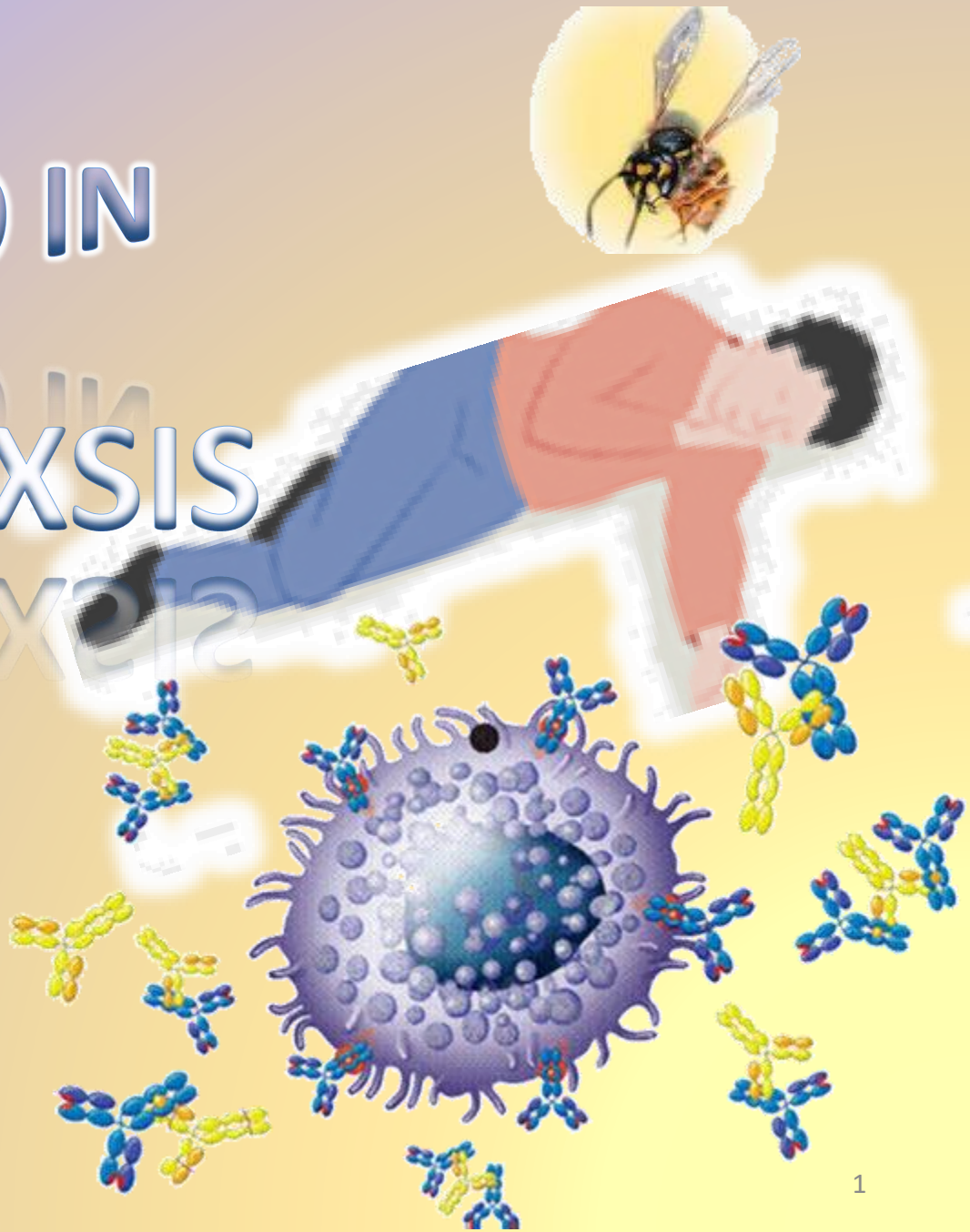
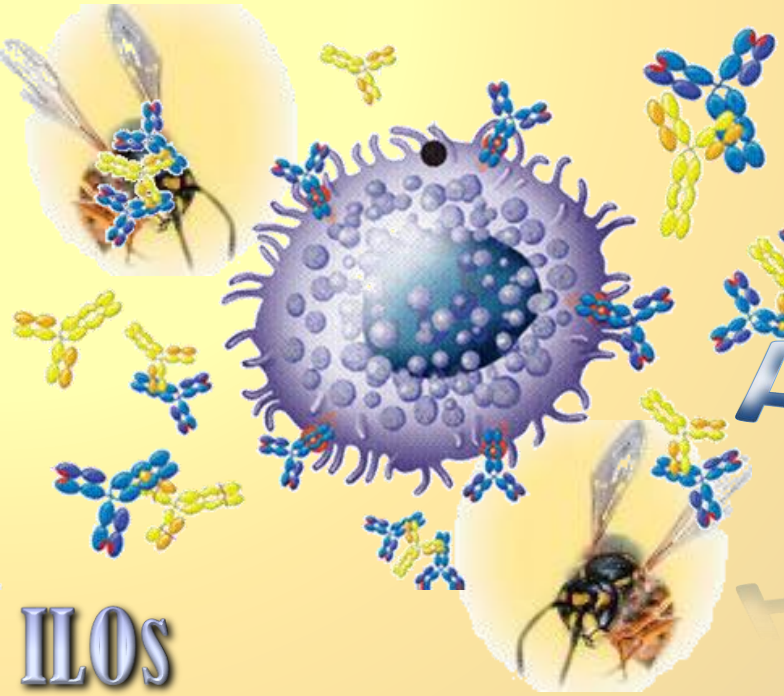
DRUGS USED IN ANAPHYLAXSIS



