



# Anaphylaxis

- Red : important
- Black : in male / female slides
- Pink : in female's slides only
- Blue : in male's slides only
- Females doctor notes
- Grey: Males doctor notes

## OBJECTIVES:

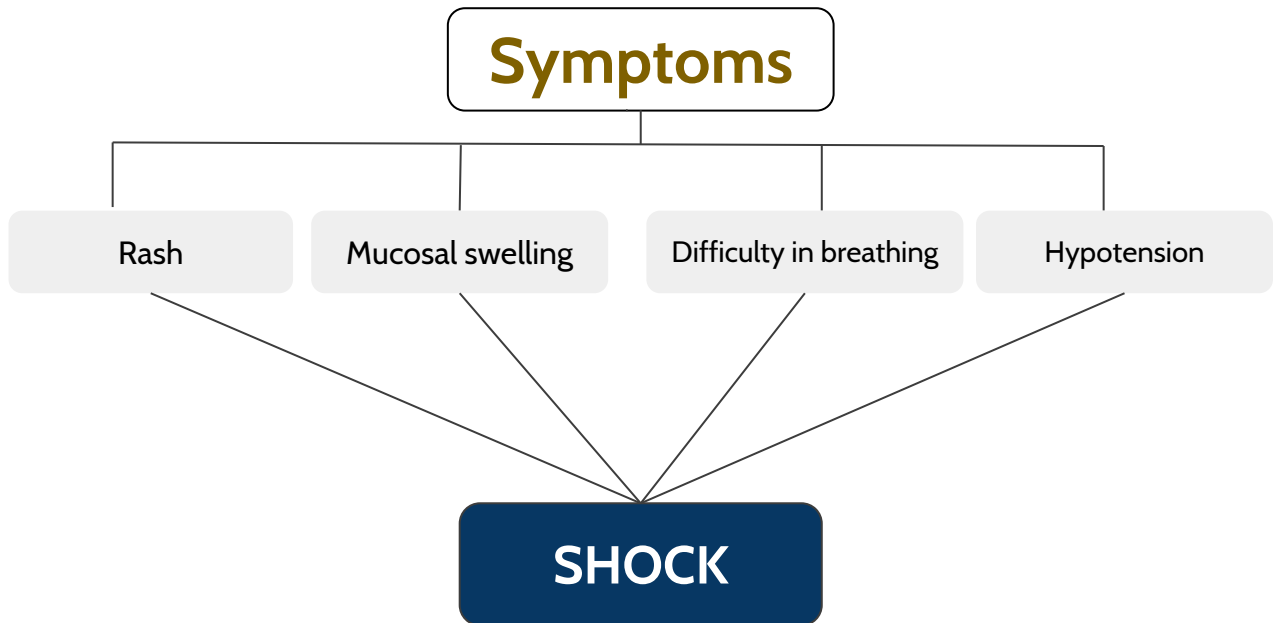
By the end of this lecture , you should be able to:

- ✓ 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.

Editing File

# Anaphylaxis

Anaphylaxis is a sudden, severe allergic reaction affecting the whole body (generalized or systemic) in response to allergen.



**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 long enough, it will lead to irreversible derangements sets then to permanent functional deficit or death.

## What type of shocks is the anaphylactic shock?

	Hypovolemic	Obstructive	Cardiogenic	Distributive
Types of shock	<ul style="list-style-type: none"> <li>• Hemorrhage</li> <li>• Fluid loss (plasma, EFC)</li> </ul>	<ul style="list-style-type: none"> <li>• Extra-cardiac obstruction. E.g. Cardiac tamponade, Pulmonary embolism</li> </ul>	<ul style="list-style-type: none"> <li>• Inability to contract &amp; pump. E.g. myocardial infarction.</li> </ul>	<ul style="list-style-type: none"> <li>• Decreased Peripheral Resistance E.g. septic shock, Neurogenic shock</li> <li><b>Anaphylactic shock</b></li> </ul>

### **ANAPHYLACTIC SHOCK :**

A life-threatening allergic reaction that causes shock (hypoperfusion) and airway swelling. it is a medical emergency where immediate treatment is needed to prevent potential death.

