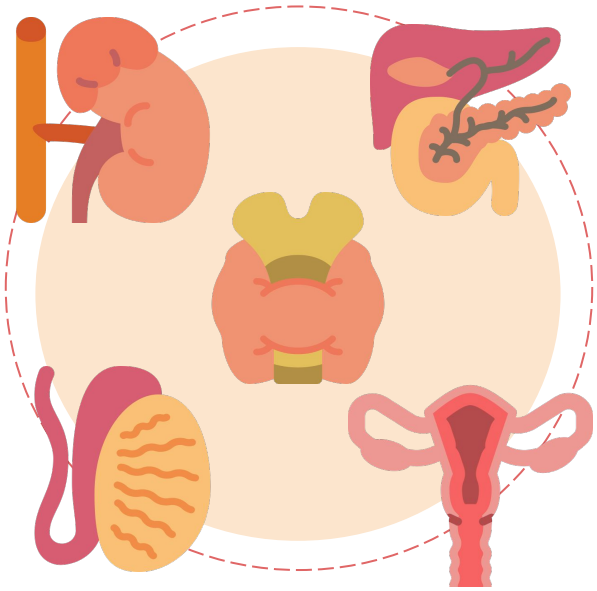

Adrenal medulla

Objectives:

- Summarize the actions of adrenal androgens.
- Describe the causes and major manifestations of hyperadrenocorticism and Hypoadrenocorticism.
- Describe circumstances in which catecholamines are released from the adrenal gland.
- List the major actions of catecholamines.

Revised By
Hadeel Awartani
Abdullah AlOmar

Done by :

➔ Team leader: Rahaf AlShammari, Abdulelah AlDossari
➔ Team members:
- Esraa AlNazzawi, Renad AlMogren
- Abdulmajeed AlWardi, Abdulelah AlSaeed
- Anas AlSaif, Saif AlMeshari
- Laila AlSabbagh, Fatimah Blasharaf
- Renad AlSwailmy, Wejdan AlShamery

Colour index:
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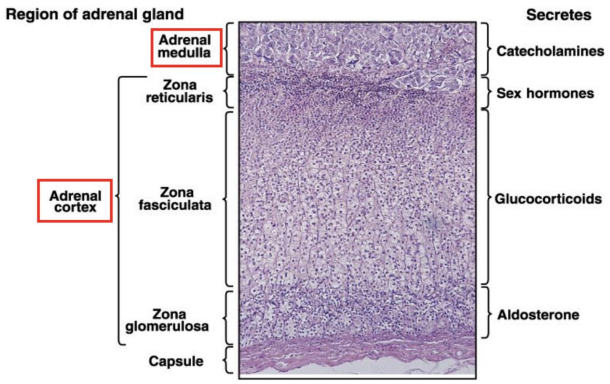
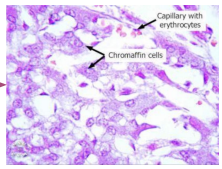
Adrenal medulla



- The adrenal medulla is the inner part or core of each adrenal gland.
- It is considered as part of sympathetic nervous system.
- It synthesizes and secretes catecholamines from Tyrosine:
  - Adrenaline (epinephrine) -- 80% of the secretion.
  - Noradrenaline (norepinephrine) -- 20 % of the secretion.
  - Small amount of dopamine



- They are released from chromaffin cells
- Secretion of these hormones causes:
  Blood to be diverted to the brain, heart, and skeletal muscle.
- Epinephrine is the more potent stimulator of the heart and metabolic activities
- Norepinephrine is more influential on peripheral vasoconstriction and blood pressure
- High levels of cortisol that drain into the medulla from the adrenal cortex induce expression of the enzyme phenylethanolamine N-methyltransferase (PNMT), which converts norepinephrine to epinephrine

Role of the adrenal medullary hormones

1. Enhance the effects of the sympathetic nervous system.

2. Prepare the body for a stressful event.

The response is known as the "fight or flight" response.

