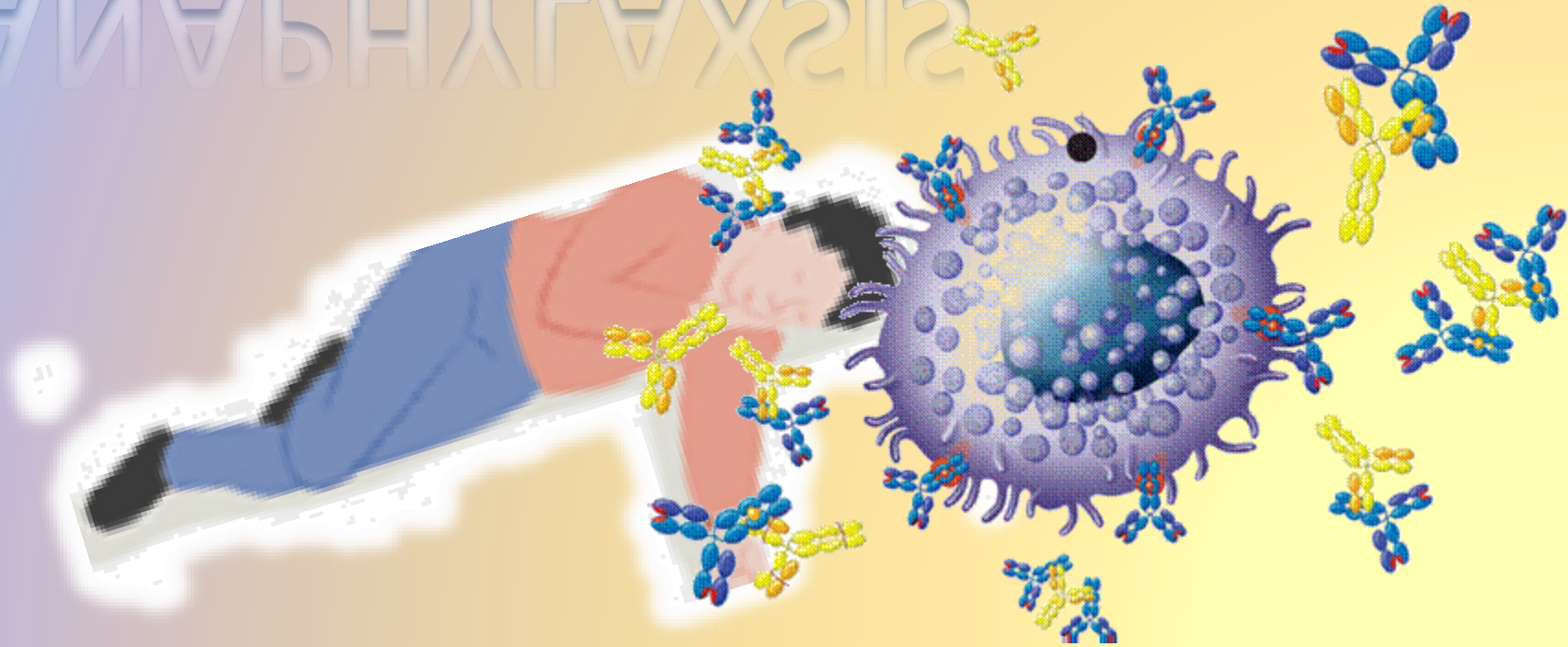


DRUGS USED IN ANAPHYLAXIS





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

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

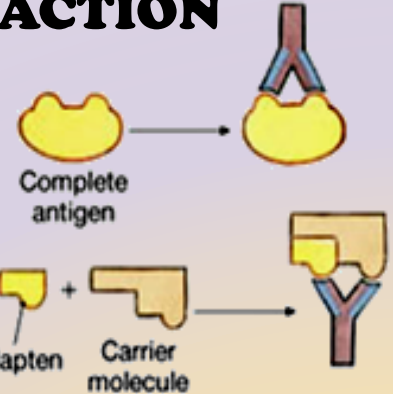
Severe, life-threatening, generalized or systemic hypersensitivity reaction in response to allergen

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_H 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

Mast Cell DEGRANULATION

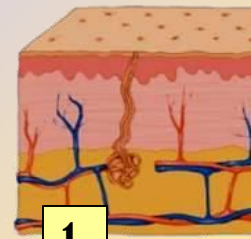
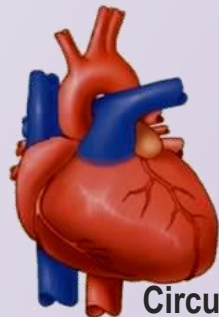
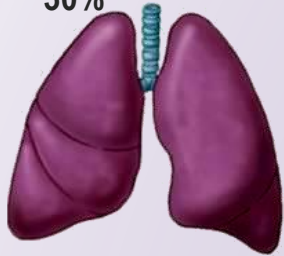
Histamine, Leukotrienes, others

Antigen Re-exposure



2.

