



# Anaphylactic shock

## Objectives:

- 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.

Rise up, start fresh, see the opportunity in each day.

- Titles
- Very important
- Extra information
- Doctor's notes

## Anaphylaxis

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

### Symptoms

Mucosal swelling

Difficulty breathing

↓ Blood pressure (hypotension)

Rash

## 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.

#### Adrenoceptors:

Alpha1: vasoconstriction.

Beta1: restore heart function (heart muscles contraction).

Beta2: bronchodilation.

## Types of shock

Type	Caused by
<b>Hypovolemic</b>	<ul style="list-style-type: none"><li>• Hemorrhage</li><li>• fluid loss (plasma, ECF) e.g. Excessive vomiting</li></ul>
<b>Cardiogenic</b>	Inability to contract & pump. E.g.: <ul style="list-style-type: none"><li>• myocardial infarction</li></ul>
<b>Obstructive</b>	Extra-cardiac obstruction: <ul style="list-style-type: none"><li>• Pulmonary embolism.</li><li>• Cardiac Tamponade.</li></ul>
<b>Distributive</b>	Decreased Peripheral* Resistance vasodilation hypotension. As in: septic shock, Neurogenic shock, <b>anaphylactic shock</b> .

\*Peripheral resistance is the resistance of the arteries to blood flow. As the arteries constrict, the resistance increases and as they dilate, resistance decreases.

Peripheral resistance is determined by three factors:

**Autonomic activity:** sympathetic activity constricts peripheral arteries.

**Pharmacologic agents:** vasoconstrictor drugs increase resistance while vasodilator drugs decrease it.

**Blood viscosity:** increased viscosity increases resistance.

• **What we need for normal blood pressure :**

1. Good cardiac output

2. Good vessels walls constriction

• If the patient is taking B2 blockers salbutamol won't work so antimuscarinics like ipratropium is the drug of choice.

# ANAPHYLACTIC SHOCK

## Immunologic Anaphylaxis (known as ANAPHYLAXIS)

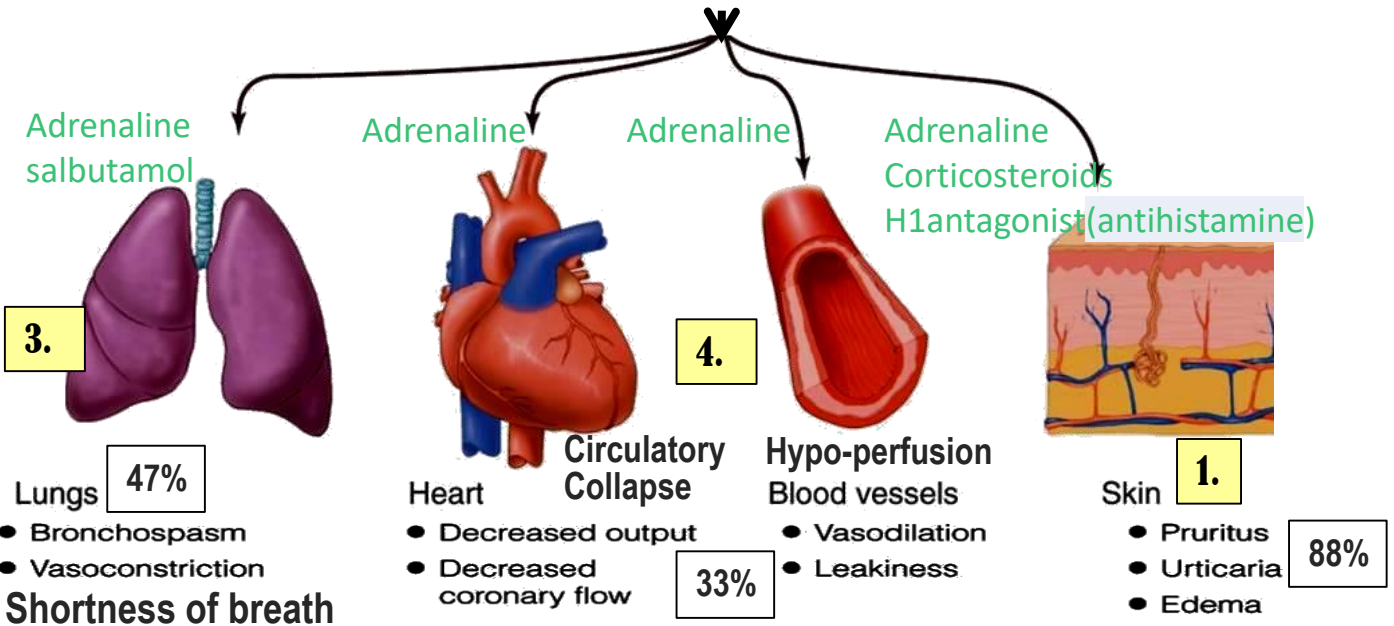
It belongs to type I hypersensitivity reaction (IgE)  
Occurs after exposure to foreign substances [antigen] such as food, insect or animal venom, drugs, blood products.  
The immune system will then develop antibodies for this antigen and it will remain in the body for a while.  
After a 2<sup>nd</sup> 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.  
**NO need for second exposure**