Effects of Catecholamines

1. △ Blood glucose level by: **Glycogenolysis** in liver and skeletal muscle (can lead to hyperglycemia)
2. Vasoconstriction of blood vessels
3. Mobilization of free fatty acids
4. △ Heart rate & BP
5. △ Metabolic rate
6. △ O2 consumption

Actions of Adrenal Medullary Hormones

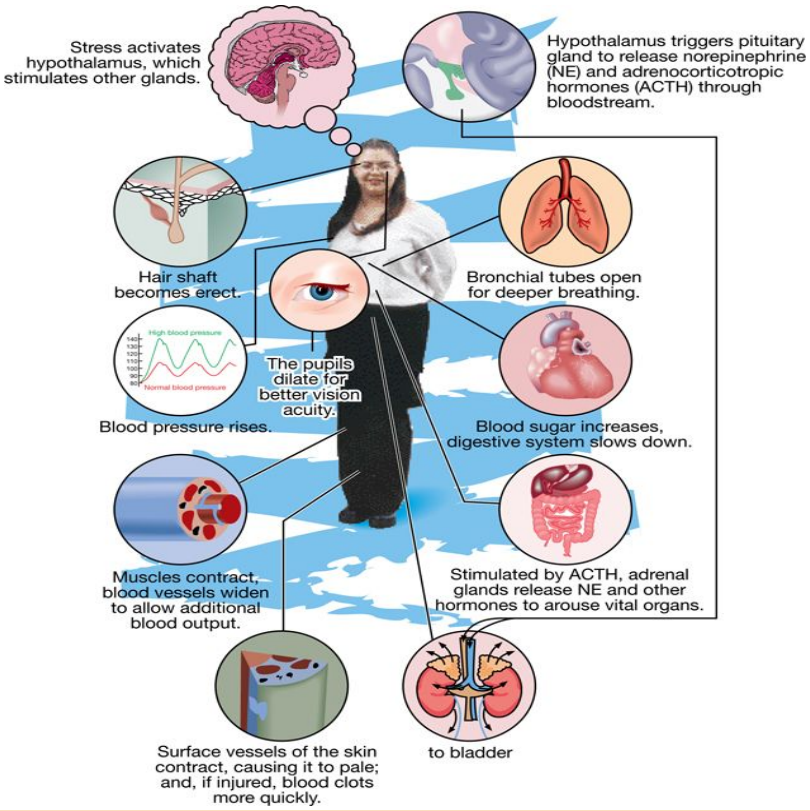
Typical Responses to stimulation of the adrenal medulla

Target		Responses	Receptor
Cardiovascular system			
Heart		↑ Frequency and rate of contraction	-
		↑ Conduction	β
		↑ Blood flow (dilation of coronary arteries) & platelet aggregation	β
		↑ Glycogenolysis	α
Arterioles: 1. Skin 2. Mucosae 3. Skeletal muscle		1. Constriction	α
		2. Constriction	α
	3.	Constriction	α
	3.	**Dilation**	β
Metabolism			
Fat		↑ Lipolysis & brown fat thermogenesis	β
		↑ Blood FFA & Glycerol	β
Liver		↑ Glycogenolysis & gluconeogenesis	β & α_1
		↑ Blood sugar	β & α_1
Muscle		↑ Glycogenolysis	β
		↑ Lactate & pyruvate release	β

Actions of Adrenal Medullary Hormones con.

Typical Responses to stimulation of the adrenal medulla		
Target	Responses	Receptor
Bronchial muscle	Relaxation	β
Stomach and intestines	↓ Motility	β
	↑ Sphincter contraction	α
Urinary bladder	↑ Sphincter contraction	α
Skin	↑ Sweating	α
Eyes	Contraction of radial muscle of the iris (Dilation)	α
Uterus	Contraction	α
pancreas	↓Insulin & ↑glucagon	α
Kidneys	↑ Renin	β

- The effects of the adrenal medullary hormones underlie the role of these hormones in preparation of body for fight or flight.
- The overall effect is to ensure that all requirements for increased muscle activity are available. What are these?

