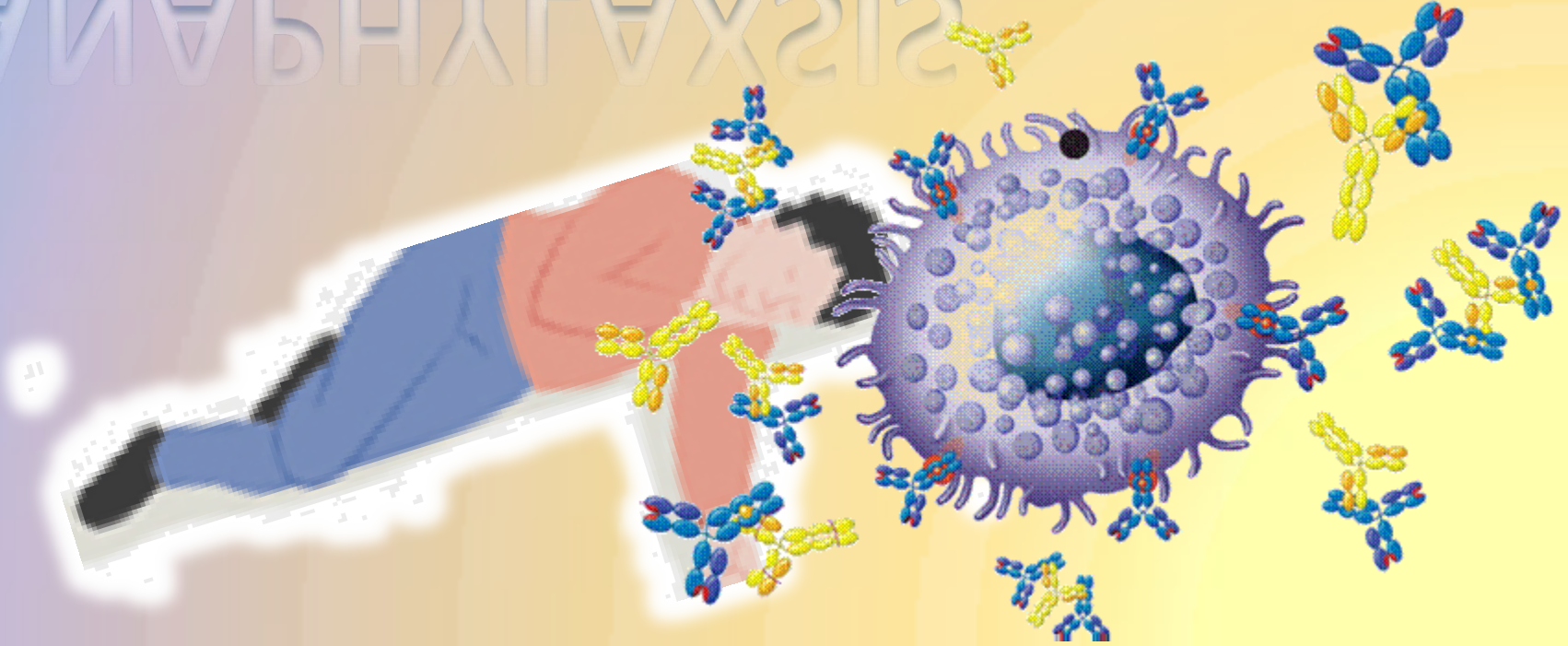
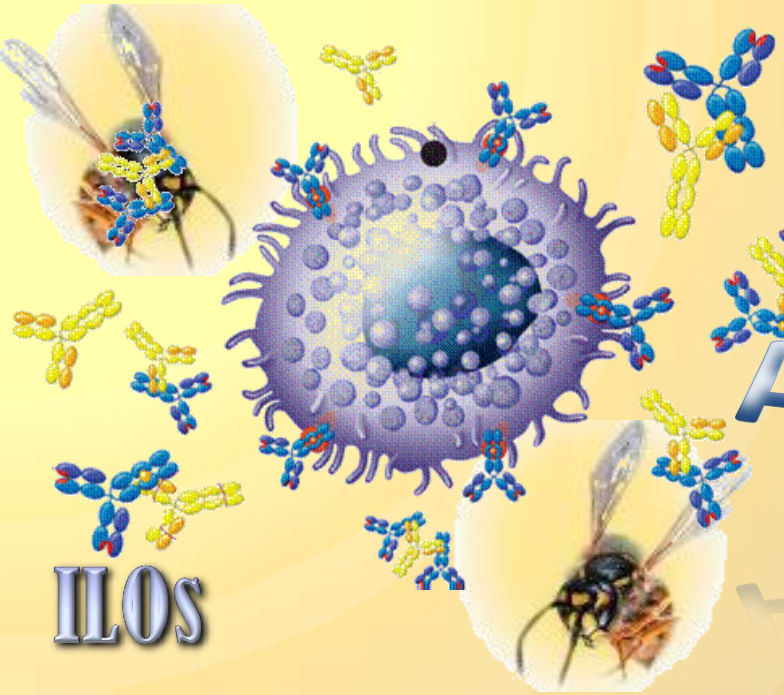
DRUGS USED IN ANAPHYLAXSIS