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



3.

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

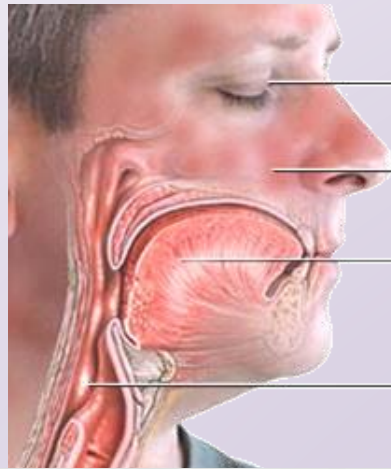
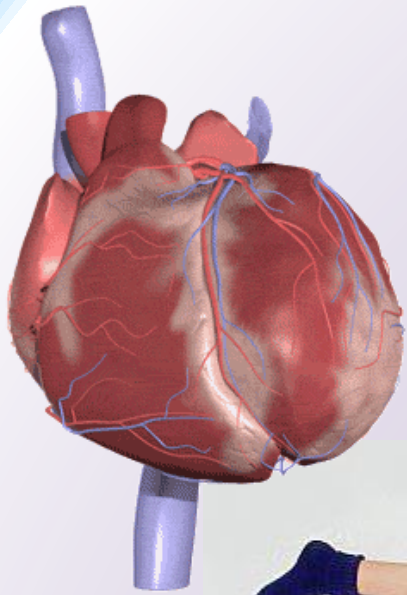
4.

- Heart Circulatory Collapse Hypo-perfusion Blood vessels
- Decreased output
 - Decreased coronary flow
 - Vasodilation
 - Leakiness
- 33%

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%)



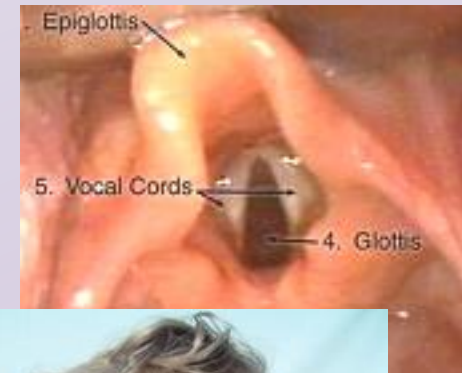
Anaphylaxis

Loss of consciousness

Hives

Swelling of tongue, inability to swallow

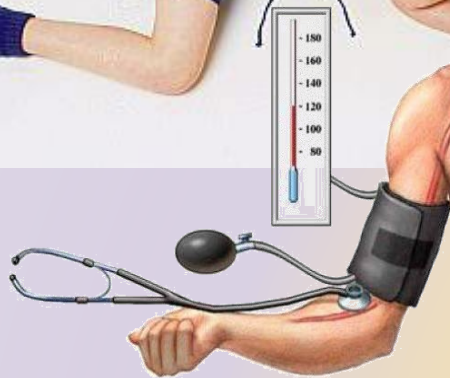
Rapid swelling of throat tissues



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
O₂ 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, SpO₂ < 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 2ND LINE

6. Bronchodilators 7. Glucagon 8. H₂ 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 \rightarrow 1 mg IV q 5 minutes until hypotension
resolves

H₂ 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

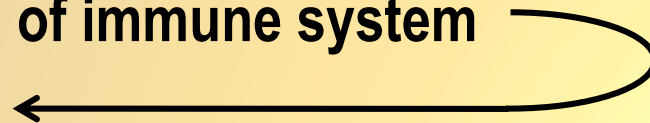
- ✚ To support the respiratory & circulatory deficits
- ✚ To halt the existing hyper-reaction
- ✚ To prevent further hyper-reaction of immune system

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 nasopharynx & 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

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

If hypotension persist → start dopamine. Why not noradrenaline?