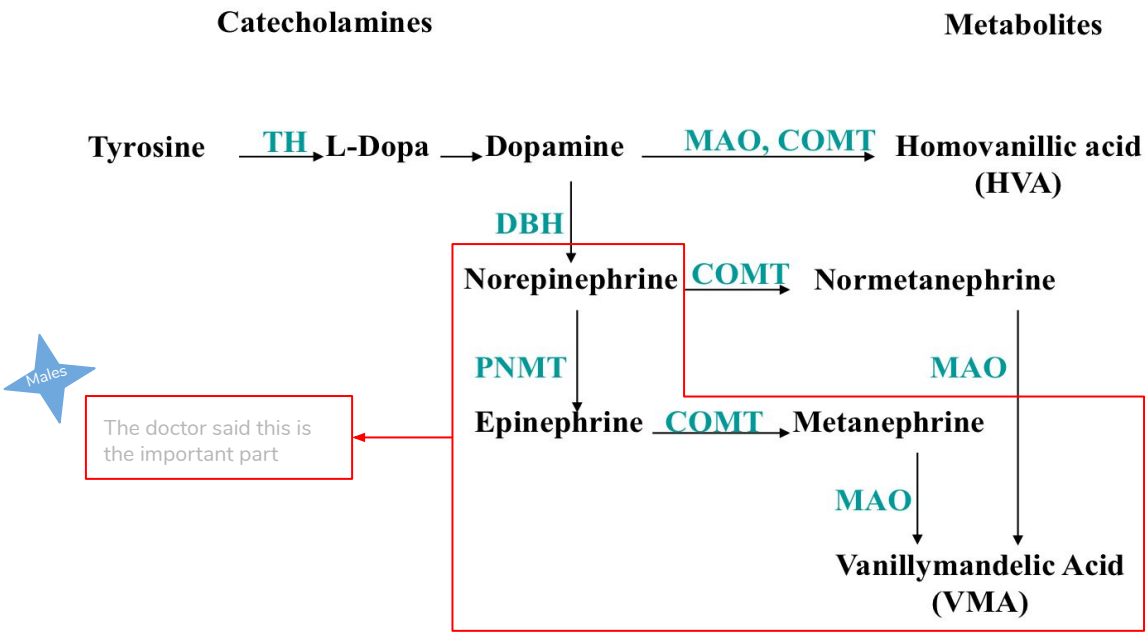


Exercise as an example of Adrenal Medulla activation

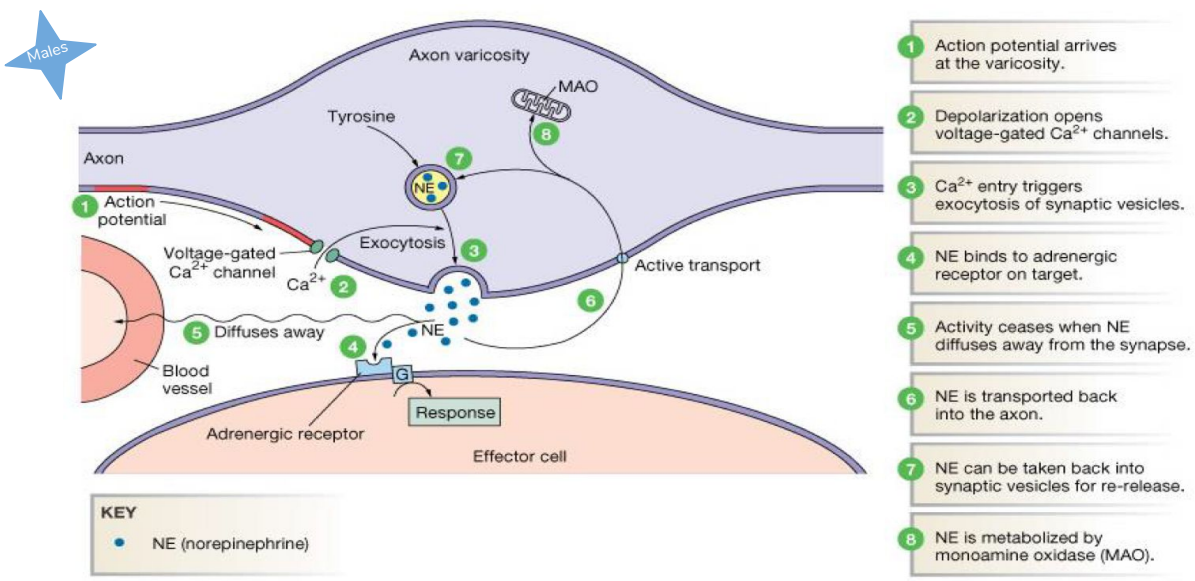
- Exercise is similar to the "fight-or-flight" response but without the subjective element of fear.
- It involves a greater adrenomedullary response (i.e., endocrine role of epinephrine) than a sympathetic nervous response (i.e., neurotransmitter role of norepinephrine).