# The Nature of anaphylactic shock

## Immunologic Anaphylaxis (known as ANAPHYLAXIS)

❖ It belongs to type I hypersensitivity reaction

- 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, Depolarizing drugs, Dextrans**

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 :

### Lungs

-bronchospasm -vasoconstriction  
-shortness in breath

### skin

1-pruritus 2- urticaria 3-edema

### heart

-↓ output - ↓ coronary flow  
- Circulatory Collapse

### blood vessels

-vasodilation -leakiness  
-Hypo-perfusion

### Mucous Swelling

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

## characters of anaphylactic shock:

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

# Anaphylactic Shock Therapy Protocol:

Rescue	When the diagnosis is made as an anaphylactic shock (after calling the ambulance), emergency treatment should be immediately start as follows:	
	<b>Life Threatening Problems:</b>	<b>Management</b>
	<p><b>Airway:</b> swelling, hoarseness, stridor .</p> <p><b>Breathing:</b> rapid breathing, wheezing, cyanosis, fatigue, confusion, oxygenated Hb (SpO2) &lt; 92%</p>	<p><b>Respiratory support</b></p> <ul style="list-style-type: none"> <li>• Open airway for O2 inhalation</li> </ul>
	<p><b>Circulation:</b> pale, clammy, low BP, faintness, drowsy /coma.</p>	<p><b>Circulatory support</b></p> <ul style="list-style-type: none"> <li>• Lay down and raise legs up</li> <li>• Fluid replacement</li> </ul>
1 <sup>st</sup> Line Therapy	<ul style="list-style-type: none"> <li>• Adrenaline (give IM by Auto injector or by syringe, unless there is a specialist to give IV)</li> <li>• IV fluid challenge Crystalloid is given for children to increase the blood plasma level.</li> </ul>	
2 <sup>nd</sup> line	<ul style="list-style-type: none"> <li>• Chlorpheniramine (first generation H1 blocker) (IM or slow IV).</li> <li>• Hydrocortisone (Glucocorticoids) (IM or slow IV).</li> </ul>	
Adjuvant to 2 <sup>nd</sup> line	<ul style="list-style-type: none"> <li>• <b>Bronchodilators:</b> Salbutamol (nebulizer), Ipratropium (nebulizer), Aminophylline (IV).</li> <li>• <b>Glucagon:</b> "to increase cardiac output" For patients taking beta-blockers &amp; with refractory hypotension .</li> <li>• <b>H2 blocker:</b> "we mainly want to block H1 so we give H2 blocker to support the action of H1 antagonist "</li> <li>• Ranitidine: I.V</li> <li>• Cimetidine: contraindicated in elderly renal/hepatic failure, or if on beta-blockers.</li> </ul>	<p><b>Why do we use the 2<sup>nd</sup> line adjuvants?</b></p> <p><b>Objective of Therapy:</b></p> <ul style="list-style-type: none"> <li>• To support the respiratory &amp; circulatory deficits.</li> <li>• To halt the existing hyper-reaction.</li> <li>• To prevent further hyper-reaction of immune system (prevent biphasic phenomenon).</li> </ul> <p><b>Biphasic Phenomenon:</b></p> <ul style="list-style-type: none"> <li>• 2<sup>nd</sup> release of mediators without re-exposure to antigen *leukotrienes and histamines are still active* in up to 20% ).</li> <li>• Clinically evident 3-4h after the initial manifestations clear.</li> </ul>

# 1<sup>st</sup> line Therapy

## Adrenaline

(A Sympathomimetic)