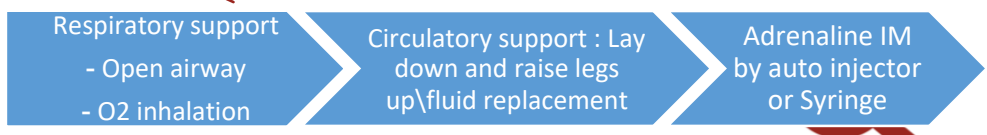
Because anaphylactic and anaphylactoid reactions produce the same clinical manifestations and are treated exactly the same way, we use the term anaphylaxis to refer to both conditions.

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



Remember when there is to much vasodilatation the body has to compensate by causing tachycardia as a reflex

**ANAPHYLACTIC SHOCK** → When the diagnosis is made → Call ambulance → START EMERGENCY TREATMENT



# 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

To compensate for vasodilation BC vasodilation means you need more blood

## 2ND LINE

In skin 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

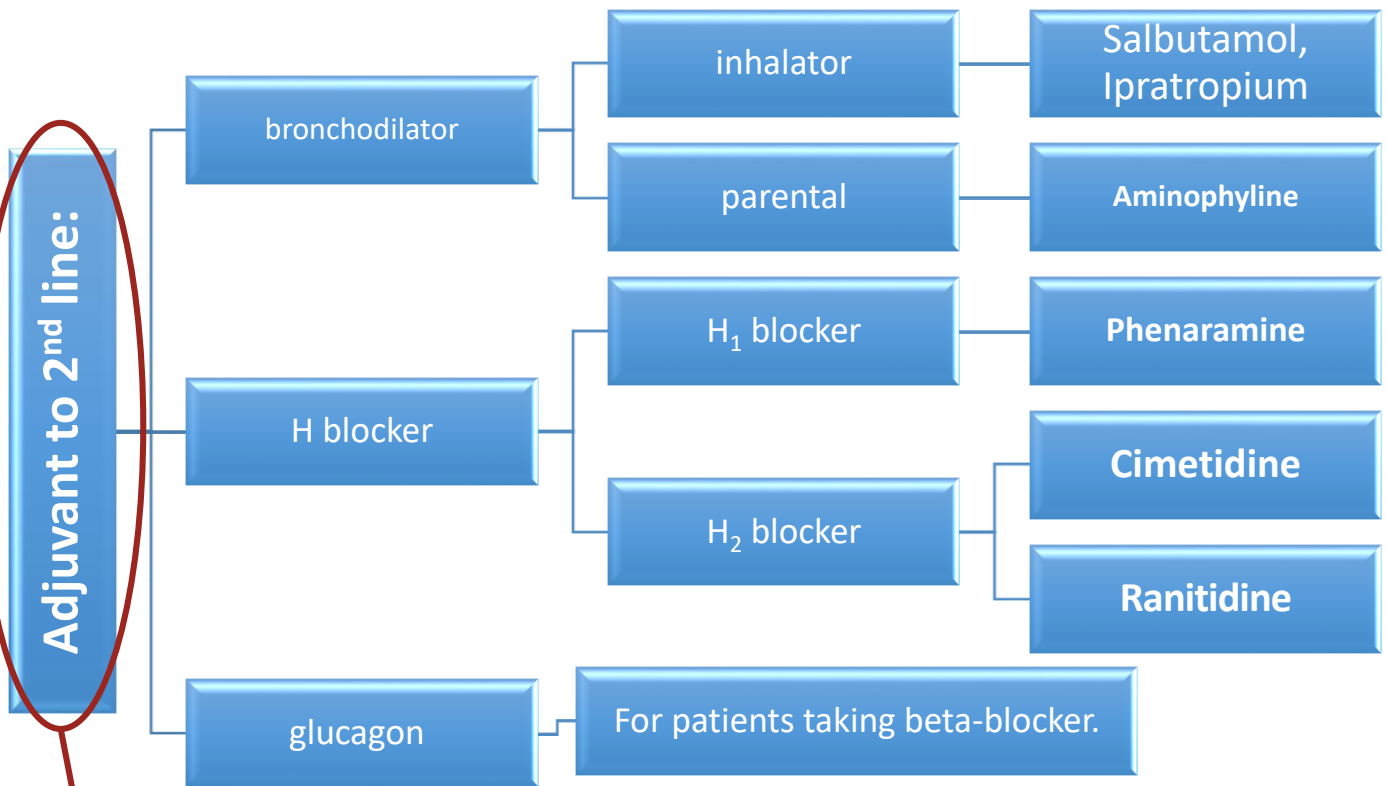
100 mg

50 mg

25 mg

The doctor said we won't be asked about doses.

# ANAPHYLACTIC SHOCK THERAPY PROTOCOL



## Objective of therapy:

- To support the respiratory & circulatory deficits
- To halt (to stop) the existing (the excessive) hyper-reaction
- To prevent further hyper-reaction of immune system (Biphasic phenomenon): 2<sup>nd</sup> release of mediators without re-exposure to antigen (in up to 20%) Clinically evident 3-4h after the initial manifestations clear



## Adrenaline

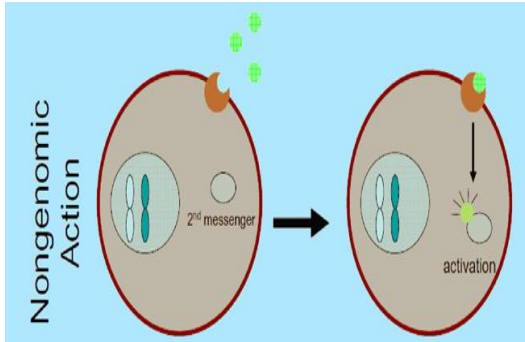
Mechanism of action	A nonselective Adrenergic agonist [ $\alpha_1$ , $\alpha_2$ , $\beta_1$ , $\beta_2$ ]
Action	<p>As an adrenergic agonist:</p> <ul style="list-style-type: none"> <li>Reverses peripheral vasodilation → maintains Blood Pressure &amp; directs blood flow to major organs</li> <li>↓ edema → reverse hives* ,swelling around face &amp; lips &amp; angioedema** in nasopharynx &amp; larynx</li> </ul> <p>As a <math>\beta</math>-adrenergic agonist:</p> <ul style="list-style-type: none"> <li><math>\beta_2</math> effect: Dilates bronchial airways + ↓ histamine &amp; leukotriene release from