Metabolism of Catecholamines

Two primary enzymes are involved in the degradation of catecholamines:
1. monoamine oxidase (MAO)
2. catechol-O-methyltransferase(COMT).



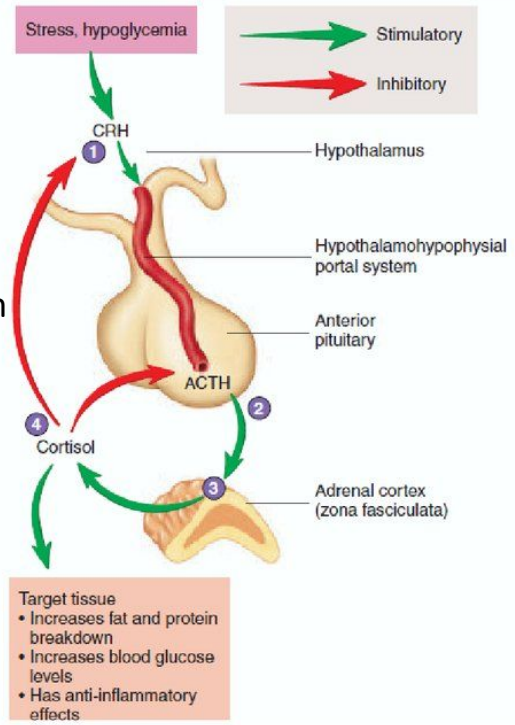
Mechanism: Norepinephrine Release and Recycling



Control of Secretion of Adrenal Medullary Hormones

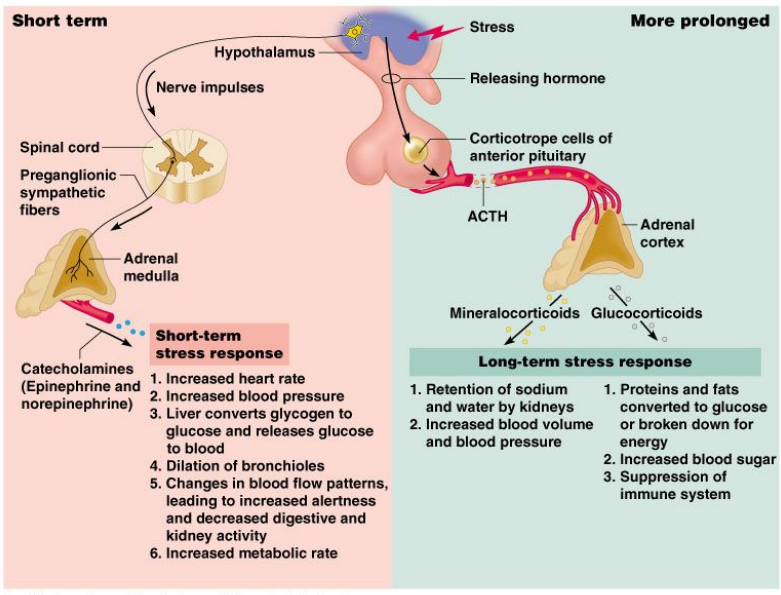
The adrenal medulla is innervated by the sympathetic nervous system.