DRUGS USED IN ANAPHYLAXSIS

ILOs

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

- 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

ANAPHYLAXSIS

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

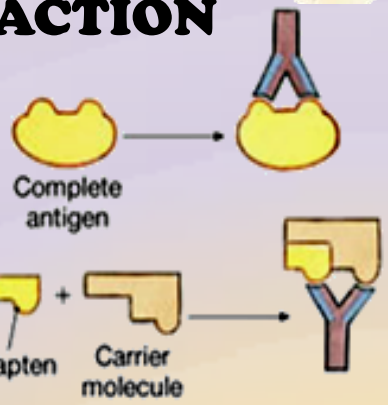
Severe, life-threatening, generalized or systemic hypersensitivity reaction in response to allergen

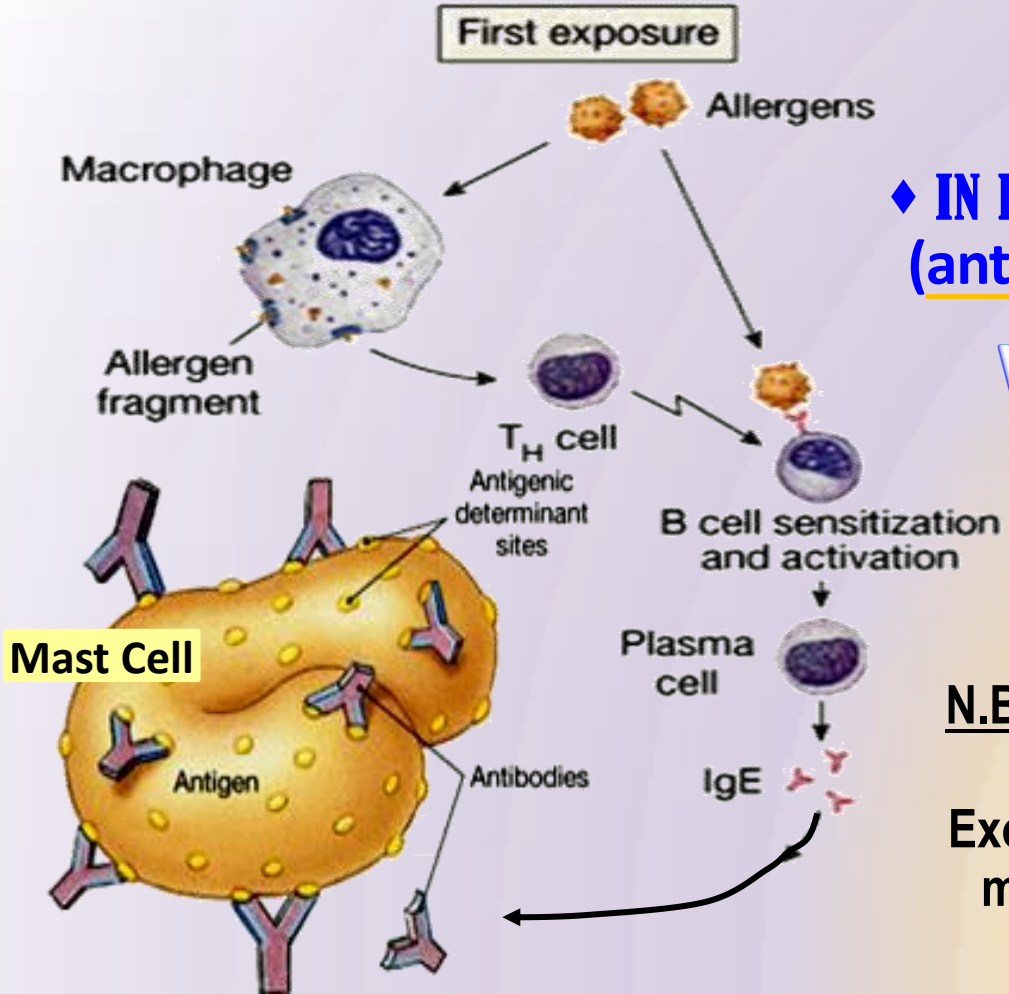
ANAPHYLACTIC SHOCK

Nature

♦ Belong to **TYPE I HYPERSENSITIVITY REACTION**

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





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

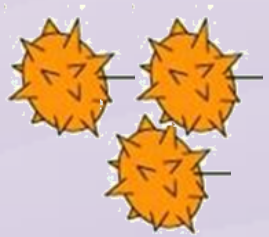
What happens ???