mast cells</li> <li><math>\beta_1</math> effect: ↑ force of myocardial contraction</li> <li><b>PHYSIOLOGICAL ANTAGONIST:</b> Attenuates the severity of IgE-mediated allergic reactions</li> <li><b>Indication:</b> drug of choice</li> </ul> <p>* allergic skin reaction causing localized redness, swelling, and itching (see more <a href="http://medical-dictionary.thefreedictionary.com/hives">http://medical-dictionary.thefreedictionary.com/hives</a>)</p> <p>** a localized edematous reaction of the deep dermis or subcutaneous or submucosal tissues appearing as giant wheals (see more <a href="http://medical-dictionary.thefreedictionary.com/angioedema">http://medical-dictionary.thefreedictionary.com/angioedema</a>)</p>
Contraindications	<ul style="list-style-type: none"> <li>Not given more than 40 years cardiac patient</li> <li>Rare in a setting of anaphylaxis</li> </ul>
Adverse effect	Dysrhythmias
Administration	<p>Intamuscular (IM), due to:</p> <ul style="list-style-type: none"> <li>Easily accessible (<b>Auto-injectors Kits:</b> Disposable (use for once) , prefilled devices → automatically administer a single dose of epinephrine in emergency)</li> <li>Greater margin of safety, so no dysrhythmias as with IV</li> <li>No need to wait for IV line, if IV present it given by physician under monitoring</li> </ul>
Repeat every 5-10 min as needed Patients observed for 4-6 hours. <b>Why?</b> Fear of biphasic anaphylaxis	If hypotension persist → start dopamine
Caution	<p>For patients taking <math>\beta</math>-blockers because they either:</p> <ul style="list-style-type: none"> <li>Refractory (<b>not response</b>); as it may antagonize <math>\beta</math> effects of adrenaline</li> <li>Rebound hypertension: [ unopposed <math>\alpha</math> effect], specially when adrenaline is repeated يعني يبجي الأدرينالين مكان مستقبلات الألفا ويسبب ارتفاع ضغط</li> </ul>





