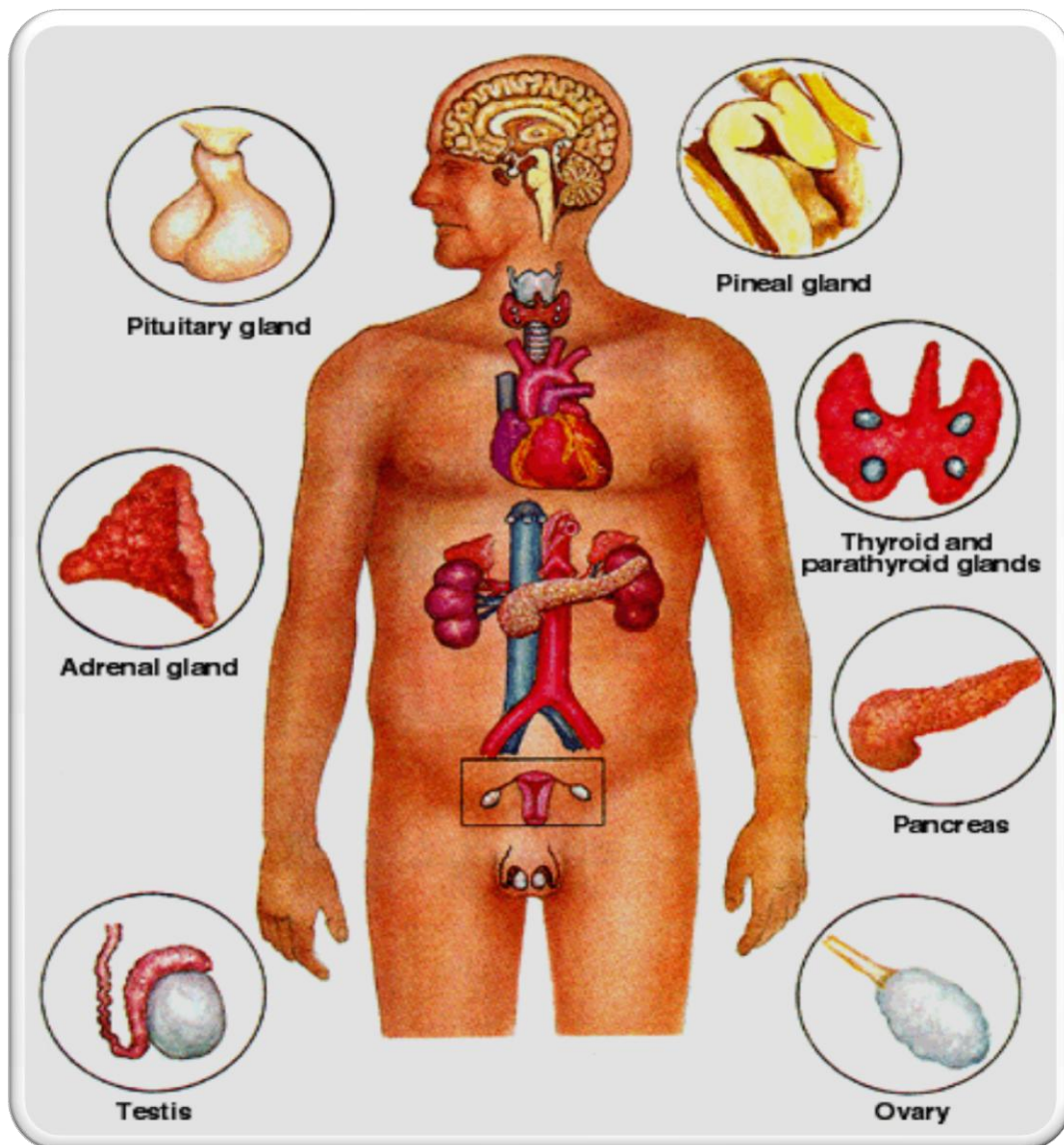


ENDOCRINE BLOCK
PHYSIOLOGY TEAM 431



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Physiology of Adrenal Medulla

The adrenal medulla is a modified sympathetic ganglion in which the postganglionic neurons have lost their axons and become secretory cells (chromaffin cells). The cells secrete when stimulated by the preganglionic nerve fibers (secreting Ach) that reach the gland via the splanchnic nerves.



