

# DRUGS USED IN

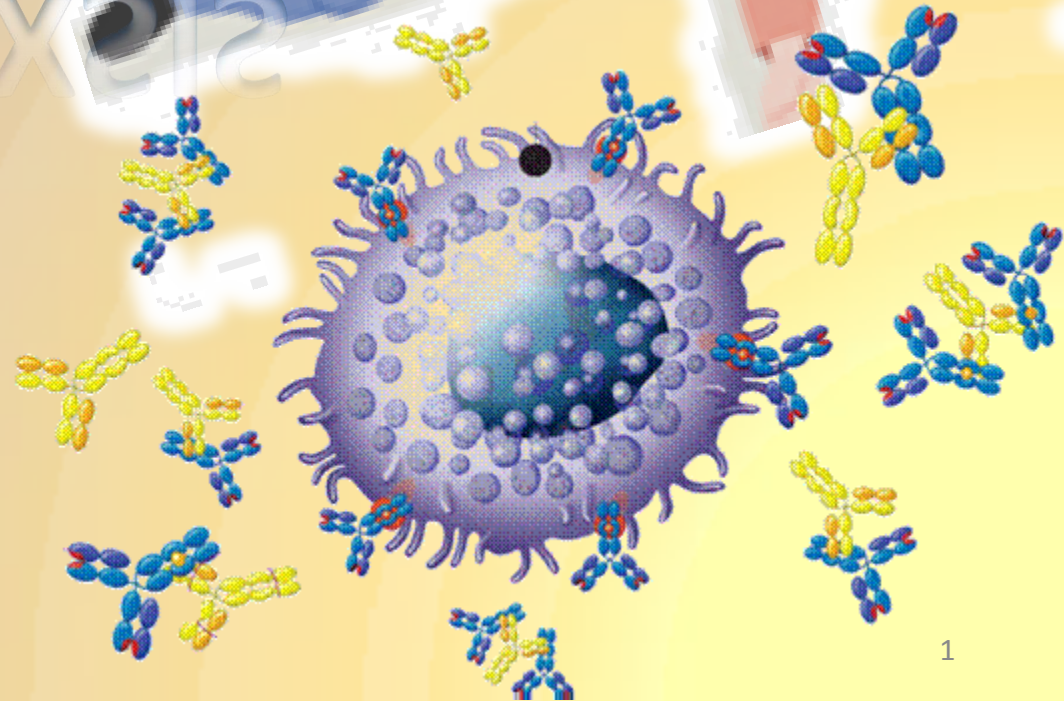


# ANAPHYLAXIS



Dr. Ishfaq

Dr. Aliah



An illustration showing a large purple cell with many small receptors on its surface. Some receptors are bound to blue and yellow Y-shaped molecules. Two bees are shown: one at the top left and one at the bottom center, both with these Y-shaped molecules on their bodies. The background is a gradient from yellow to blue.

# DRUGS USED IN ANAPHYLAXIS

## ILOs

**By the end of this lecture you will be able to:**

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

# ANAPHYLAXIS



Is a sudden, severe allergic reaction affecting the whole body

symptoms including:

- Rash
- Mucosal swelling
- Difficulty breathing
- Reduced blood pressure



## SHOCK



## ANAPHYLACTIC SHOCK

A life-threatening allergic reaction that causes shock (hypoperfusion) and airway swelling.

**What TYPE of shock is it ???**

# SHOCK



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

→ when intense or sustained enough, irreversible derangements sets → permanent functional deficit or death

## ✚ **Hypovolemic**

Haemorrhage / fluid loss (plasma, ECF)

## ✚ **Cardiogenic**

Inability to contract & pump → myocardial infarction

## ✚ **Obstructive**

Extracardiac obstruction → Pul. embolism, cardiac tamponade

## ✚ **Distributive**

↓ PR → septic shock, neurogenic, anaphylactic shock.