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

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

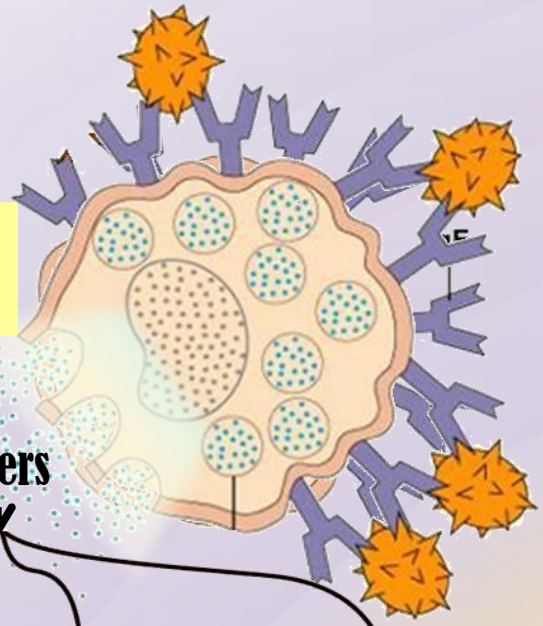
ANAPHYLACTIC SHOCK

Second or later exposure



Antigen Re-exposure

Mast Cell DEGRANULATION

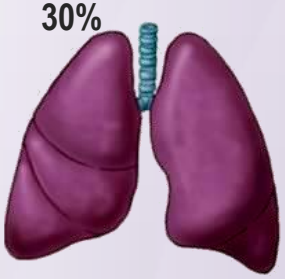


Characters

Histamine, Leukotrienes, others

2.

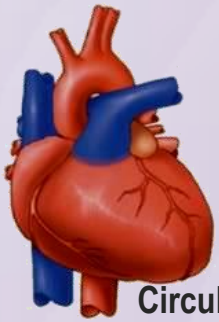
Mucous Swelling
Rhinitis 16%
Angioedema 88%
Airway 56%
GIT 30%



3. Lungs **47%**

- Bronchospasm
- Vasoconstriction

Shortness of breath



Heart — Circulatory Collapse

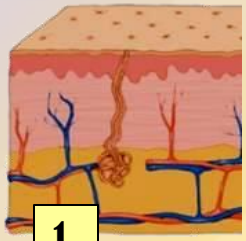
- Decreased output
- Decreased coronary flow

33%

4.