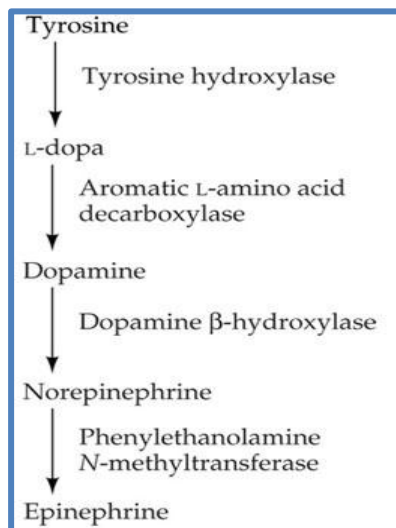
Hormones of the Adrenal Medulla

- Adrenaline (epinephrine)
- Noradrenaline (norepinephrine)
 - *Norepinephrine (Noradrenaline) is metabolized into normetanephrine and Vanillyl mandelic acid (VMA) .
 - *High urine VMA is one of the diagnostic tests for Pheochromocytoma.
- As well as little amount of dopamine (dopamine is cardiotoxic meaning it increases the heart contractility)

80% of released catecholamines are epinephrine (only source of epinephrine in the circulation)

Hormones are secreted and stored in the adrenal medulla and released in response to appropriate stimuli

Biosynthesis of catecholamines



(Remember that catecholamines are derivatives of amino acid tyrosine just like thyroid hormones, however catecholamines behave like peptide hormones while thyroid hormones behave like steroids hormones)(So you have to revise the differences between steroids hormones and peptide hormones, for examples in their receptors and so on)

Receptor	α	β
Norepinephrine	+++++	++
Epinephrine	++++	++++

Mechanism of Action of catecholamines

Receptor mediated: **adrenergic receptors**

Peripheral effects are **dependent upon the type and ratio of receptors in target tissues**

(Norepinephrine has high affinity for the alpha receptors that's why it will mainly induce vasoconstriction, epinephrine has equal affinity for the alpha and beta receptors, so it is more acting on the heart than NE)

Differences between Epinephrine and Norepinephrine

1. **Epinephrine** >> norepinephrine – in terms of **cardiac stimulation leading to greater cardiac output (Beta stimulation)**
2. **Epinephrine** < norepinephrine – in terms of **constriction of blood vessels – leading to increased peripheral resistance – increased arterial pressure.**
3. **Epinephrine** >> norepinephrine –in terms of **increasing metabolism**, Epinephrine = 5-10 x Norepinephrine = 100% normal (Epinephrine has 5 to 10 times as great a metabolic effect as norepinephrine)

Effects of Epinephrine

In general Catecholamines are secreted mainly in emergency conditions to prepare the body for the "fight or- flight" responses, and have almost the same effects throughout the body as direct sympathetic stimulation.

1. **Metabolism**
 - **Stimulation of glycogenolysis** in liver and skeletal muscle so can lead to **hyperglycemia**
(One of the strong stimuli for catecholamines secretion is acute hypoglycemia)
 - **Mobilization of free fatty acids (FFA)** (from adipose tissue)also this cause elevated blood sugar
 - **Increase the metabolic rate and O2 consumption** (leading to increase heat production and increase sweating)
2. **Cardiovascular**
 - **Increase both heart rate and force of contraction**
 - **increase blood pressure**
3. **Respiration**
 - **Increase Oxygen consumption & respiratory rate**

In general, to remember the action of catecholamines think of someone doing exercise

Pheochromocytoma (90% is benign)

- A catecholamine-secreting tumor of **chromaffin cells**, almost 90% is in the adrenal medulla

Adrenal Pheochromocytoma (90%)

- **Paraganglioma** - a catecholamine secreting tumor of the sympathetic paraganglia

Extra-Adrenal Pheochromocytoma

Signs and Symptoms of Pheochromocytoma

- **Resistant Hypertension (95%)**
- **Headache**
- **Sweating**
- Palpitations
- Chest Pain
- Anxiety
- Glucose Intolerance
- Increased Metabolic Rate

Note the ones in red are the classic triad

You could think of the signs and symptoms systematic wise:

- On CNS: headache, anxiety, insomnia, panic attacks, tremors and hyperreflexia
- On CVS: uncontrolled hypertension, palpitations also as a complication the patient could undergo hypertrophy of the heart and can suffer from ischemic heart attack
- Metabolic effects: hyperglycemia, increase O₂ consumption, increase heat and sweating

How will the patient present in the ER?

He/she would have one of these complications: acute ischemic heart disease, uncontrolled hypertensive crisis, stroke or palpitations (ventricular tachycardia)

Diagnosis and Treatment

- Diagnosed by **high plasma catecholamines and increased metabolites [VMA] in urine**