Dr. Ishfaq

Dr. Aliah



DRUGS USED IN ANAPHYLAXSIS

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.

ANAPHYLAXSIS

Is a sudden, severe allergic reaction affecting the whole body

symptoms including:

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

SHOCK

ANAPHYLACTIC SHOCK

What TYPE of shock is it ???

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

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

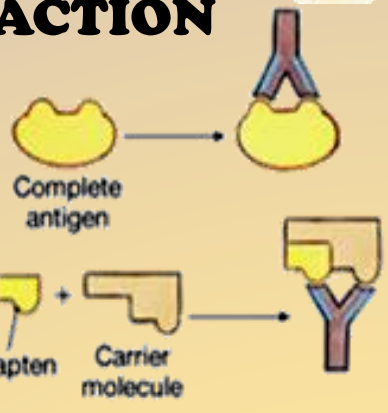
- **Hypovolemic**
  Haemorrhage / fluid loss (plasma, ECF)
- **Cardiogenic**
  Inability to contract & pump➔ myocardial infarction
- **Obstructive**
  Extracardiac obstruction ➔ Pul. embolism, cardiac tamponade
- **Distributive**
  ↓ PR ➔ septic shock, neurogenic, anaphylactic shock.

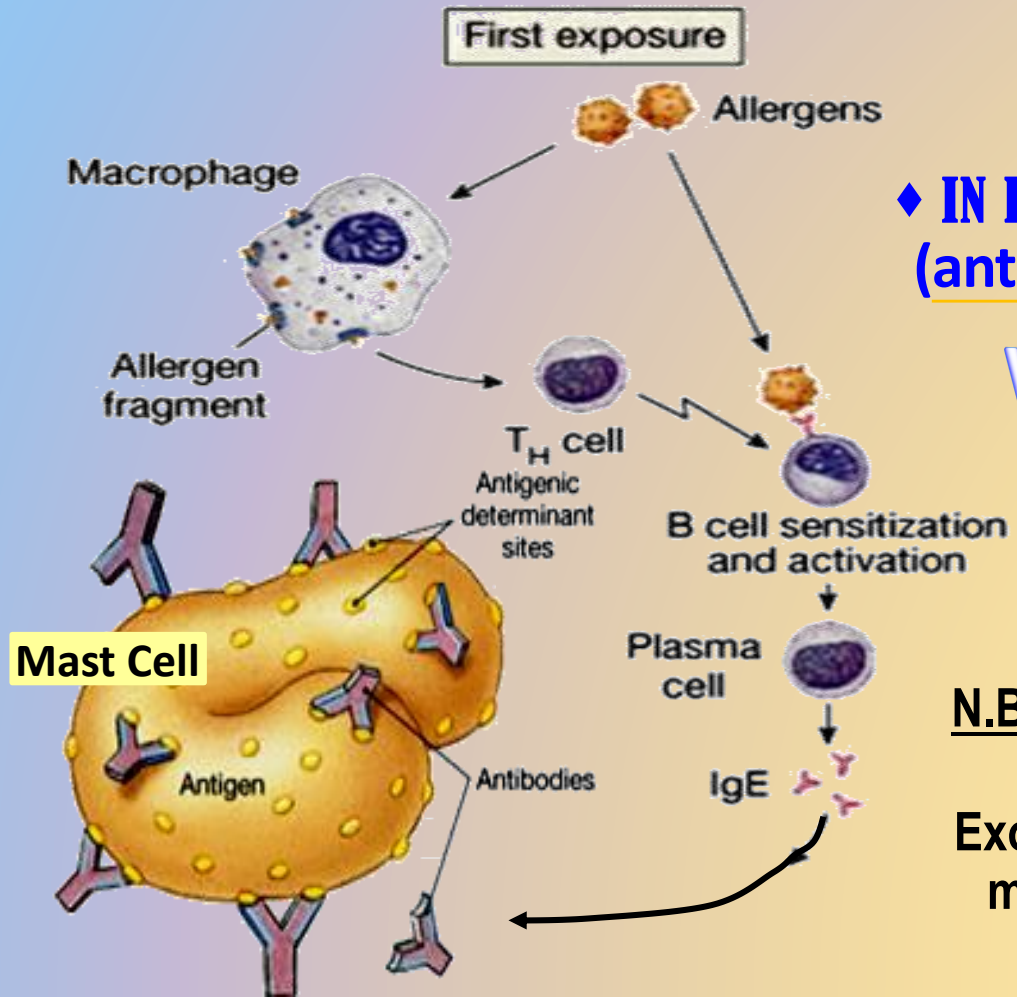
Severe, life-threatening, generalized or systemic hypersensitivity reaction in response to allergen.