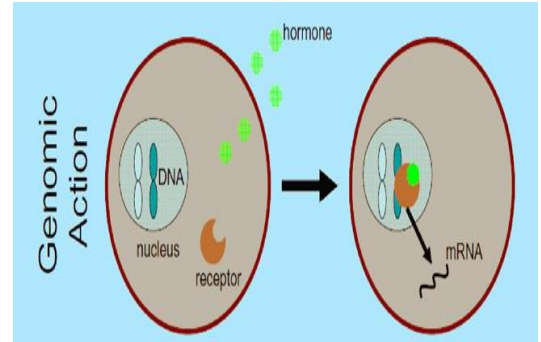
	corticosteroids	H <sub>1</sub> blockers	H <sub>2</sub> blockers	Salbutamol		Aminophylline	glucagon
Mechanism of action	through immediate GCs actions on Membrane-bound receptors → modulating levels of 2nd messengers → (within seconds or minutes) which means <b>Non-genomic action</b>	Though mast cells have already degranulated (e.g. phenaramine)	(anti-ulcer drugs, used for epigastric pain)	<b>β<sub>2</sub>-adrenergic agonist</b>	Ipratropium		Has both positive inotropic & chronotropic effects on heart → increase cardiac cyclic AMP → an effect entirely independent of adrenergic that is why effective in spite of β-adrenergic blockade. Efficacy of acting on bronchi less than in heart (no evident bronchodilation)
					Anticholinergic		
Action	<ul style="list-style-type: none"> <li>Reverse hypotension and bronchoconstriction, so it will decrease the releasing of inflammatory mediators (anti-chemotactic &amp; mast cell stabilizing effects).</li> <li>Decrease mucosal swelling and skin reaction</li> <li>May help to limit biphasic reactions by decrease allergic mediators</li> </ul>	<ul style="list-style-type: none"> <li>help to counteract histamine-mediated vasodilation &amp; bronchoconstriction.</li> <li>May help to limit biphasic reactions by decrease histamine release</li> </ul>	The significance of H <sub>2</sub> blockers is not established (e.g. Ranitidine & cimetidine)	1- Short acting, rapid relief onset relax bronchial smooth muscle and may decrease mediator release from mast cells and basophils. 2- Inhibit airway microvascular leakage.	Decrease secretion Less rapid in action	treatment of anaphylaxis when inhaled Bronchodilators are not effective & bronchospasm is persistent	patients with refractory hypotension  Drug of choice for severe anaphylaxis in <b>patients taking β-blockers</b> .
Contraindications	<ul style="list-style-type: none"> <li>Not given more than 40 years cardiac patient</li> <li>Rare in a setting of anaphylaxis</li> </ul>		No cimetidine in elderly, renal/hepatic failure, or if on β-blockers			Given in hospital setting as levels of drug should be	
Adverse effect	<b>Dysrhythmias</b>		associated with serious adverse drug interactions		Inhalational longer duration of action	<b>Therapeutically Monitored</b> because it has narrow therapeutic index	
Administration	slowly intravenously or intramuscularly	Ranitidine 50 mg IV		Inhalational			1 mg IV q 5 min until hypotension resolves

