

بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ





BENHA UNIVERSITY

FACULTY OF MEDICINE

1st Year Medical Students



Chemical transmission in autonomic nervous system (Noradrenaline)

BY

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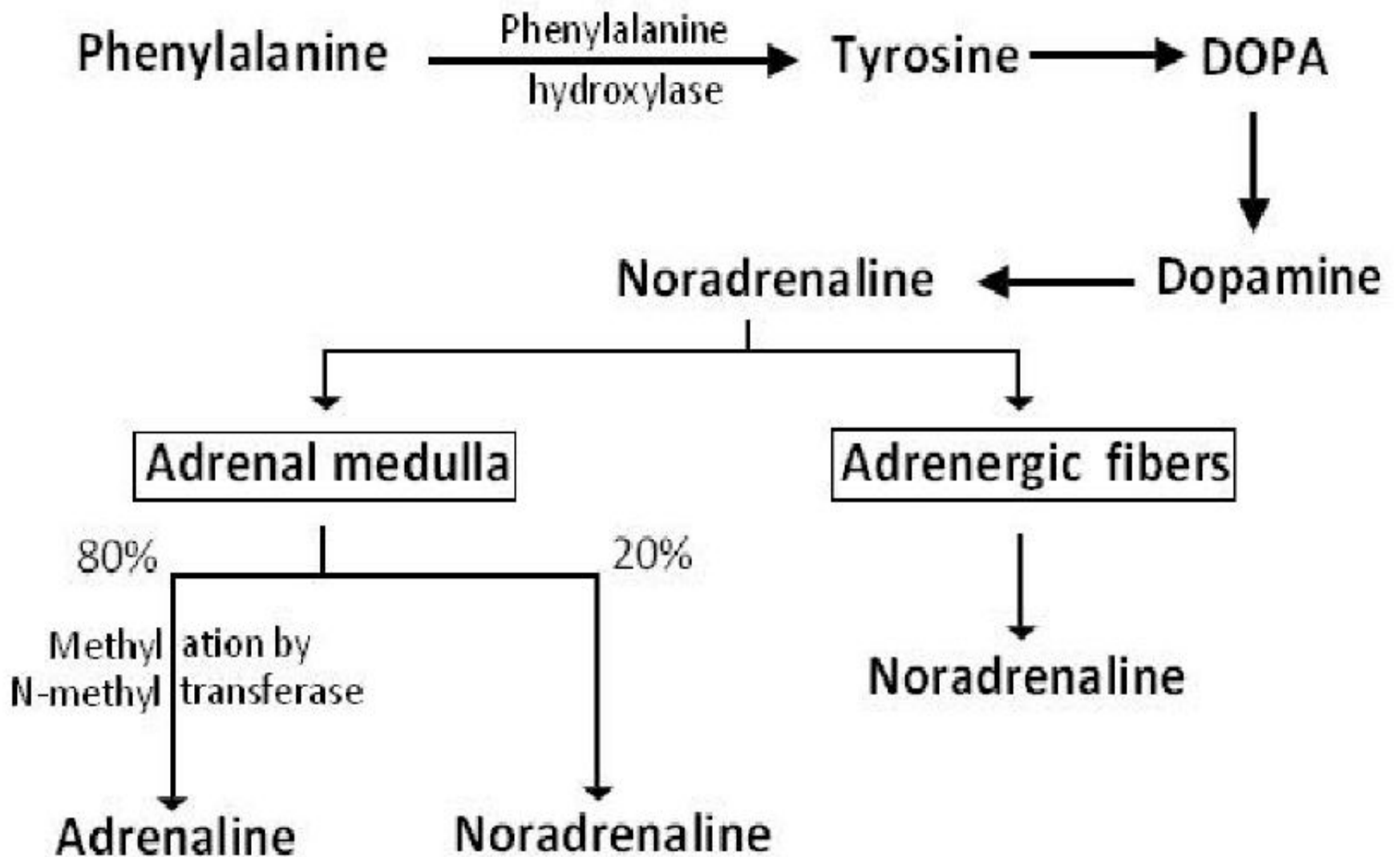
II- Noradrenaline (Norepinephrine; N.A)



★ Formation (Synthesis):

- ❖ Phenylalanine Hydroxylation Tyrosine.
- ❖ Tyrosine Hydroxylation Dihydroxy phenylalanine (DOPA).
- ❖ DOPA Decarboxylation Dopamine.
- ❖ Dopamine Hydroxylation Noradrenaline.
- ❖ Noradrenaline Methylation (N-methyltransferase) Adrenaline.





N.B.:

❖ Noradrenaline (Norepinephrine) is formed from phenylalanine (amino acid) in adrenergic nerve endings.