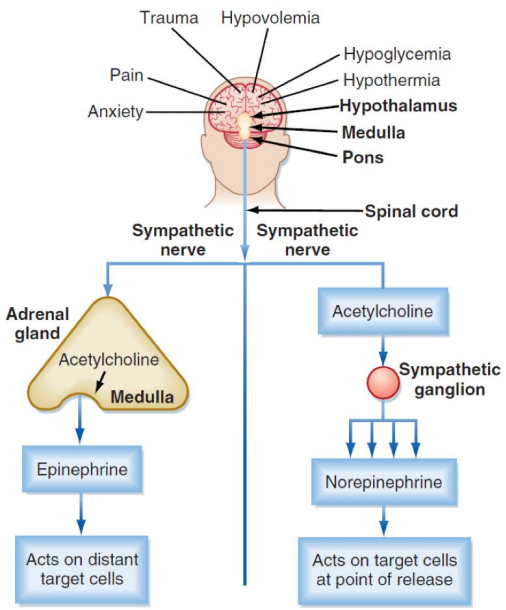
- Adrenal hormones are released from the medulla in response to signals from the cholinergic preganglionic sympathetic nervous system.
- The sympathetic nervous system is activated in response to stress also known as the “fight or flight” response. Stress can be physical (exercise), physiological (hypoglycemia, hemorrhage), or emotional.
- Cortisol when secreted from the adrenal cortex in response to stress, causes release of these hormones from the medulla.
- The adrenal medulla is, functionally, integral part تعتبر جزء لا يتجزأ of the sympathetic system.
  - 80% of its secretion is Epinephrine (EP).
  - 20% of its secretion is Norepinephrine (NE).
- EP in the bloodstream comes solely from the adrenal medulla, on the other hand, NE in blood comes from both adrenal medulla and postganglionic.



This is because postganglionic sympathetic nerves can not synthesize EP from its precursor NE, because they lack the enzyme (PNMT) needed for conversion of NE into EP.

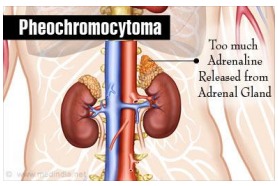
Stress and the Adrenal Gland





Pheochromocytoma

- Pheochromocytoma is a tumor of adrenal medulla.
- It can be life threatening if not recognized & not treated.
- Most often occurs in middle age.

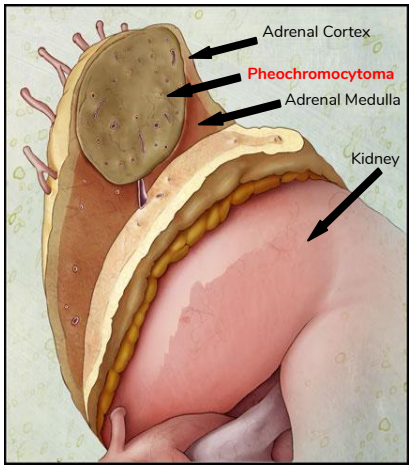


3 most common symptoms

PHEochromocytoma

- **P**alpitations
- **H**eadache
- **E**pisodic sweating (diaphoresis)

- Pheochromocytoma is derived from **chromaffin cells** (arise from neural crest) along the paravertebral sympathetic chain extending from pelvis to base of skull.
- Most tumors secrete epinephrine, NE, and dopamine and can cause episodic hypertension.
- **Urinary vanillylmandelic acid (VMA)** -a breakdown product of norepinephrine- and plasma catecholamines are **elevated**.



