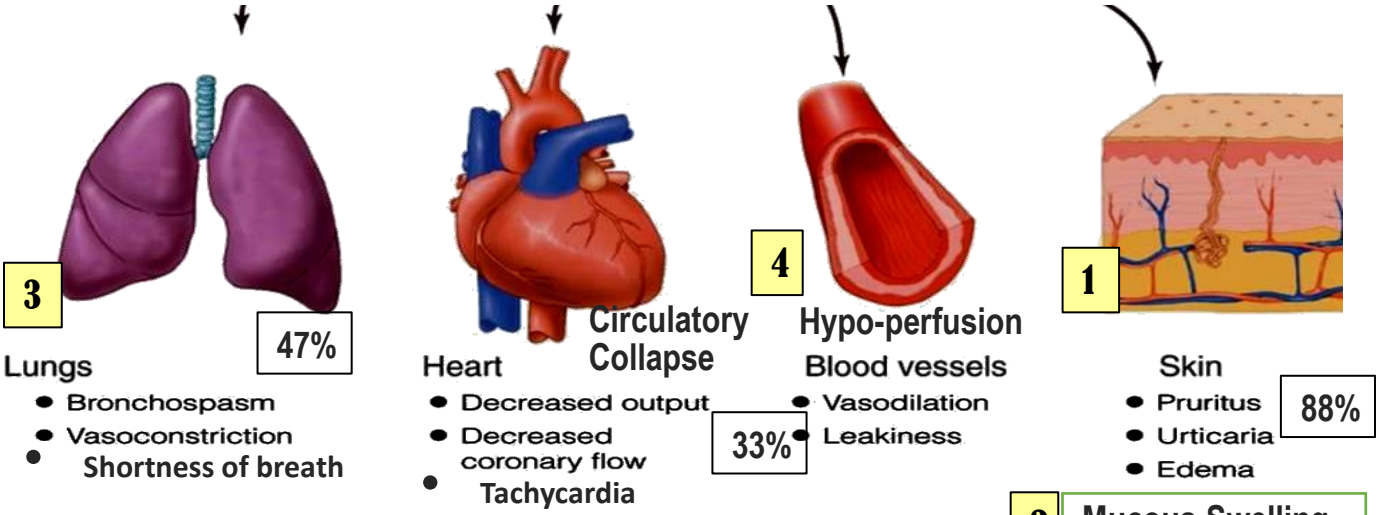
Not IgE-mediated

Exogenous substances directly degranulate mast cells. E.g. Radiocontrast dye, Opiates "analgesics", Depolarizing drugs, Dextrans "antithrombotics".

An anaphylactoid reaction can occur following a single, first-time exposure to certain agents in non-sensitized patients.

Because anaphylactic and anaphylactoid reactions produce the same clinical manifestations and are treated exactly the same way, we use the term anaphylaxis to refer to both conditions.

The degranulation of the mast cells will release histamine, Leukotrienes and other inflammatory substances and will lead to:




## characters of anaphylactic shock:

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

# Anaphylactic Shock Therapy Protocol:

## Rescue

**When the diagnosis is made as an anaphylactic shock (after calling the ambulance), emergency treatment should be immediately started as follows:**

| Life-threatening Problems: | Management |
|---|---|
| **Airway:** swelling, hoarseness, stridor "a harsh or grating sound" **Breathing:** rapid breathing, wheezing, cyanosis, fatigue, confusion, oxygenated Hb (SpO2) < 92% | **Respiratory support**<br>• Open airway<br>• O2 inhalation |
| **Circulation:** pale, clammy "sticky ", low BP, faintness, drowsy " sleepy" /coma | **Circulatory support**<br>• Lay down and raise legs up (to direct blood towards brain and prevent edema in legs)<br>• Fluid replacement |

### 1st line therapy

- Adrenaline (give IM by Auto-injector or by syringe, unless there is a specialist to give IV)
- IV fluid challenge "small amount of **fluid** in a short period of time"

## 2nd line

- Chlorophenamine (first generation H1 blocker, has sedating effect) (IM or slow IV)
- Hydrocortisone (**Glucocorticoids**, used for severe acute asthma) (IM or slow IV)

## Adjuvant to 2nd line:

### ❖ Bronchodilators

Salbutamol (nebulizer), Ipratropium (nebulizer), Aminophylline (IV)

### ❖ Glucagon

**For patients taking beta-blockers & with refractory hypotension** → 1 mg IV every 5 minutes until hypotension resolves.

