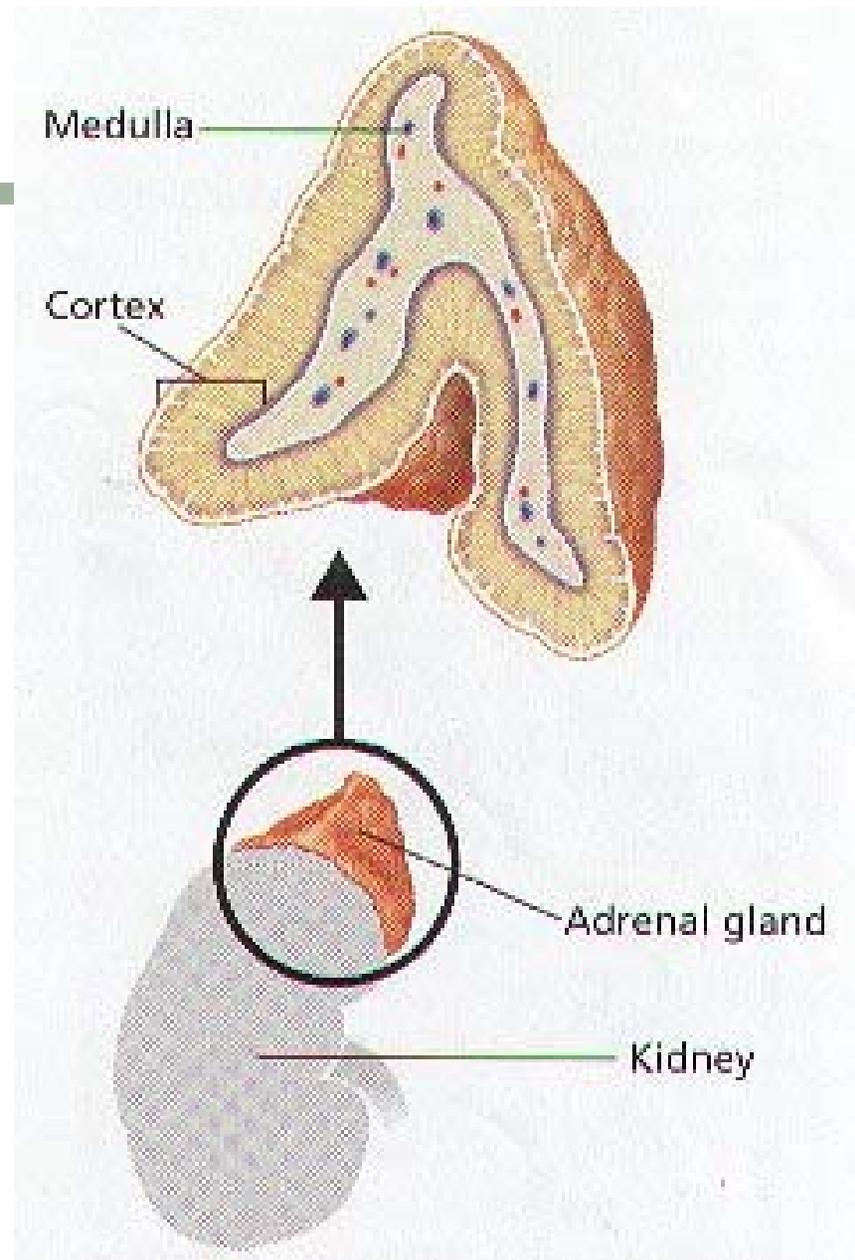




Adrenal Medulla

Amelyn R. Rafael, M.D.



Adrenal Medulla

- Exodermal in origin
- Cells derived from the sympathogonia of the primitive neuroectoderm
- A sympathetic ganglion in which the post-ganglionic cells have lost their axons and have become specialized for secretion of their products directly into the blood stream

[Active principles]

- Catecholamines:
 - Epinephrine (Adrenaline)
 - Norepinephrine (noradrenaline)
 - Dopamine
- Secreted by chromaffin cells in response to nervous stimulation

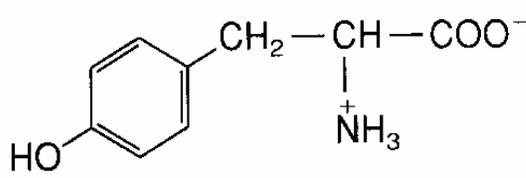
[Neural Stimuli]