ANAPHYLACTIC SHOCK

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

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





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

What happens ???

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

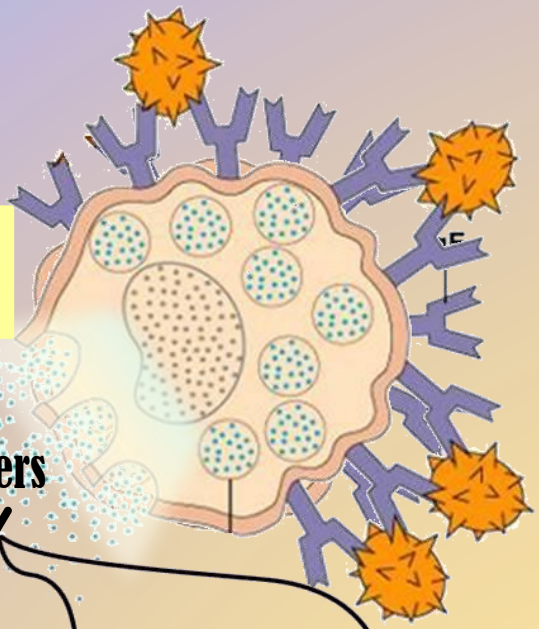
Exogenous substances directly degranulate mast cells➔ Radiocontrast dye, Opiates, Depolarizing drugs, Dextrans

ANAPHYLACTIC SHOCK

Second or later exposure

Antigen Re-exposure

Mast Cell DEGRANULATION

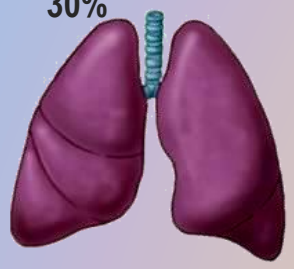


Histamine, Leukotrienes, others

Characters

2.

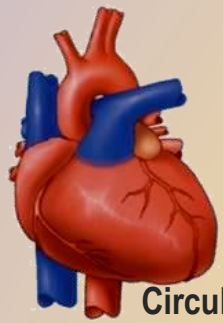
Mucous Swelling
Rhinitis 16%
Angioedema 88%
Airway 56%
GIT 30%



3. Lungs **47%**

- Bronchospasm
- Vasoconstriction

Shortness of breath



Heart — Circulatory Collapse

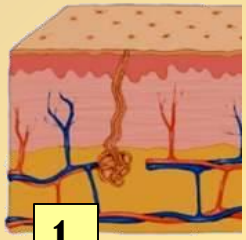
- Decreased output
- Decreased coronary flow

33%

4.