❖ Adrenaline (Epinephrine) is formed only in adrenal medulla (not at adrenergic nerve endings) due to absence of N-methyltransferase in adrenergic nerve endings.



★ Storage:

It is stored in dark vesicles in the adrenergic nerve terminal.

★ Release:

It is released by exocytosis in presence of Ca^{++} .



★ Sites of formation and release:

- ❖ All postganglionic sympathetic fibers except postganglionic sympathetic fibers to sweat glands and skeletal muscles' blood vessels.
- ❖ Adrenal medulla secretes 80% adrenaline and 20% noradrenaline.
- ❖ Neurotransmitter in CNS.



★ Removal of noradrenaline:

- ❖ Mainly (50 - 80%) by active reuptake by nerve terminal.
- ❖ Small amounts are removed by diffusion into surrounding tissues.

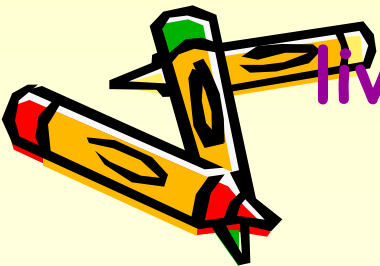




❖ Small amounts are removed by enzymatic destruction into inactive products either by:

- **Oxidation:** By monoamine oxidase (MAO) enzyme present in mitochondria of nerve endings.

- **Methylation:** By catechol-O-methyltransferase (COMT) enzyme present in liver and kidney.



★ Adrenergic receptors:

They are classified according to their site into:

	Presynaptic Receptors	Postsynaptic Receptors
Site	Postganglionic nerve endings.	Effector organ
Types	Alpha (α) & Beta (β)	Alpha (α) & Beta (β)
Action	They control release of noradrenaline from nerve endings. Similar to α_2 postsynaptic receptors ($\downarrow\downarrow$ cAMP).	

★ Postsynaptic drenergic receptors:



	Alpha (α) Receptors	Beta (β) Receptors
Types and functions	<p><u>α_1 (Excitatory):</u></p> <ul style="list-style-type: none">● Contraction of dilator pupillae muscle.● Contraction of pilo-erector muscle.● Contraction of splenic capsule.● Vasoconstriction.● Contraction of GIT & urinary sphincters.● Ejaculation. <p><u>α_2 (Inhibitory):</u></p> <ul style="list-style-type: none">● Relaxation of GIT and urinary walls.	<p><u>β_1 (Excitatory):</u></p> <ul style="list-style-type: none">● \uparrow heart rate.● \uparrow cardiac contractility. <p><u>β_2 (Inhibitory):</u></p> <ul style="list-style-type: none">● Vasodilatation.● Bronchodilatation.● Relaxation of GIT and urinary walls.● Uterine relaxation.● Glycogenolysis.● Lipolysis.

	Alpha (α) Receptors	Beta (β) Receptors
Mechanism of action	<p><u>$\alpha 1$</u>: \uparrow Intracellular Ca^{++}</p> <p><u>$\alpha 2$</u>: Inhibit adenylyl cyclase enzyme $\rightarrow \downarrow$ cAMP</p>	<p><u>$\beta 1$ & $\beta 2$</u>: Stimulate adenylyl cyclase enzyme \rightarrow \uparrow cAMP</p>
Relative sensitivity	<p>More sensitive to <u>noradrenaline</u> than adrenaline</p>	<p>Equally sensitive to <u>noradrenaline</u> and <u>adrenaline</u></p>



* Drugs acting on adrenergic receptors:



Site of action	Stimulant drugs (Sympathomimetics)	Inhibitor drugs (Sympatholytics)
Sympathetic ganglia	<ul style="list-style-type: none"> ● Nicotine small dose. ● Anticholine esterases. 	<ul style="list-style-type: none"> ● Nicotine large dose. ● Hexamehonium.
Release of noradrenaline from postsynaptic fibers	<p style="text-align: center;"><u>↑ release:</u></p> <ul style="list-style-type: none"> ● Ephedrine. ● Amphetamine. 	<p style="text-align: center;"><u>↓ release:</u></p> <ul style="list-style-type: none"> ● Reserpine. ● α-methyl dopa.
Alpha (α) receptors	<p style="text-align: center;"><u>α stimulant:</u></p> <ul style="list-style-type: none"> ● Noradrenaline. ● Adrenaline. ● Phenylephrine. 	<p style="text-align: center;"><u>α blockers:</u></p> <ul style="list-style-type: none"> ● Phentolamine. ● Ergot alkaloids.
Beta (β) receptors	<p style="text-align: center;"><u>β stimulant:</u></p> <ul style="list-style-type: none"> ● Adrenaline. ● Isoprenaline. 	<p style="text-align: center;"><u>β blocker:</u></p> <ul style="list-style-type: none"> ● Propranolol.