<b>Mechanism</b>	<b>nonselective</b> Adrenergic agonist ( $\alpha_1$ , $\alpha_2$ , $\beta_1$ , $\beta_2$ , $\beta_3$ ).
<b>Actions</b>	<ul style="list-style-type: none"><li>• <b><math>\alpha</math> agonist:</b><ul style="list-style-type: none"><li>- Reverses peripheral vasodilation, thus maintains BP and directs blood flow to major organs.</li><li>- Vasoconstriction leads to decreasing edema → reverse hives, swelling around face &amp; lips &amp; angioedema in nasopharynx &amp; larynx.</li></ul></li><li>• <b><math>\beta</math> agonist:</b><ul style="list-style-type: none"><li>-<b><math>\beta_2</math></b>: Dilates bronchial airways + ↓ histamine &amp; leukotriene release from mast cells.</li><li>-<b><math>\beta_1</math></b>: ↑ force of myocardial contraction.</li></ul></li><li>• <b>Adrenaline is the physiological antagonist of histamine:</b><ul style="list-style-type: none"><li>-Attenuates “reduce” the severity of <b>IgE-mediated</b> allergic reactions.</li></ul></li></ul>
<b>Indications</b>	<b>Drug of choice for anaphylactic shock.</b>
<b>Contraindications</b>	<ul style="list-style-type: none"><li>• Rare in a setting of anaphylaxis</li><li>• Not given for cardiac patient who are older than 40 years</li><li>• Patients taking <b><math>\beta</math>-blockers</b> either are: <i>why? because of the <math>\beta</math> blocking action</i><ul style="list-style-type: none"><li>• <b>Refractory</b>; as it may antagonize <math>\beta</math> effects of adrenaline. (<math>\beta_2</math> receptors won't be stimulated since they're blocked, no ↑ cAMP, no effect)</li><li>• <b>Rebound hypertension</b> (unopposed <math>\alpha</math> effect), specially when adrenaline is repeated (glucagon is used in this case).</li></ul></li></ul>
<b>ARDs</b>	<b>Causes dysrhythmias if given IV.</b>
<b>Administration</b>	<p><b>IM: why?</b></p> <ol style="list-style-type: none"><li>1-Easily accessible by using Auto-injectors Kits, they are disposable prefilled devices, automatically administer a single dose of epinephrine in emergency.</li><li>2-Greater margin of safety → no dysrhythmias as with IV.</li><li>3-No need to wait for IV line, if present, it should be given by physician under monitoring.</li><li>4- Repeat every 5-10 min as needed</li><li>5- Patient should be observed for 4-6 hours <b>(fear of biphasic anaphylaxis)</b></li></ol> <p>It could also be administered subcutaneously, which is safer, but won't produce as rapid effect as IM injection for the rescue of anaphylaxis..</p>

**IMPORTANT NOTE:** • If hypotension persists, start **Dopamine** (To protect the kidney), Why not noradrenaline? \*Noradrenaline is nonselective on ( $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ ). It has no effect on  $\beta_2$  stimulation of  $\alpha_1$  (vasoconstriction) causes hypertension, but this vasoconstriction is not opposed by the stimulation of  $\beta_2$  (vasodilatation) Therefore, noradrenaline will cause a very severe vasoconstriction, much more than what is required in the case of anaphylactic shock.

## 2<sup>nd</sup> line therapy

### Corticosteroids

(anti-inflammatory)

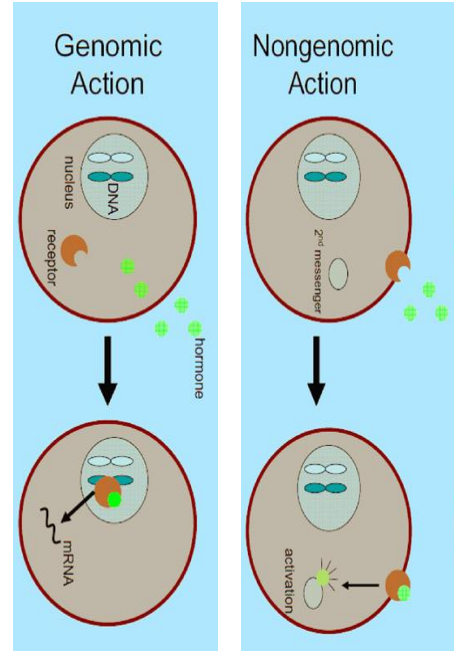
#### Mechanism

##### Genomic Action: \*For chronic use.

- Intracellular receptors (cytosol or nucleus)
- Takes hours to days to be activated.
- Used for maintenance of asthma as it suppresses airway inflammation