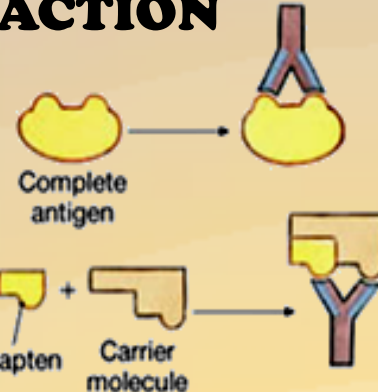
*Severe, life-threatening, generalized or systemic hypersensitivity reaction in response to allergen.*



# ANAPHYLACTIC SHOCK

**Nature** ♦ Belong to **TYPE I HYPERSENSITIVITY REACTION**

♦ Occurs after exposure to foreign substances [antigen];  
*food, insect or animal venom, drugs, blood products, .....*



First exposure

Allergens

Macrophage

Allergen fragment

T<sub>H</sub> cell

Antigenic determinant sites

B cell sensitization and activation

Plasma cell

IgE

Mast Cell

Antigen

Antibodies

♦ **IN PREVIOUSLY SENSITIZED PERSONS**  
**(antigen-specific IgE are present)**

What happens ???

N.B. **Non-Immunologic Anaphylaxis**  
**(ANAPHYLACTOID)**

Exogenous substances directly degranulate mast cells → Radiocontrast dye, Opiates, Depolarizing drugs, Dextrans

# ANAPHYLACTIC SHOCK

Second or later exposure

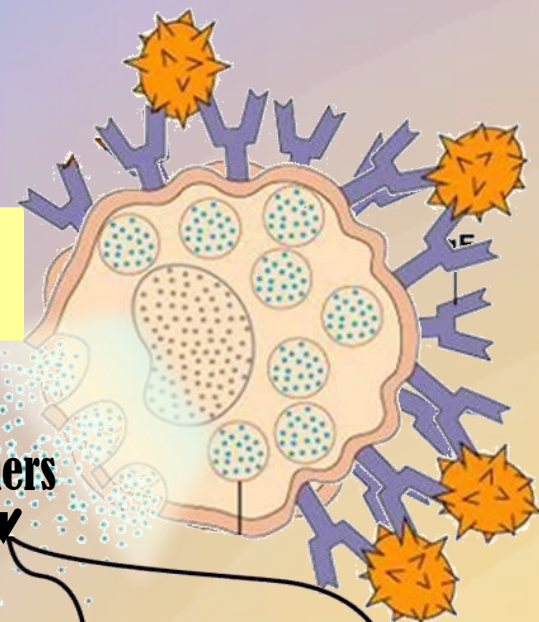
## Characters

2.

- Mucous Swelling
- Rhinitis 16%
- Angioedema 88%
- Airway 56%
- GIT 30%

**Mast Cell DEGRANULATION**

Histamine, Leukotrienes, others

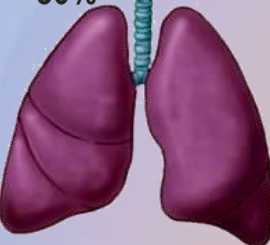


Antigen Re-exposure



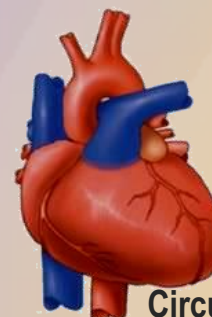
3.

- Lungs 47%
- Bronchospasm
  - Vasoconstriction
- Shortness of breath



4.