Adrenal medulla



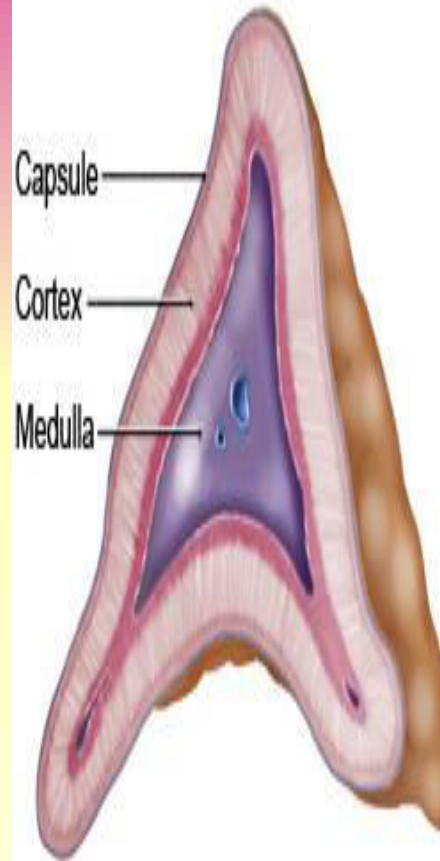
★ Site: The adrenal (suprarenal) gland is present above the kidney. It is divided into 2 parts;

- ❖ Adrenal cortex.
- ❖ Adrenal medulla.

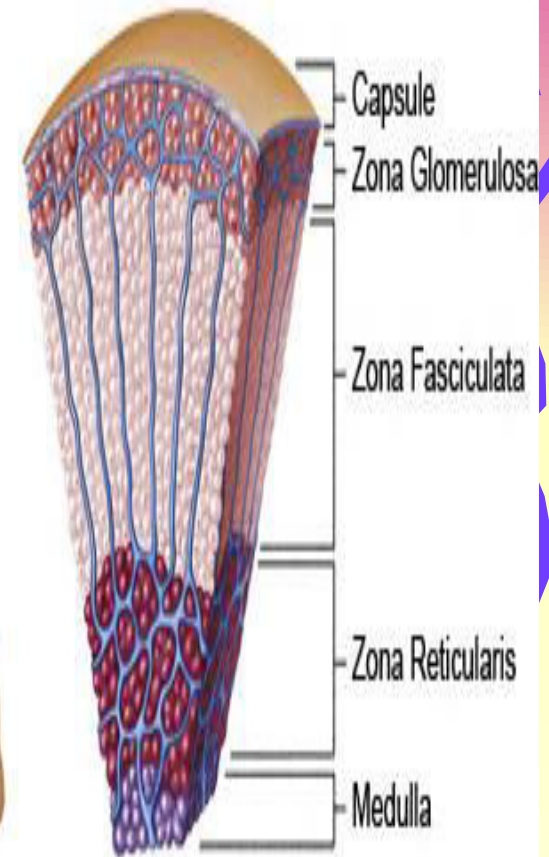




Transverse Section



Microscopic Section




✱ N.B: Adrenal medulla is considered as modified sympathetic ganglia.

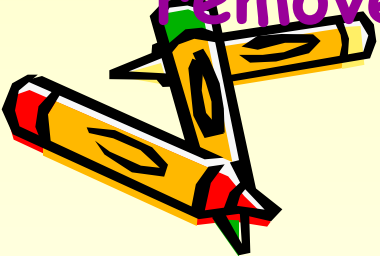
❖ It is supplied by preganglionic fiber from greater splanchnic nerve.

❖ The postganglionic neuron lose its axon and the cell bodies are modified into secretory cells.





★ Secretion: Adrenal medulla secretes 80% adrenaline (epinephrine) and 20% noradrenaline (norepinephrine). They have the same effects as sympathetic stimulation however, the secreted noradrenaline has prolonged effect (10 times as noradrenaline released from adrenergic nerve endings) as it is slowly removed from the blood.



★ Differences between adrenaline and noradrenaline:



	Noradrenaline (NA)	Adrenaline
Source	<ul style="list-style-type: none">● Adrenal medulla (20%).● Adrenergic nerve endings.	<ul style="list-style-type: none">● Adrenal medulla (80%).
Chemistry	Adrenaline - methyl group.	Noradrenaline + methyl group.
Sensitivity on receptor	Mainly α receptor.	Equal sensitivity on α and β receptor.
Action	<ul style="list-style-type: none">● More V.C.● Less stimulant effect on heart.● Less bronchodilatation.● Less metabolic effect.	<ul style="list-style-type: none">● Less V.C.● More stimulant effect on heart.● More bronchodilatation.● More metabolic effect