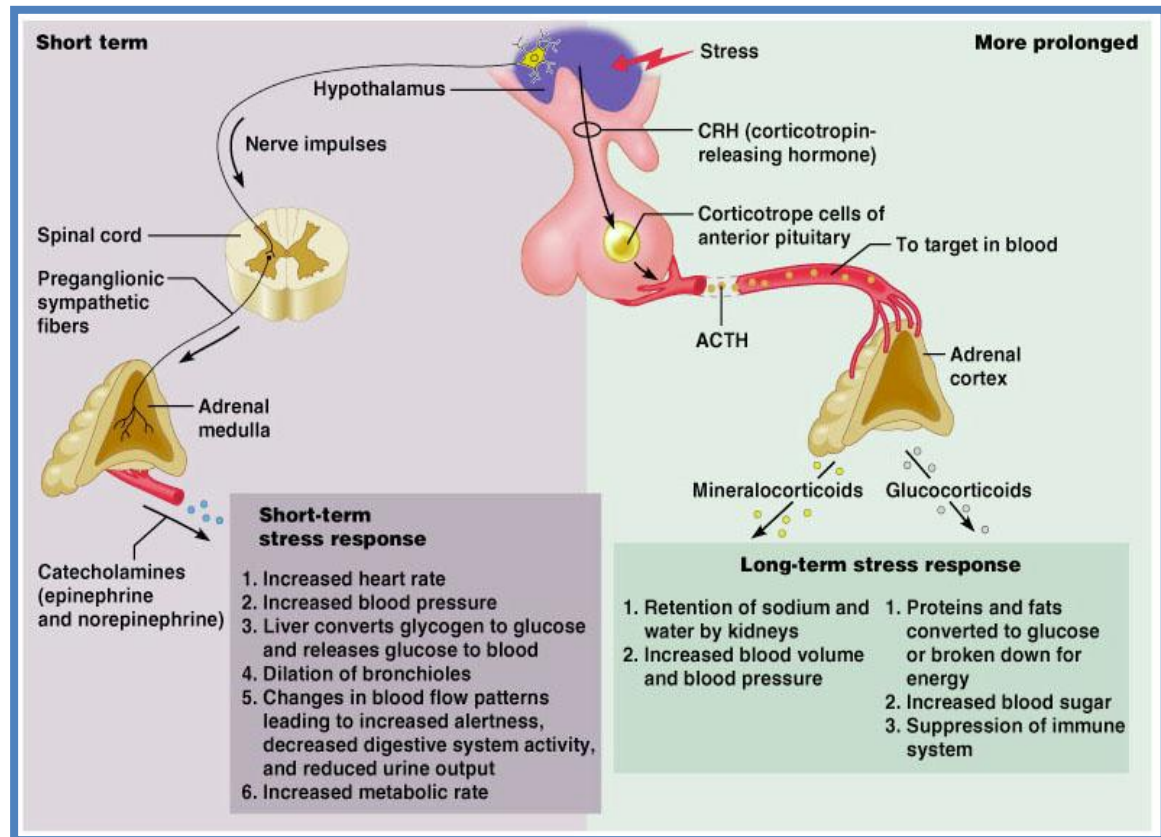
VMA Urine Test: This test measures the amount of vanillylmandelic acid (VMA) that is excreted into the urine, typically over a 24-hour period. VMA is one of the metabolites of the catecholamines epinephrine (adrenaline) and norepinephrine.

- **Treatment is surgical resection**

(Surgical resection of the tumor is the treatment of choice and usually results in cure of the hypertension)

This is extra info: but think of it as a way to revise what you have learned so far

This illustration is demonstrating how the adrenal gland copes with stress



Summary

*Adrenal medulla is the inner part of adrenal gland and comprises about 20% of the adrenal gland.

*It is not essential to life if the animal is kept under sheltered conditions without any external stress (but is real life devoid of any stress ?)

*The adrenal medulla is actually a ganglion of the sympathetic nervous system , since its origin is the embryonic neural crest (i.e. its cells are actually neurons)

*It is made of Chromaffin cells that secrete catecholamines (Epinephrine, NE, and to a lesser extent dopamine)

*NE & Epinephrine Effects are those of the sympathetic nervous system (on the pupil, CVS, CNS, GIT, Skin, bronchioles, liver, skeletal muscle).

*Pheochromocytoma is a tumor that arises from Chromaffin cells in the adrenal medulla.

*Symptoms of Pheochromocytoma are an exacerbation of catecholamines effects.

Questions

1/What is the diagnostic metabolite for detecting Pheochromocytoma?

1-normetanephrine

2- Vanillyl mandelic acid (VMA)

3-Dopamine

2/ A-Why do we consider the adrenal medulla as a sympathetic ganglion

B- and why is an endocrine gland?

A- Because it developed from the neural crest and because they represent the post ganglionic fibers of sympathetic system

B- It is an endocrine organ because it releases its hormones into the circulation to reach the target.

3/ How do catecholamines increase blood sugar?

Due primarily to catecholamine stimulation of lipolysis (breakdown of stored fat) leading to high levels of free fatty acids and the subsequent inhibition of glucose uptake by muscle cells. Further more , stimulation of beta-adrenergic receptors leads to glycogenolysis and gluconeogenesis and thus elevation of blood glucose levels).