- Over 95% are abdominal.
- More than 90% are in the adrenal medulla.
- 80% occur unilaterally.
- About 10% of pheochromocytomas are malignant.

Characteristics

Males

It can occur in combination with other tumors, conditions and in some familial (inherited) syndromes.

-Causes a surgically correctable form of hypertension.

-Associated with neurofibromatosis.

The symptoms occur in Paroxysms or Crisis (episodes): frequent or sporadic, occurring at intervals as long as weeks or months. With time, the paroxysms usually increase in frequency, duration, and severity.

Signs and Symptoms of Pheochromocytoma

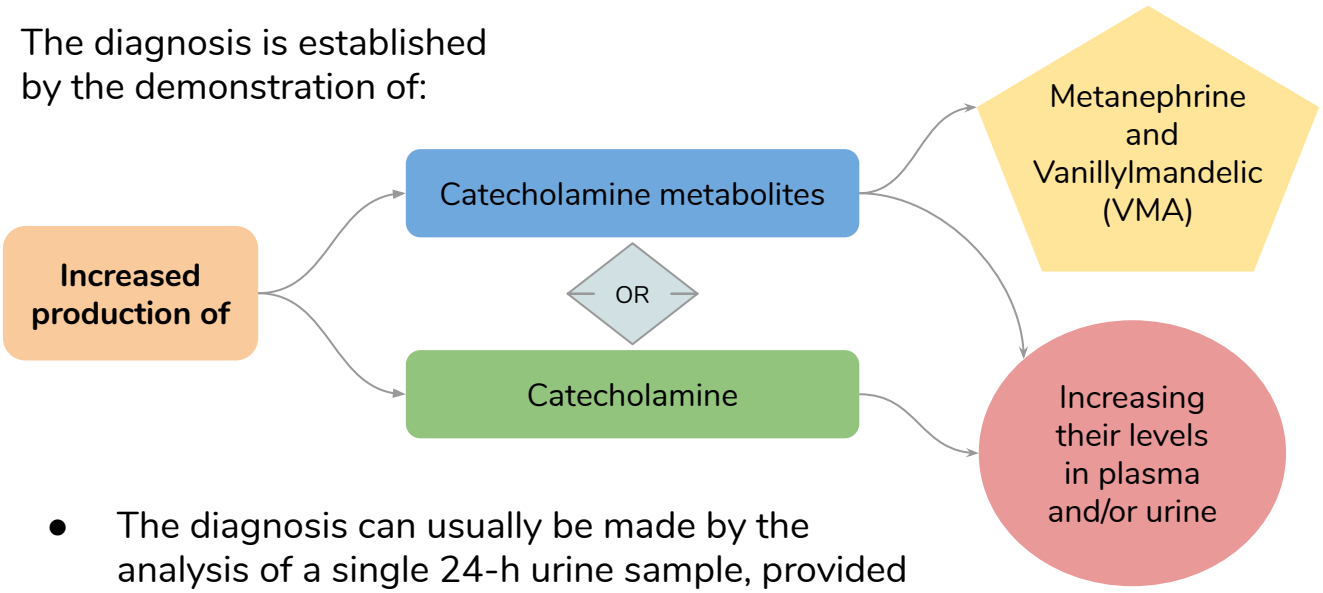
- Resistant **hypertension** (occasionally malignant) (95%)
- **Headache**
- **Sweating** (Perspiration)
- **Palpitations**