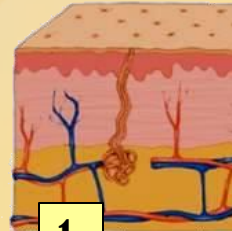
- Heart
- Circulatory Collapse
- Decreased output
  - Decreased coronary flow
- 33%



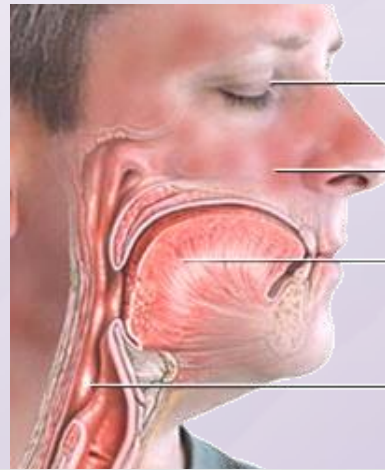
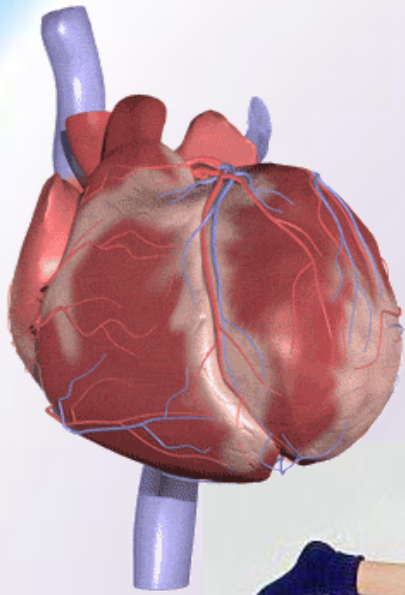
- Hypo-perfusion Blood vessels
- Vasodilation
  - Leakiness

1.

- Skin
- Pruritus
  - Urticaria
  - Edema
- 88%



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



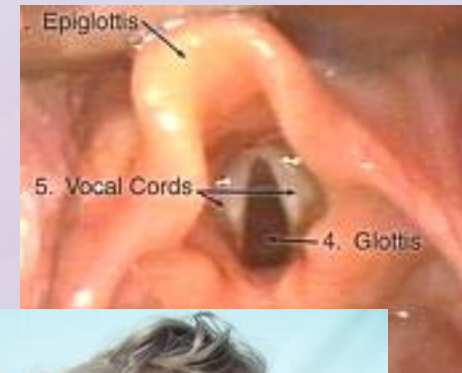
Anaphylaxis

Loss of consciousness

Hives

Swelling of tongue, inability to swallow

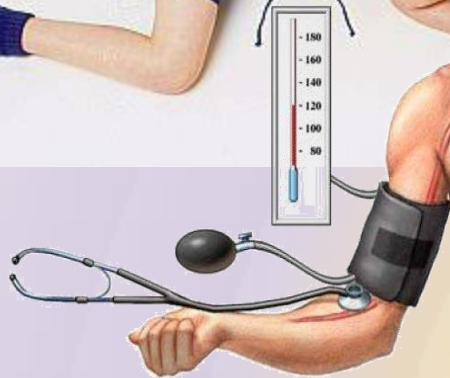
Rapid swelling of throat tissues



Fainting, Syncope



# ANAPHYLACTIC SHOCK



**IS A MEDICAL EMERGENCY WHERE IMMEDIATE TREATMENT IS NEEDED TO PREVENT POTENTIAL DEATH.**



# ANAPHYLACTIC SHOCK

DIAGNOSIS IS MADE



START EMERGENCY TREATMENT

**Respiratory Support**

Open Airway  
O<sub>2</sub> Inhalation

**Circulatory Support**

Lay down / Legs up  
Fluid Replacement

**Adrenaline**

IM by Auto-injector  
Or by syringe





# ANAPHYLACTIC SHOCK THERAPY PROTOCOL

RESCUE

## 1 Life-threatening problems:

**Airway:** swelling, hoarseness, stridor

**Breathing:** rapid breathing, wheeze, fatigue, cyanosis, SpO<sub>2</sub> < 92%, confusion

**Circulation:** pale, clammy, low blood pressure, faintness, drowsy/coma

1ST LINE

## 2 Adrenaline (give IM unless experienced with IV adrenaline)

IM doses of 1:1000 adrenaline (repeat after 5 min if no better)