##### Non-genomic actions:

- Immediate Glucocorticoids actions on **Membrane-bound receptors**, which leads to modulating 2nd messengers levels.
- Rapid onset of action (seconds or minutes). \*That's why we use it in anaphylactic shock.



#### Action

##### Non-genomic action in anaphylactic shock:

- Reverse hypotension & bronchoconstriction.
- ↓ release of inflammatory and allergic mediators (anti-chemotactic & mast cell stabilizing effects.)
- ↓ mucosal swelling and skin reaction.
- May help to limit biphasic reactions by decreasing allergic mediators.

#### Administration

- Given slowly IV or IM.
- Not used alone (**not life saving**).

## 2<sup>nd</sup> line therapy

## Adjuvant 2<sup>nd</sup> line therapy

### H1 Blockers

### H2 Blockers

#### Examples

pheniramine

Ranitidine, Cimetidine, Pantoprazole

#### Action

- Though mast cells have already de-granulated, yet these drugs can still help to counteract histamine-mediated vasodilation & bronchoconstriction.
- May help to limit biphasic reactions by blocking histamine receptors.

- The significance of H2 blockers is not established, these drugs are associated with serious adverse drug interactions.
- **Pantoprazole** is a Proton pump inhibitor it is safer and given once. "to decrease GIT acidity, it's safer than H2 blockers"

#### Administration

- Given slowly I.V or I.M
- It can not be used alone (**not life saving**).

-

#### Contra-indication

-

**Cimetidine** shouldn't be given to elderly, renal/ hepatic failure, or if on b-blockers.  
Why? Because it inhibits cytochrome P450 which controls drug-drug interactions. So when given it may increase the toxicity of other drugs, therefore it's replaced by ranitidine.

# Bronchodilators

(used for asthma as well)

Salbutamol	Ipratropium	Aminophylline
Inhalation		Parenteral IV
$\beta 2$ agonist	Anticholinergic Antimuscarinic	Methylxanthine
<ul style="list-style-type: none"> <li>Short acting.</li> <li>Rapid onset of acting.</li> <li>Relaxation of bronchial smooth muscle. (Bronchodilation)</li> <li>Decrease mediators released from mast cell and basophils. .</li> <li>inhibit airway microvascular leakage.</li> </ul>	<ul style="list-style-type: none"> <li>Longer acting.</li> <li>Less rapid in action.</li> <li>Slower onset of action.</li> <li>Decrease secretion</li> <li>Decreases cGMP , therefore decreases the contractility of smooth muscles.</li> </ul>	<ul style="list-style-type: none"> <li>IV is useful for anaphylactic shock.</li> <li>may be useful in the treatment of anaphylaxis when inhaled bronchodilators are not effective &amp; bronchospasm is persistent.</li> <li>Given in hospital setting as levels of drug <b>should be therapeutically monitored</b> because it has narrow therapeutic index.</li> <li>Increase cAMP</li> <li>Smooth muscle relaxation</li> </ul>
<ul style="list-style-type: none"> <li>Not effective in Patients taking <math>\beta</math> blockers,</li> </ul>	<ul style="list-style-type: none"> <li>Effective for bronchodilation in spite of <math>\beta</math>-adrenergic blockade.</li> </ul>	