- Pain
- Cold
- Volume receptors in the circulatory system stimulated
- Emotional states

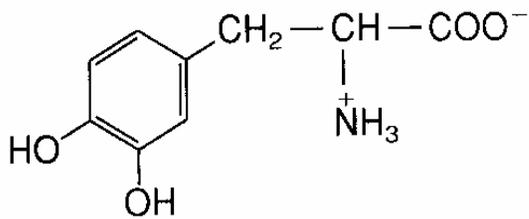
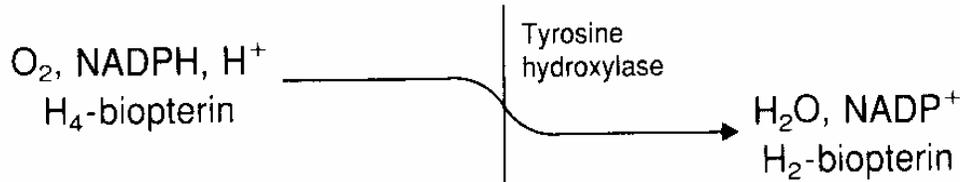
[Humoral or Chemical stimuli]

- Oxygen lack
- Insulin hypoglycemia
- Poisons
- Drugs: nicotine, acetylcholine

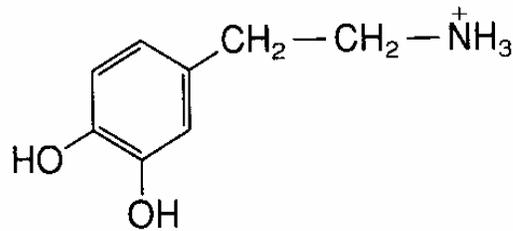
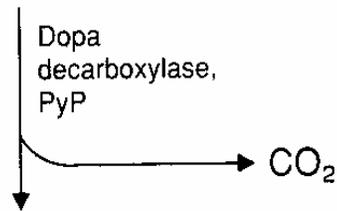
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- A large left square bracket is on the left side, and a large right square bracket is on the right side. A horizontal line with a light green gradient runs across the top of the slide, positioned between the two brackets.
- → CNS → hypothalamus stimulated
 - → sends impulse to the spinal cord through the splanchnic nerves which synapse in the pre-aortic ganglia and continue to
 - → adrenal medulla causing the release of Ach at the nerve endings
 - → Ach stimulate the chromaffin cells to secrete NE & E



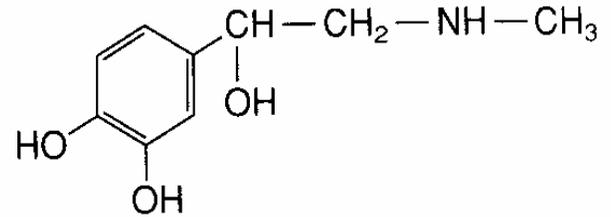
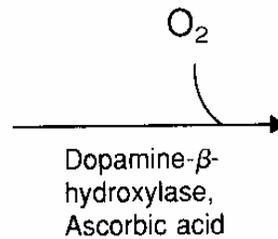
Tyrosine



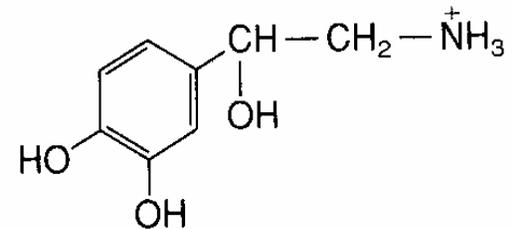
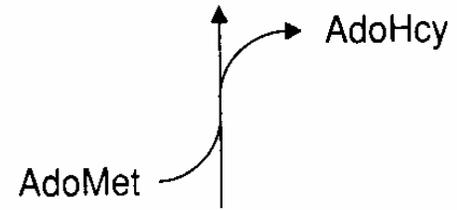
Dopa



Dopamine



Epinephrine



Norepinephrine

Biosynthesis of Catecholamines

- The enzyme responsible for the conversion of NE to E is found in high concentration only in the AM
- 2 – 4 mg/gm of tissue: average combined NE-E content of the normal human adrenal medulla in the adult
- 30% is NE
- In the extra-medullary catecholamine-secreting tissue most of the catecholamine is NE

Metabolism of Catecholamines

- Liver
- Breakdown:
 - Orthomethylation (80%)
 - Oxidation deamination (20%)
 - Catechol-o-methyl transferase (COMT)
 - Mono-amine oxidase
- Urine: metanephrine, normetanephrine, and VMA