### ❖ $H_2$ blocker

(anti-ulcer drugs, used for epigastric pain)

- **Ranitidine**: 50 mg IV
- **Cimetidine:** contraindicated in elderly, renal/hepatic failure, or if on beta-blockers (not used anymore due to many drug interactions)

### Why do we use the 2nd line adjuvants?

**Objective of Therapy:**

- To support the respiratory & circulatory deficits
- To halt the existing hyper-reaction
- To prevent further hyper-reaction of immune system (prevent biphasic phenomenon)

### Biphasic Phenomenon:

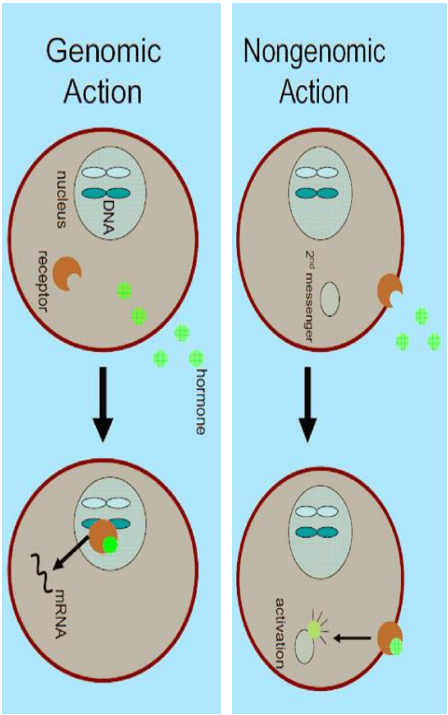
2nd release of mediators without re-exposure to antigen. (in up to 20% ) Clinically evident 3-4h after the initial manifestations clear

# First line therapy

## Adrenaline

| | |
|---|---|
| **Mechanism** | A Sympathomimetic, **nonselective** Adrenergic agonist [α1, α2, β1, β2, β3 ]. |
| **Actions** | • **α agonist:**<br>- Reverses peripheral vasodilation (vasoconstriction), thus maintains BP and directs blood flow to major organs.<br>- Vasoconstriction leads to decreasing edema ➔ reverse hives "urticaria", swelling around face & lips & angioedema in nasopharynx & larynx. angioedema = swelling of deep dermis, subcutaneous, or submucosal tissue due to vascular leakage<br>• **β agonist:**<br>-β2 :Dilates bronchial airways +↓ histamine & leukotriene release from mast cells .<br>-β1 :↑ force of myocardial contraction.<br>• **Physiological antagonist of histamine:**<br>-Attenuates "reduce " the severity of **IgE-mediated** allergic reactions. |
| **Indications** | Drug of choice for anaphylactic shock |
| **Contra-indications** | - Rare in a setting of anaphylaxis<br>- Not given for cardiac patient who are older than 40 years<br>- Patients taking **β-blockers** either are:<br>➢ **Refractory**; as it may antagonize β effects of adrenaline. (β2 receptors won't be stimulated since they're blocked, no ↑ cAMP, no effect)<br>➢ **Rebound hypertension** [unopposed α effect], specially when adrenaline is repeated (glucagon is used in this case) |
| **ADRs** | Causes dysrhythmias if given IV. |
| **Administration** | IM: why?<br>- Easily accessible. (Auto-injectors Kits are disposable prefilled devices, automatically administer a single dose of epinephrine in emergency)<br>- Greater margin of safety → no dysrhythmias as with IV.<br>- No need to wait for IV line, if present, it should be given by physician under monitoring.<br>- Repeat every 5-10 min as needed<br>- Patient should be observed for 4-6 hours (**fear of biphasic anaphylaxis)**<br>It could also be administered subcutaneously, which is safer, but won't produce as rapid effect as IM injection for the rescue of anaphylaxis. |
| **Notes** | • If hypotension persists, start **Dopamine** (To protect the kidney),<br>Why not noradrenaline?<br>Noradrenaline is nonselective on (α1, α2, β1). It has no effect on β2<br>stimulation of α1(vasoconstriction) causes hypertension, but this vasoconstriction is not opposed by the stimulation of β2(vasodilatation)<br>Therefore, noradrenaline will cause a very severe vasoconstriction, much more than what is required in the case of anaphylactic shock. |

# Second line therapy

| | Corticosteroids [anti- inflammatory] |
|---|---|
| **Mechanism** | **Genomic action:**<br>• Intracellular receptors (cytosol or nucleus)<br>• takes hours to days to be activated.<br>• Used for maintenance of asthma as it suppresses airway inflammation<br>**non-genomic actions:**<br>• Immediate Glucocorticoids actions on on Membrane-bound receptors, which leads to modulating 2nd messengers levels.<br>• Rapid onset of action (minutes).<br>• That's why it is used in anaphylactic shock<br>  |
| **Action** | **non-genomic action in anaphylactic shock:**<br>- Reverse hypotension & bronchoconstriction<br>- ↓ release of inflammatory and allergic mediators (anti-chemotactic & mast cell stabilizing effects).<br>- ↓ mucosal swelling and skin reaction.<br>- May help to limit biphasic reactions by decreasing allergic mediators |
| **Administration** | Given slowly IV or IM |
| **Notes** | Not used alone **(not life saving)** |

## H1 Blockers:

- It can not be used alone → not life saving
- Given slowly intravenously or intramuscularly (e.g. **phenaramine**)
- Though mast cells have already de-granulated, yet these drugs can still help to counter act histamine-mediated vasodilation & bronchoconstriction.
- May help to limit biphasic reactions by ↓ of more histamine release
- E.g. **Chlorphenamine** (sedating), loratidine (no sedating effects)

# Adjuvant 2nd line therapy

## H2 Blockers:

The significance of H2 blockers is not established , these drugs are associated with serious adverse drug interactions.