## Non-genomic action



هنا يدخل الدواء ويرتبط بالمستقبلات التي على الغشاء البلازمي ويعطي تأثير سريع

## Genomic action



genomic action is slow may take hours to days

هنا يدخل الدواء ويرتبط بمستقبل جوا الخلية، هذا المستقبل يبدخل جوا DNA وبيأثر بتكوين البروتين بعدين يطلع التأثير، يأخذ وقت طويل عشان يعطي تأثيره

لو كان المريض يأخذ  $\beta$ -blockers ماراح يصير عندي cAMP بالتالي مافيه contraction عشان أسوي contraction استخدم

قلوكاجون اللي بيأثر على مستقبلات خاصة فيه تحفز  $G_s$  وبالتالي تزيد cAMP وبيصير عندي contraction

## Glucagon



## Sympathomimetics

## Ipratropium

A 12-year-old boy is brought to the emergency department after being stung by a bee. He had been well until he was stung on his right forearm, while playing in the yard. He initially complained of localized pain and swelling. Fifteen minutes later, he began to complain of shortness of breath. His parents observed him to be wheezing, very weak and dizzy. His parents brought him immediately to the local emergency department. His medical history shows that he has allergy.

## Q1: what is the most likely diagnose in this case ?

Anaphylactic shock.

## Q2: What is the drug of choice in this case ?

Adrenaline.

## Q3: What is the best route of administration for this drug ?

Intra-muscular (IM).

although we can use IV line but should be given by physician under monitoring.

## Q4: What is the mechanism of its action ?

It is Sympathomimetic drug, so it mimics the effect of Sympathetic system by working as Adrenergic agonist .

It is nonselective agonist which act on [ $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ,  $\beta_2$ ,  $\beta_3$  ], some of its action:

1\ In blood vessel, act as  $\alpha$  agonist which cause vasoconstriction.

2\ In heart, act as  $\beta_1$  agonist which lead to increase the force of myocardial contraction.

3\ In bronchi & bronchioles, act as  $\beta_2$  agonist which cause bronchodilator and decrease histamine & leukotriene release from mast cells .

- **After 3-4 hours, he may develop what we called Biphasic Phenomenon.**

## Q5:What do we mean by Biphasic Phenomenon?

It is a second episode of anaphylaxis with 2nd release of mediators without re-exposure to antigen.

## Q6: List some drugs we can use it to prevent Biphasic Phenomenon ?

2<sup>nd</sup> line anaphylaxis's drugs. Such as 1\ Glucocorticoids : Hydrocortisone

2 \ First generation H1 blocker : Chlorphenamine

## Q7: Later, we can give him some bronchodilators as Adjuvant 2<sup>nd</sup> line therapy, list some of them?

Salbutamol as  $\beta_2$  Agonist.

Ipratropium as Anti-muscarinic.

Aminophylline as Methyl-xanthine.

**Zoom in to see the answers**

## QUIZ



Boys	Girls
عبدالرحمن ذكري	غادة المهنا
عبدالعزيز رضوان	اللولو الصليهم
مؤيد أحمد	روان القحطاني
فيصل العباد	درة الحمدي
فارس النفيسة	شروق الصومالي
خالد العيسى	سما الحربي
عبدالرحمن العريفي	انوار العجمي
عبدالرحمن الجريان	وتين الحمود
محمد خوجة	رنا باراسين
عمر التركستاني	امل القرني

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