Hypo-perfusion Blood vessels

- Vasodilation
- Leakiness

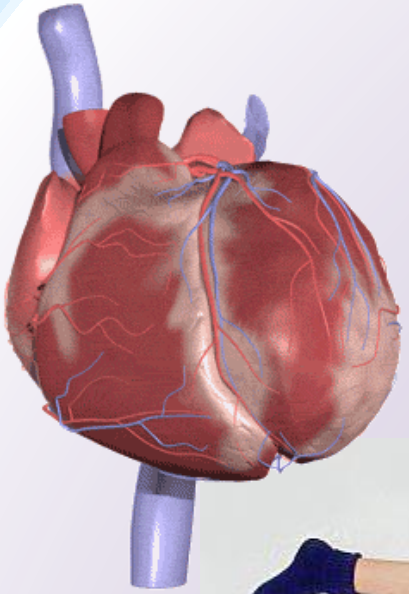


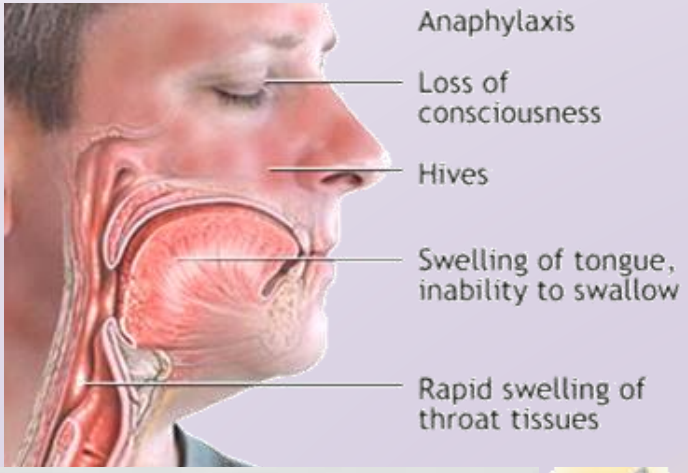
1. Skin

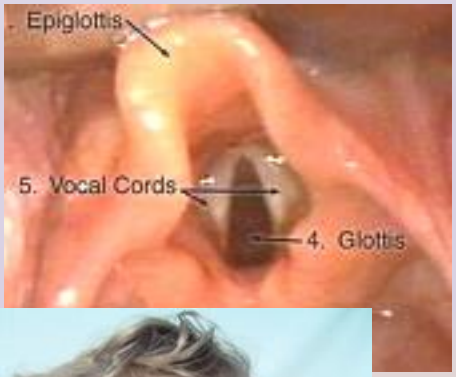
- Pruritus
- Urticaria
- Edema

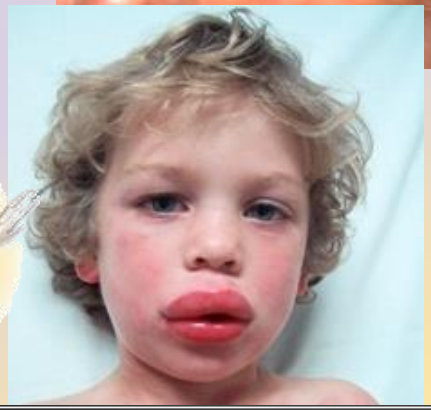
88%

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









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_2 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_2 < 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)	5 Hydrocortisone (IM or slow IV)
Adult or child more than 12 years	10 mg	200 mg
Child 6 - 12 years	5 mg	100 mg
Child 6 months to 6 years	2.5 mg	50 mg
Child less than 6 months	250 micrograms/kg	25 mg

ADJUVANT TO 2ND LINE

6. Bronchodilators 7. Glucagon 8. H_2 Blockers

ANAPHYLACTIC SHOCK THERAPY PROTOCOL

ADJUVANT TO 2ND 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

2nd 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 [α_1, α_2, β_1, β_2]

Actions

As an α-AD agonist ➔

- Reverses peripheral vasodilation ➔ maintains BP & directs blood flow to major organs
- ↓ edema ➔ reverse hives, swelling around face & lips & angioedema in nasopharynex & larynx

As a β-AD agonist ➔

- Dilates bronchial airways + ↓ histamine & leukotriene release from mast cells ➔ β_2 effect
- ↑ force of myocardial contraction ➔ β_1 effect

PHYSIOLOGICAL ANTAGONIST

Attenuates the severity of IgE-mediated allergic reactions.