Classic Triad

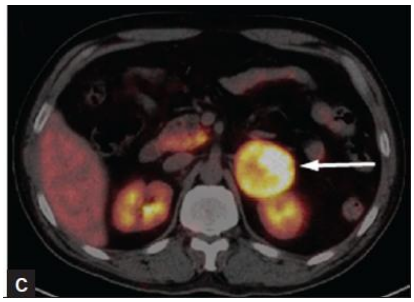
- Chest pain (angina)
- Anxiety
- Glucose intolerance
- Increased metabolic rate
- Ventricular premature contractions
- Sinus tachycardia
- Sinus bradycardia
- Supraventricular arrhythmias
- Pallor

Diagnosis

The diagnosis is established by the demonstration of:



- The diagnosis can usually be made by the analysis of a single 24-h urine sample, provided the patient is hypertensive or symptomatic at the time of collection.
- Imaging: CT, MRI



Treatment

- Laparoscopic Adrenalectomy
- Pre-op:

1. Control of hypertension.
2. α blockers to prevent intraoperative hypertensive crisis due to tumor manipulation and release of catecholamines.
3. Fluid resuscitation(restoration) to prevent circulatory collapse (caused by sudden vasodilation) after removal of the catecholamine secreting tumor.

Summary

Adrenal Medulla is an integral part of sympathetic systems, it secretes:		
1. Epinephrine	2. Norepinephrine	3.Dopamine
- 80% of secretions - Acts on heart and metabolic activity - Comes solely from Adrenal Medulla - Postganglionic sympathetic nerves lack the enzyme (PNMT) required for EP synthesis from NE.	- 20% - Peripheral vasoconstriction and blood pressure - Comes from Adrenal medulla and postganglionic sympathetic nerves	Small amount

Stress and Adrenal Gland		
Short- term stress response	Long_term stress response	
Hypothalamus → nerve impulses → Adrenal **medulla**	Hypothalamus → Hormone release → anterior pituitary → ACTH → Adrenal **cortex**	
↑ heart rate ↑ B.P ↑ alertness ↑ metabolic rate ↓ digestive and kidney activity Bronchioles dilation and conversion of glycogen to glucose	Mineralocorticoids	Glucocorticoids
	1. Water & Na retention 2. ↑ blood volume and pressure	1. ↑ blood sugar 2. Conversion of fat and proteins to glucose 3. Immune suppression

MCQs

1.Cells of the adrenal medulla receive synaptic input from which of the following types of neurons?
A) Preganglionic sympathetic neurons
B) Postganglionic sympathetic neurons
C) Preganglionic parasympathetic neurons
D) Postsynaptic parasympathetic neurons

2.After extensive testing, a 60-year-old man is found to have a pheochromocytoma that secretes mainly epinephrine. Which of the following signs would be expected in this patient?
A) Decreased heart rate
B) Decreased arterial blood pressure
C) Decreased excretion rate of 3-methoxy-4-hydroxymandelic acid (VMA)
D) Cold, clammy skin

3.Which autonomic receptor mediates an increase in heart rate?
A) Adrenergic α receptors
B) Adrenergic β1 receptors
C) Adrenergic β2 receptors
D) Cholinergic muscarinic receptors

4.Which autonomic receptor mediates secretion of epinephrine by the adrenal medulla?
A) Adrenergic α receptors
B) Adrenergic β1 receptors
C) Cholinergic muscarinic receptors
D) Cholinergic nicotinic receptors

5.Which autonomic receptor is activated by low concentrations of epinephrine released from the adrenal medulla and causes vasodilation?
A) Adrenergic α receptors
B) Adrenergic β1 receptors
C) Adrenergic β2 receptors
D) Cholinergic muscarinic receptors

6.Which catecholamine has higher affinity for alpha receptor ?
A) Epinephrine
B) Norepinephrine
C) Ach
D) Serotonin

SAQ

What is the role of adrenal medulla hormones?

1. Enhance the effect of the sympathetic nervous system.
2. Prepare the body for a stressful event.

Answers
1. A
2. D
3. B
4. D
5. C
6. B