Hypo-perfusion Blood vessels

- Vasodilation
- Leakiness

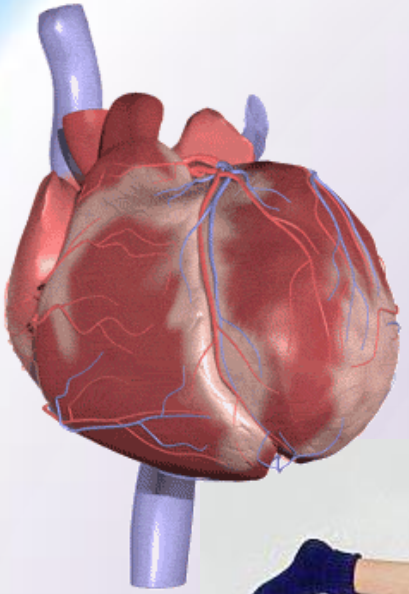


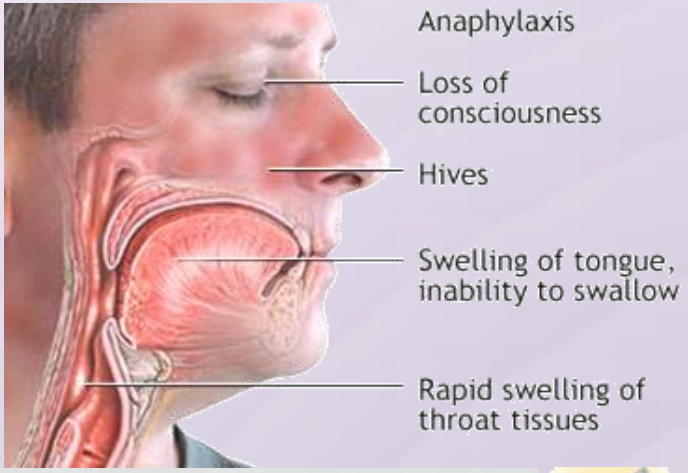
1. Skin

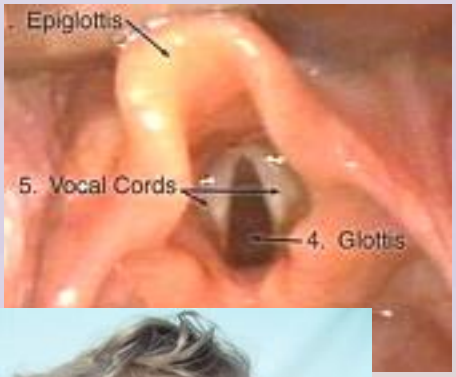
- Pruritus
- Urticaria
- Edema

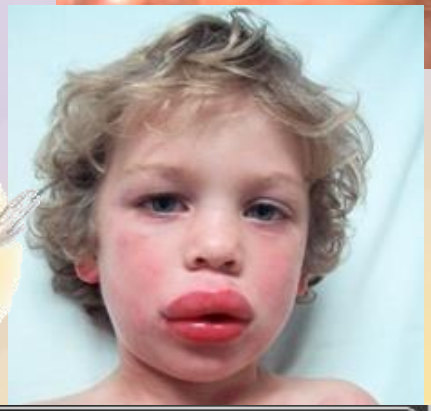
88%

- 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

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 50 mg IV / No cimetidine in elderly, renal/hepatic failure, or if on β-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 3-4h 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.