## Glucagon

Mechanism	<ul style="list-style-type: none"> <li>Main action: act on glucagon receptors in the heart.</li> </ul>
Action	<ul style="list-style-type: none"> <li>Has both positive inotropic &amp; chronotropic effect on heart → increase cardiac cyclic AMP.</li> <li><b>This effect is completely independent of Adrenergic Receptors</b>, That is why effective in spite of <math>\beta</math>-adrenergic blockade.</li> <li>Efficacy of acting on bronchi is less prominent than that of the heart → no evident bronchodilation</li> </ul>
Clinical uses	<ul style="list-style-type: none"> <li><b>Drug of choice for severe anaphylaxis in patients taking <math>\beta</math>-blockers.</b> Because adrenaline won't be effective.</li> <li>★ <b>Important Q:</b> How a patient will benefit if he took beta blockers and developed allergic reaction, what will be the role of glucagon? Glucagon works the same way it increases cAMP BUT independent of adrenergic receptors.</li> </ul>

# QUIZ

## MCQ:

1- A 12-year-old boy who is allergic to peanuts was brought to the emergency room after accidentally consuming peanuts contained in fast food. He is in anaphylactic shock. Which of the following drugs would be most appropriate to treat this patient?

- A. Noradrenaline
- B. Phenylephrine
- C. Dobutamine
- D. Adrenaline

2- What is the drug of choice for cardiogenic and septic shock?

- A. Dopamine
- B. Phenylephrine
- C. Dobutamine
- D. Adrenaline

3- A child stung by a bee experiences respiratory distress within minutes and lapses into unconsciousness. This reaction is probably mediated by:

- A. IgE antibody
- B. IgG antibody
- C. Sensitized T cells
- D. Complement
- E. IgM antibody

4- A child disturbs a wasp nest, is stung repeatedly, and goes into shock within minutes, manifesting respiratory failure and vascular collapse. This is MOST likely due to;

- A. Systemic anaphylaxis
- B. Serum sickness
- C. An Arthus reaction
- D. Cytotoxic hypersensitivity

5- Symptoms of anaphylaxis can occur:

- A- Shortly after coming in contact with an allergen
- B- Hours after coming in contact with an allergen
- C- All of above

6- An anaphylactic reaction can be as simple as developing a rash after exposure to an allergen.

- A-True
- B-False



# QUIZ

## SAQ:

1. Why noradrenaline is used to treat shock?

2. A 7-year-old boy with a previous history of bee sting allergy is brought to the emergency department after being stung by 3 bees.

- Which are the probable signs of the anaphylactic reaction to bee stings?
- If this child has signs of anaphylaxis, what is the treatment of choice?

3. A 60-year-old immigrant from Latin America was told she had hypertension and should be taking antihypertensive medication. She decides to take an herbal medication from an online "holistic pharmacy." One week after starting the medication, she is found unconscious in her apartment. In the emergency department, her blood pressure is 60/40 mm Hg and heart rate is 40 bpm. Respirations are 20/min; pupils are slightly constricted. Bowel sounds are present. Which of the following would be the most effective cardiovascular stimulant?

4- The most important intervention for a patient experiencing shock is assessing:

5- What is an additional therapeutic goal of anaphylactic shock?

## MCQs Answers

- D
- A
- A
- A
- C

6. "False. Anaphylaxis typically involves more than one symptom in more than one part of the body at the same time"

## SAQs Answers

- Noradrenaline is used to treat shock, because it increases vascular resistance and, therefore, increases blood pressure. It has no other clinically significant uses.
- a. Bronchospasm, tachycardia, hypotension, laryngeal Edema.  
b. Adrenaline.
- Noradrenaline (Norepinephrine).
- Blood pressure.
- prevent or stop the hypersensitive inflammatory response.



# GOOD LUCK

## Team Leaders:

Nouf Alshammari

Zyad Aldosari

## Team sub-leader:

May Babaeer

## Team Members:

Alwaleed Alsaleh

Bassam Alkuwaiter

Mohaned Makkawi

### Sources:

Team 435