Indication

DRUG OF CHOICE

Contraindications

Rare in a setting of anaphylaxsis

Not given > 40 y cardiac patient

ADRs

Dysrrhythmias

ADRENALINE

1ST LINE

Administration

Best is (IM) route in anaphylaxis. Why ?

- Easily accessible
- Greater margin of safety ➔ no dysrrhythmias 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

Auto-injectors Kits;
Disposable, prefilled devices ➔ automatically administer a single dose of epinephrine in emergency

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

If hypotension persist ➔ start dopamine. Why not noradrenaline?

CORTICOSTEROIDS

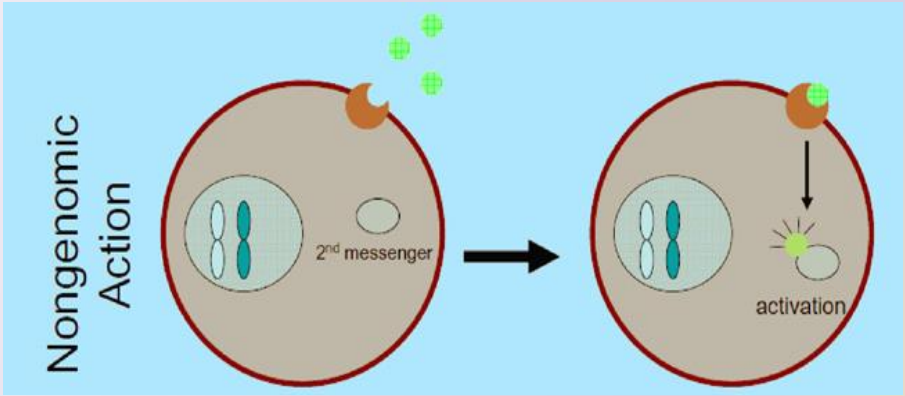
2ND LINE

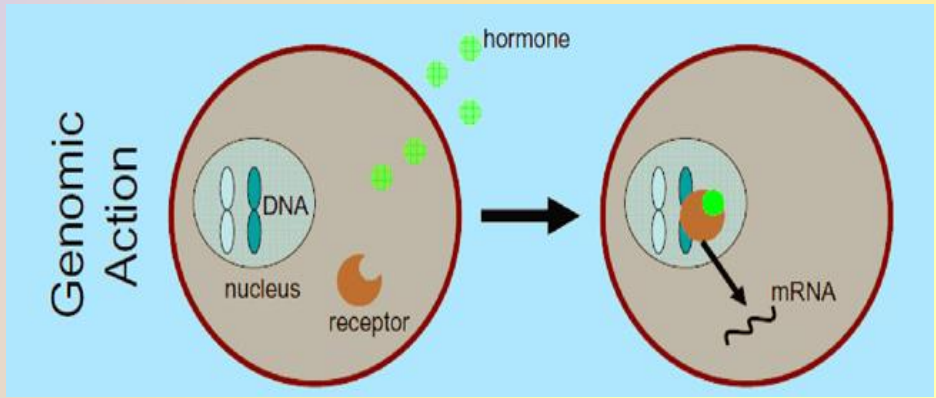
It can not be used alone → not life saving

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_1 BLOCKERS

2ND LINE

It can not be used alone ➔ not life saving
Given slowly IV or IM (e.g phenaramine)

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

H_2 BLOCKERS

The significance of H2 blockers is not established, these drugs are associated with serious adverse drug interactions. Proton pump inhibitor (e.g. Pantoprazole) is safer and given once.

ANAPHYLACTIC SHOCK THERAPY PROTOCOL

ADJUVANT TO 2ND LINE

Bronchodilators : Salbutamol nebulizer / Ipratropium nebulizer / Aminophylline IV

Glucagon: For patients taking β-blockers & with refractory hypotension➔1 mg IV q 5 minutes until hypotension resolves

H_2 blocker: Ranitidine 150 mg IV / No cimetidine in elderly, renal/ hepatic failure, or if on β-blockers.??

BRONCHODILATORS

Inhalational

- **Salbutamol** → β_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

Parentral

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 β-blockers

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