Contraindications

Rare in a setting of anaphylaxsis

Not given > 40 y cardiac patient

ADRs

Dysrrhythmias

Indication

DRUG OF CHOICE

ADRENALINE

1ST LINE

Administration

Best is (IM) route in anaphylaxsis. 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 anaphylaxsis

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

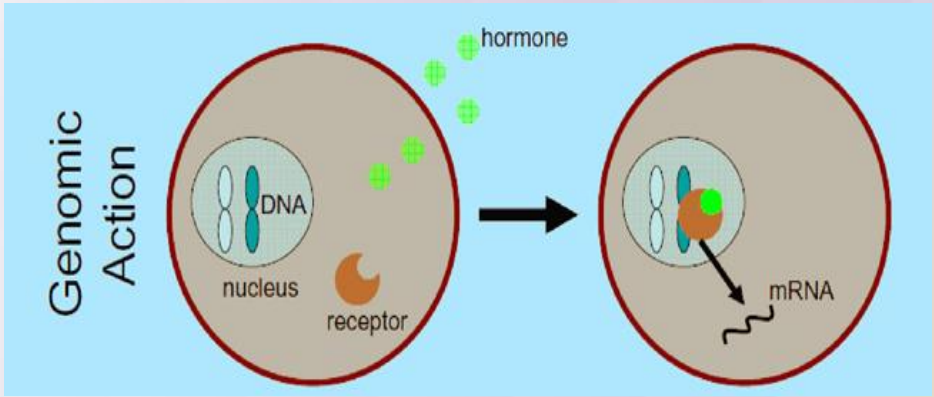
2ND LINE

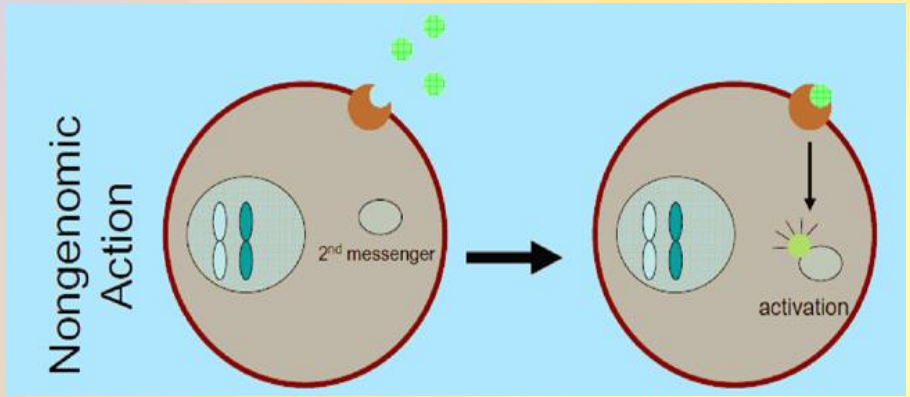
It can not be used alone → not life saving

Given slowly intravenously or intramuscularly.

- 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 actions on **Membrane-bound receptors** → modulating levels of 2nd messengers → (within seconds or minutes) → **Non-genomic action (genomic action is slow may take hrs to 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 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 ↓ more histamine release

H_2 BLOCKERS

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

BRONCHODIALATORS

Inhalational

- **Salbutamol** → β_2-AD agonist → short acting, rapid relief onset relax bronchial smooth muscle and may decrease mediator release from mast cells and basophils.
  It may also inhibit airway microvascular leakage.
- **Ipratropium** → Anticholinergic → longer duration of action → ↓ secretion
  Less rapid in action