Auto-injectors Kits;

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

CORTICOSTEROIDS

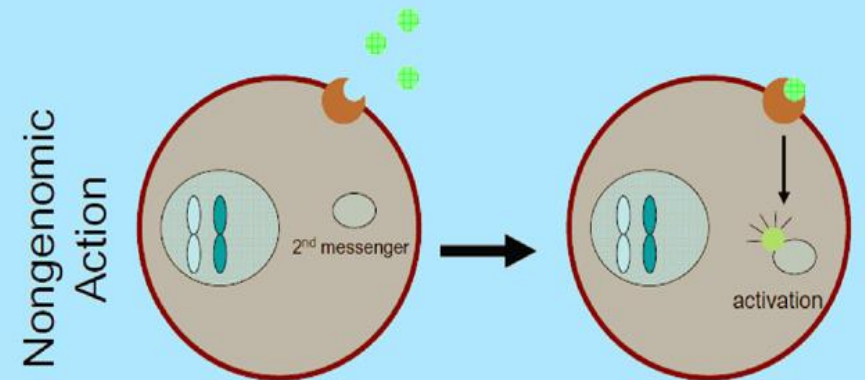
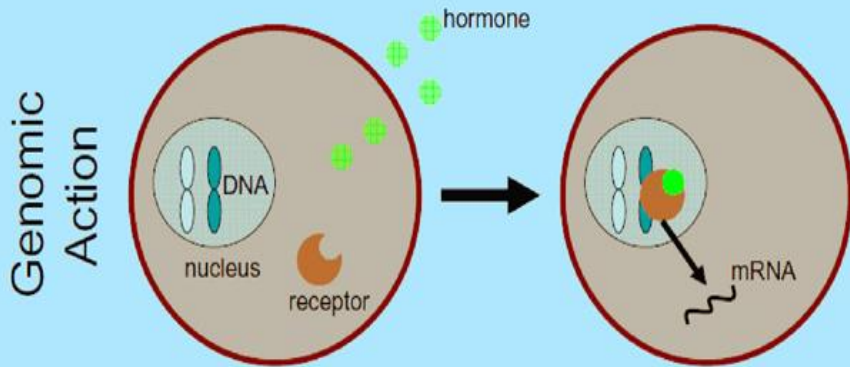
2ND LINE

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

H₁ 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

H₂ BLOCKERS

The significance of H₂ blockers is not established , these drugs are associated 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

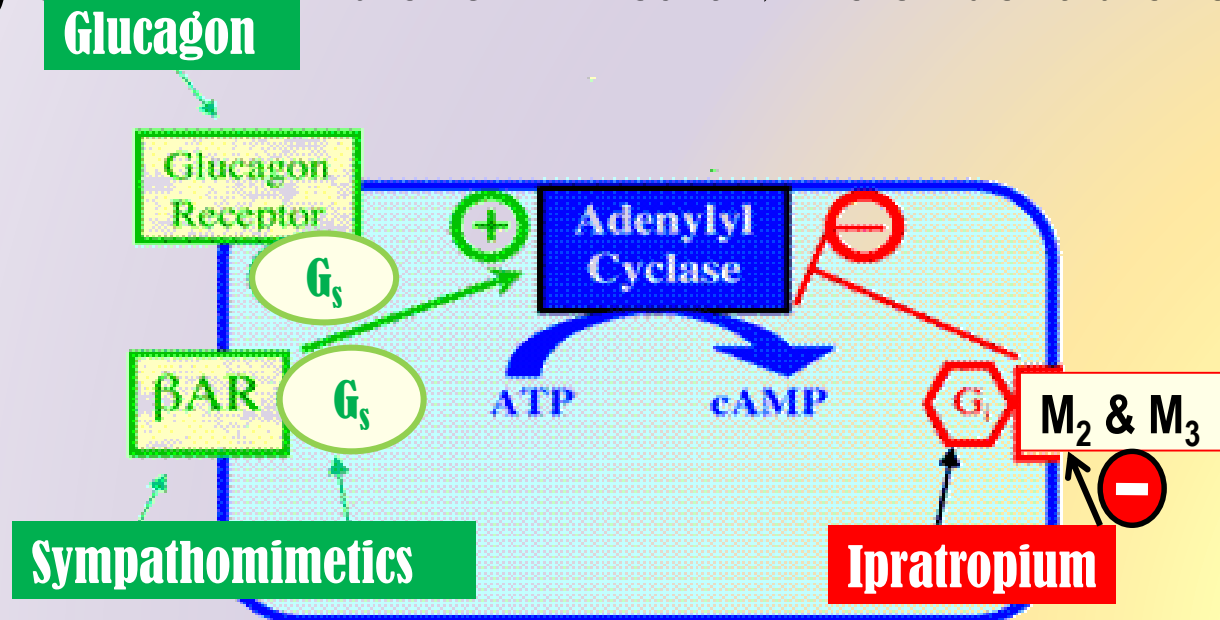
Parenteral

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

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

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





DRUGS USED IN ANAPHYLAXIS

GOOD LUCK