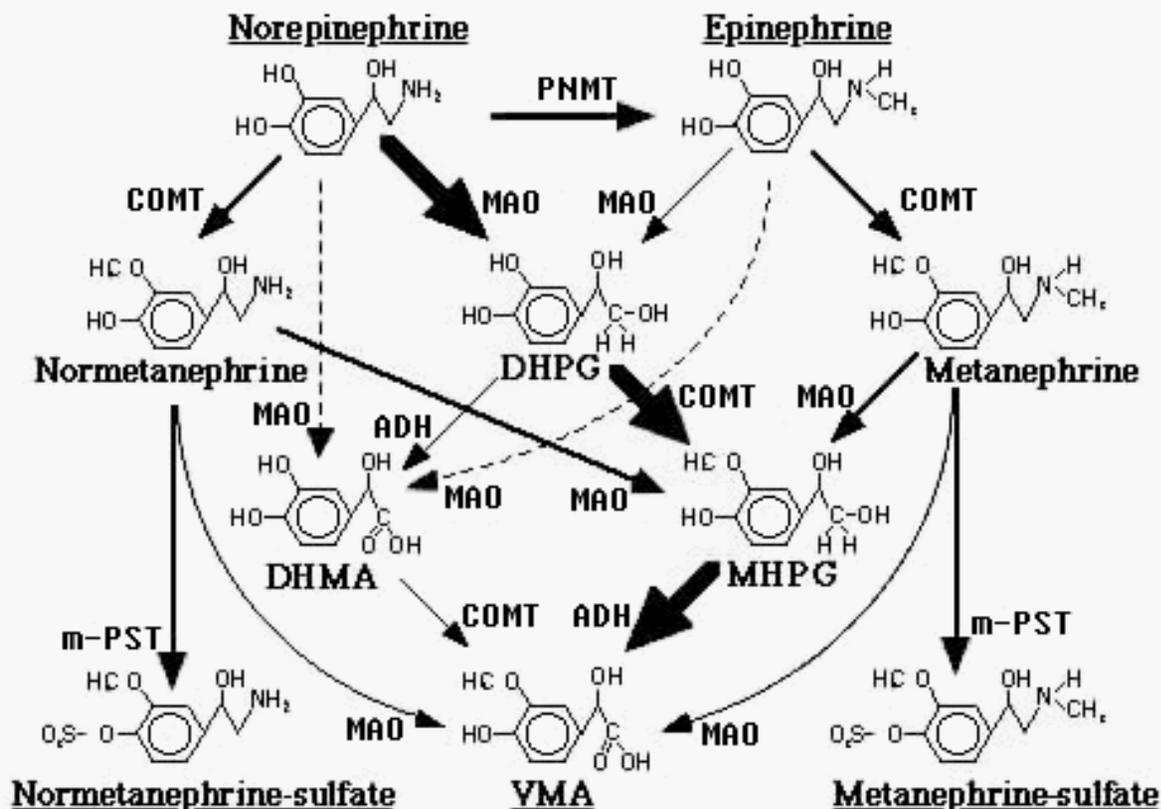


Figure 1. Pathways of metabolism of norepinephrine and epinephrine.

Enzymes responsible for each pathway are shown at the head of arrows. The more solid arrows indicate the more major pathways of metabolism, while the dotted arrows indicate pathways of negligible importance. Compounds that are routinely measured in urine or plasma for diagnosis of pheochromocytoma are underlined. Note that free normetanephrines and metanephrine are distinct metabolites from normetanephrine-sulfate and metanephrine-sulfate. The pathways of sulfate conjugation for other compounds are not shown.

Abbreviations:

PNMT, phenylethanolamine-N-methyltransferase
 MAO, monoamine oxidase
 COMT, catechol-O-methyltransferase
 ADH, alcohol dehydrogenase
 m-PST, phenolsulfotransferase

DHPG, 3, 4-dihydroxyphenylglycol
 DHMA, 3, 4-dihydroxymandelic acid
 MHPG, 3-methoxy-4-hydroxyphenylglycol
 VMA, vanillylmandelic acid

Effects of the Catecholamines

- Circulatory system:
 - Effect on the resistance blood vessels:
 - E: constrict the resistance vessels of the skin and the kidneys
 - No direct effect on the resistance vessels of the coronary and the cerebral vascular beds
 - It increases coronary blood flow by causing an increase metabolism in the stimulated heart muscle