- e.g. **Ranitidine**, **Cimetidine**


| Bronchodilators (used for asthma as well) | | |
|---|---|---|
| **Salbutamol** | **Ipratropium** | **Aminophylline** |
| Inhalation | | Parenteral IV |
| $\beta_2$ Agonist | Anticholinergic Antimuscarinic | Methylxanthine |
| - Short acting<br>- Rapid onset of acting.<br>- rapid relief<br>- Relaxation of bronchial smooth muscle.<br>- Decrease mediators released from mast cell and basophils. .<br>- inhibit airway microvascular leakage. | - Longer acting.<br>- Less rapid in action<br>- Slower onset of action.<br>- Decrease secretion. | - IV is useful for anaphylactic shock.<br>- Not effective in bronchodilation and bronchospasm if inhaled.<br>- may be useful in the treatment of anaphylaxis when inhaled bronchodilators are not effective & bronchospasm is persistent.<br>- Given in **hospital setting** as levels of drug should be therapeutically monitored because it has **narrow therapeutic index**. |
| - Not effective in Patients taking **β-blockers** | Effective for bronchodilation in spite of beta-adrenergic blockade. | |

| | **Glucagon** |
|---|---|
| **Action** | Drug of choice for severe anaphylaxis in patients taking **b-blockers** |
| **Mechanism** | Act on glucagon receptors in the heart |
| **Action** | • Has both + inotropic & chronotropic effect → increase cardiac cyclic AMP<br>• This effect is completely independent of Adrenergic Receptors , That is why effective in spite of beta-adrenergic blockade.<br>• Efficacy of acting on bronchi is less prominent than that of the heart ➔ no evident bronchodilation **(because glucagon receptors only exist on the heart, not on the bronchi)** |

# Mind map as summary

A life-threatening, Rapidly developing, Multisystem involved allergic reaction that causes Distributive shock (hypoperfusion) and airway swelling, and may lead to Mortality
Symptoms: Rash, Mucosal swelling, Difficulty breathing, Hypotension

## Anaphylactic shock

Occurs after exposure to foreign substances [antigen] such as food, insect or animal venom, drugs, blood products. It's a type I hypersensitivity reaction (IgE) in sensitized patients

ANAPHYLAXIS

ANAPHYLACTOID

Exogenous substances directly degranulate mast cells. E.g. Radiocontrast dye, Opiates Depolarizing drugs, Dextrans

### Therapy of anaphylactic shock

Rescue:
**Call an ambulance**

**Respiratory support:**
- Open airway
- O2 inhalation

**Circulatory support:**
- Lay down and raise legs up
- Fluid replacement

1st line

**Adrenaline**

- Causes Vasodilation
- maintains BP
- ↓edema
- Dilates bronchi
- ↑ force of myocardial contraction
- ↓ **IgE-mediated** allergic reactions
- Administered IM
- Causes dysrhythmias if given IV.
- Not used along with **β-blockers**

Adjuvant to 2nd line

**Glucagon**

- Drug of choice for severe anaphylaxis in patients taking **b-blockers**
- Has + inotropic & chronotropic

**Bronchodilators**

**Salbutamol**
- Short acting and has rapid relief
- Relaxation of bronchial smooth muscle.

**Ipratropium**
- Longer acting & Slower onset of action.
- Decrease secretion.

**Aminophylline**
- IV is useful for anaphylactic shock.
- narrow therapeutic index

**H2 Blockers**

serious adverse drugs interaction

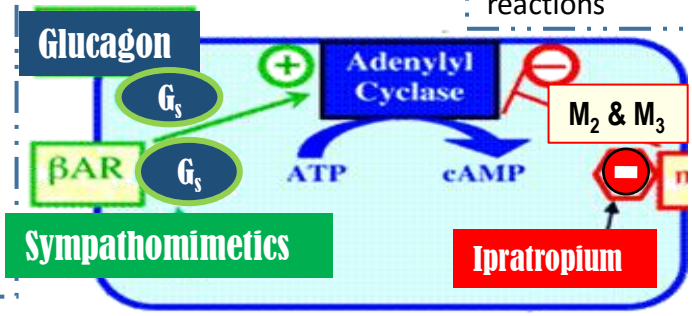
2nd line

**Corticosteroids**

**non-genomic action:**
- Reverse hypotension & bronchoconstriction
- ↓ release of inflammatory and allergic mediators
- limit biphasic reactions
- Given slowly IV or IM
- Not used alone **(not life saving)**

**H1 Blockers (phenaramine)**

- It can not be used alone → not life saving
- Given IV or IM to counter act histamine-mediated vasodilation & bronchoconstriction
- helps to limit biphasic reactions



# QUIZ

## THANK YOU FOR CHECKING OUR WORK

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