- Adult 500 micrograms IM (0.5 mL)
- Child more than 12 years: 500 micrograms IM (0.5 mL)
- Child 6 -12 years: 300 micrograms IM (0.3 mL)
- Child less than 6 years: 150 micrograms IM (0.15 mL)

Adrenaline IV to be given only by experienced specialists

Titrate: Adults 50 micrograms; Children 1 microgram/kg

## 3 IV fluid challenge:

Adult - 500 – 1000 mL

Child - crystalloid 20 mL/kg

Stop IV colloid if this might be the cause of anaphylaxis

2ND LINE

## 4 Chlorphenamine (IM or slow IV)

Adult or child more than 12 years

10 mg

Child 6 - 12 years

5 mg

Child 6 months to 6 years

2.5 mg

Child less than 6 months

250 micrograms/kg

## 5 Hydrocortisone (IM or slow IV)

200 mg

100 mg

50 mg

25 mg

ADJUVANT TO 2<sup>ND</sup> LINE

6. Bronchodilators 7. Glucagon 8. H<sub>2</sub> Blockers

# ANAPHYLACTIC SHOCK THERAPY PROTOCOL

## ADJUVANT TO 2<sup>ND</sup> LINE

- ✚ To support the respiratory & circulatory deficits
- ✚ To halt the existing hyper-reaction
- ✚ To prevent further hyper-reaction of immune system

### Objective of Therapy

#### Biphasic phenomenon

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

# ADRENALINE

A Sympathomimetic.

1ST LINE

## Mechanism

A nonselective AD agonist [ $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_2$ ]

## Actions

As an  $\alpha$ -AD agonist →

+ **Reverses** peripheral vasodilation → maintains BP & directs blood flow to major organs

+ **↓** edema → reverse hives, swelling around face & lips & angioedema in nasopharynx & larynx

As a  $\beta$ -AD agonist →

+ **Dilates** bronchial airways + **↓** histamine & leukotriene release from mast cells →  $\beta_2$  effect

+ **↑** force of myocardial contraction →  $\beta_1$  effect

## Contraindications

Rare in a setting of anaphylaxis

Not given > 40 y cardiac patient

## ADRs

Dysrhythmias

## PHYSIOLOGICAL ANTAGONIST

Attenuates the severity of IgE-mediated allergic reactions.

## Indication

**DRUG OF CHOICE**



## Administration

Best is (IM) route in anaphylaxis. Why ?

- ✚ Easily accessible
- ✚ Greater margin of safety → no dysrhythmias as with IV
- ✚ No need to wait for IV line → if present  
→ given by physician under monitoring

Repeat every 5-10 min as needed

Patients observed for 4-6 hours. Why ?

Fear of biphasic anaphylaxis

### N.B. Caution

Patients taking **β-blockers** either are →

- ✚ Refractory; as it may antagonize β effects of adrenaline
- ✚ Rebound hypertension → [unopposed α effect], specially when adrenaline is repeated

### **Auto-injectors Kits;**

Disposable, prefilled devices → automatically administer a single dose of epinephrine in emergency