Parentral

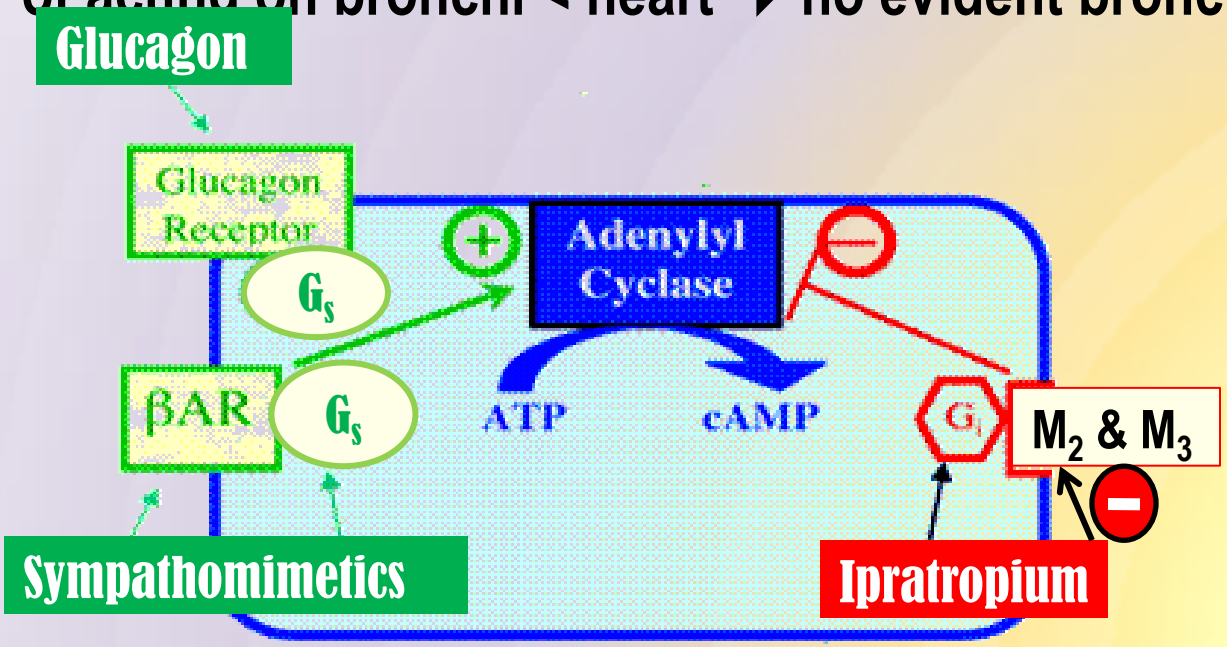
Aminophylline IV → may be useful in the treatment of anaphylaxis when inhaled broncho-dilators are not effective & bronchospasm is persistent.
Given in hospital setting as levels of drug should be **Therapeutically Monitored** → has narrow therapeutic index

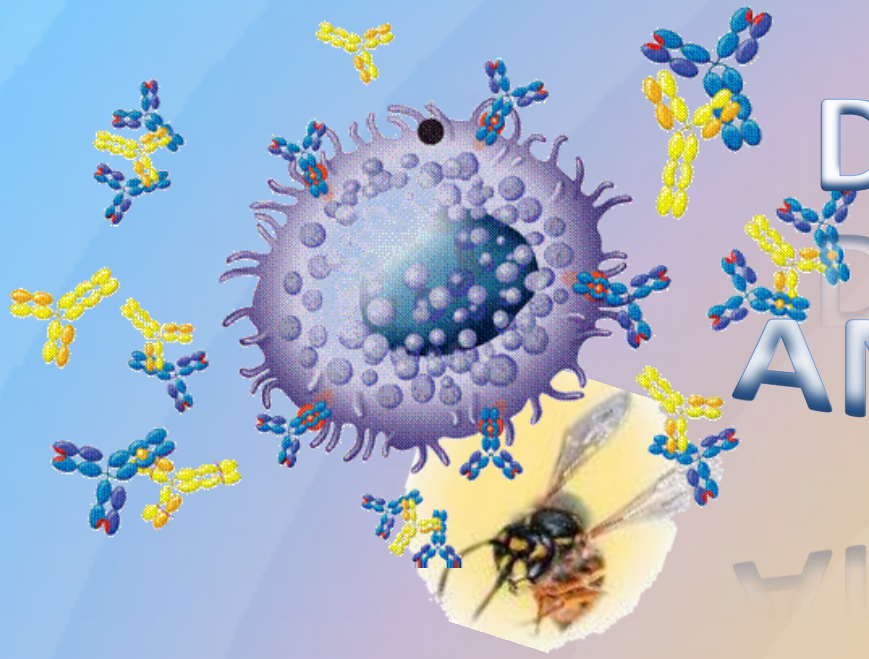
GLUCAGON

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 AR
That is why effective in spite of beta-adrenergic blockade.
Efficacy of acting on bronchi < heart ➔ no evident bronchodilation





DRUGS USED IN ANAPHYLAXSIS

GOOD LUCK