Effect on resistance blood vessels

- Epinephrine: has a dual action on the resistance vessels of the skeletal muscle and the mesenteric vascular beds (dose dependent):
 - Small or moderate doses – dilation
 - Large doses - constriction

Effect on resistance blood vessels

- Norepinephrine: constricts the resistance vessels of the skin, renal mesenteric and skeletal muscle vascular beds
 - Has no direct effect on the resistance vessels of the coronary and cerebral vascular beds
 - It exerts only a constrictor effect on the resistance vessels of the skeletal muscle and mesenteric vascular beds
 - Exerts overall VC → increase TPR

Effect on the capacitance vessels

- Epinephrine in physiological concentrations has no consistent effect on the capacitance vessels in the skeletal muscle vascular bed.

Effects on the heart

- Epinephrine: produces an increase in rate and in the force of cardiac constriction
 - Also enhances conduction in the bundle of His and increases cardiac muscle excitability leading to ectopic ventricular beat
- NE has very weak direct effects on the myocardium

Respiratory System

- E and NE infusions 10 – 20 ug/min increases depth and rate of breathing
 - Direct effect of epinephrine on the respiratory center
 - Epinephrine: relaxes the bronchiolar smooth muscle, causes shrinkage of the mucosa, and reduces the secretion of mucus by the mucosal cells
 - NE: less potent bronchodilator agent

Actions on other smooth muscles

- GIT: E decreases GI tone and motility; produces contraction of the pyloric and ileocolic sphincters
- UB: E relaxes the detrussor and contracts the trigone and sphincter of the bladder

Actions on other smooth muscles

- Uterus:

- In vivo, epinephrine inhibits the human uterus in late pregnancy and during labor and puerperium. NE stimulates contraction.
- In vitro, both amines stimulate contractions of the isolated human myometrium at any stage of its development.

Actions on the skeletal muscle

- The muscles work to better advantage owing to their improved BS
- Adrenaline increases the force of contraction both of normal and fatigued muscle in response to stimulation of its motor nerve

Metabolic Actions

■ Blood Sugar:

- Epinephrine raises the BS, sometimes to levels high enough to produce glycosuria.
- The hyperglycemia is due to accelerated breakdown of glycogen in liver and muscle.
- NE is only about 1/5 as potent as E in this respect

Metabolic Actions

- Blood Lactate:

- The blood lactate is increased as a result of rapid muscle glycogenolysis.
- The lactate is carried to the liver where it is converted to glycogen, and to the heart where it is utilized as a source of energy for contraction.

Metabolic Actions

- Blood Fatty Acids:
 - The FFA level in the blood rises immediately following E and NE administration.

Calorigenic Actions

- The usual therapeutic dose of epinephrine increases total oxygen consumption by up to 30%.
 - Stimulation of cellular oxidations throughout the tissues of the body generally
 - Increase utilization of CHO and FFA
 - Contributing factors:
 - Cutaneous VC → diminished heat loss
 - Increased muscular tone

[Blood]

- Epinephrine shortens the coagulation time
 - Subcutaneous injection (0.8 mg) increases the RBC, Hct value, Hgb concentration, and plasma protein concentration
 - Attributed to hemoconcentration due to movement of fluid out of the blood

[Skin]

- Epinephrine and NE produce pallor due to capillary constriction and erection of hair or goose flesh due to contraction of erector pili muscles

[CNS

]

- Stimulant or depressant actions

Pheochromocytoma

- Benign chromaffin tissue tumors which occur in:
 - The adrenal gland itself (90%)
 - The course of the aorta along the sympathetic chain
 - The spleen, ovaries, and testes (occasionally)
 - The organ of Zuckerkandl, at the bifurcation of the aorta

Adrenal pheochromocytoma

- Flesh-colored, hemorrhagic breakdown at the site of tumor
- Affect both adrenals (10%)
- Low incidence

Clinical Manifestation

- Intermittent (paroxysmal) hypertension
- Sustained (chronic) hypertension
- Paroxysm
 - Headache, severe palpitations, sweating, nausea and vomiting, increased depth and rate of breathing, anxiety, weakness, dizziness, and substernal pain

[Diagnosis]

- Urinary assay of catecholamines and their methoxy derivatives
- The upper limits of normal are:
 - Free catecholamines (NE and E) = 100ug
 - Metanephrine + normetanephrine = 1.3mg
 - VMA = 6.5 mg



Thank You.....

.....for listening!