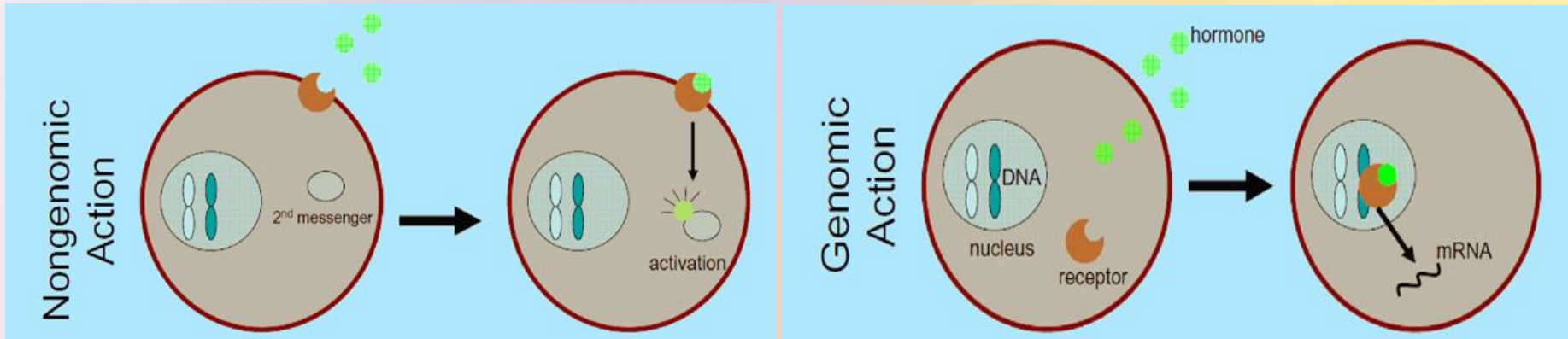
If hypotension persist → start dopamine. Why not noradrenaline?

It can not be used alone → not life saving

Given slowly IV or IM

- Reverse hypotension & bronchoconstriction → ↓ release of inflammatory mediators (anti-chemotactic & mast cell stabilizing effects)
- Also decrease mucosal swelling and skin reaction.

This is through immediate GCs action on Membrane-bound receptors → modulating levels of 2nd messengers → (within seconds or minutes) → Non-genomic action (genomic action is slow may take hrs - days)



May help to limit biphasic reactions → ↓ allergic mediators.

## H<sub>1</sub> BLOCKERS

## 2ND LINE

It can not be used alone → not life saving

Given slowly IV or IM (e.g pheniramine)

Though mast cells have already de-granulated, yet these drugs can still help to counteract histamine-mediated vasodilatation & bronchoconstriction

May help to limit biphasic reactions by blocking histamine receptors

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## H<sub>2</sub> BLOCKERS

The significance of H<sub>2</sub> blockers is not established, these drugs are associated with serious adverse drug interactions. Proton pump inhibitor (e.g. Pantoprazole) is safer and given once.



**Bronchodilators** : Salbutamol nebulizer / Ipratropium nebulizer /  
Aminophylline IV

**Glucagon**: For patients taking  $\beta$ -blockers & with refractory  
hypotension  $\rightarrow$  1 mg IV q 5 minutes until hypotension resolves

**H<sub>2</sub> blocker**: Ranitidine 150 mg IV / No cimetidine in elderly, renal/  
hepatic failure, or if on  $\beta$ -blockers.??

# BRONCHODILATORS

## Inhalational

• **Salbutamol** →  $\beta_2$ -AD agonist → short acting, rapid relief onset relax bronchial smooth muscle & may decrease mediators release from mast cells & basophils

It may also inhibit airway microvascular leakage

• **Ipratropium** → Anticholinergic → longer duration of action → ↓ secretion  
Less rapid in action

## Parenteral

**Aminophylline IV** → may be useful in the treatment of anaphylaxis when inhaled broncho-dilators are not effective & bronchospasm is persistent

Given in hospital setting as levels of drug should be **Therapeutically Monitored** (has narrow therapeutic index).

# GLUCAGON

## 2ND LINE

Drug of choice for severe anaphylaxis in patients taking  $\beta$ -blockers

Has both positive inotropic & chronotropic effects on heart  $\rightarrow$   $\uparrow$  cardiac cyclic AMP  $\rightarrow$  an effect entirely independent of adrenergic receptors, that is why effective in spite of  $\beta$ -adrenergic blockade. Efficacy of acting on bronchi  $<$  heart  $\rightarrow$  no evident bronchodilation.

