

تجدون في guidance مادة الفارما على موقع النادي :

للوصول الى guidance الفارما و تفاريغ المادة كاملة :



كل اعمال الفريق العلمي تنشر على قناة التليغرام





Pharmacology

Subject : Pharmacology

Lec no :

Done By : Zeyad al-ghananim

وَقَارِبْ زَيْدَانِي عَلَانَا

By

Dr/Yasmeen Mohammed Ismail

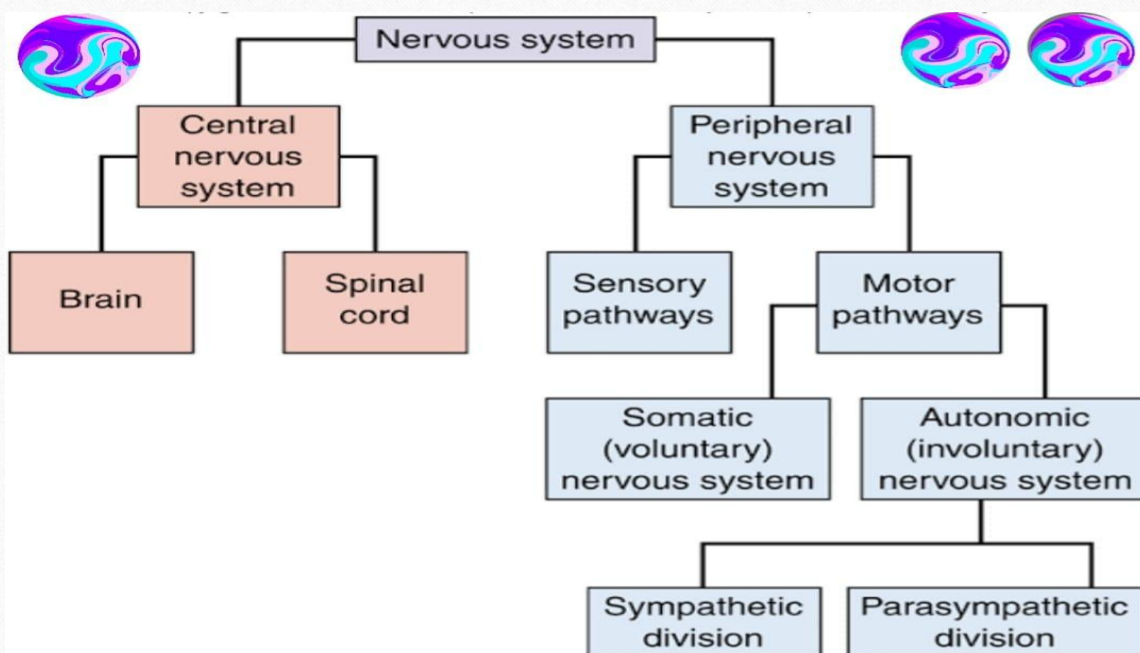
Associate professor of pharmacology

faculty of medicine

Hashemite university

***Adrenergic
Pharmacology***

(1)
sympathomimetics



Normally \Rightarrow 2 systems act together to maintain balance.

in stress situations \Rightarrow Sympathetic system become predominance
fear

* يعني مثلا وبتحتاج ليلتك الامتحان يكون شغال S.N.S 😊

* مثلا لحدك قلبك 😊

انت هوه محتاج دم يوصل للعقدات فيسر (VC) + تحتاج اكسجين

عشان تتنفس فيسر Bronchi Dilation لما تتوسع الشعبات بيسر يوصلك اكسجين.

وكمان بتلاقي شدقة العين واسعا (مين الخوف يوجهل)

وانت بعالي الحالة مش بحاجة انه تفوت الحمام قنتن sphincter

in night at rest times \Rightarrow Parasympathetic system become predominance.

هوه كل اشي العكس.

* يتحكم فيه جميع
الحركات اللا ارادية

Autonomic nervous system

It regulates involuntary functions of the body which are:

- 1- Cardiovascular system (CVS)
- 2- Smooth muscles fibres (SMF)
- 3- Exocrine glands

} vital functions should occur whole day.

Autonomic nervous system includes :

- Sympathetic - Parasympathetic

Sympathetic vs. Parasympathetic Structural Differences

Symp .

Parasymp.

	<u>Symp .</u>	<u>Parasymp.</u>
<i>Point of CNS Origin</i>	T1 → L2 (thoracolumbar)	Brainstem, S2 → S4 (craniosacral)
<i>Site of Peripheral Ganglia</i>	Paravertebral – in sympathetic chain	On or near target tissue
<i>Length of preganglionic fiber</i>	Short	Long
<i>Length of postganglionic fiber</i>	Long	Short

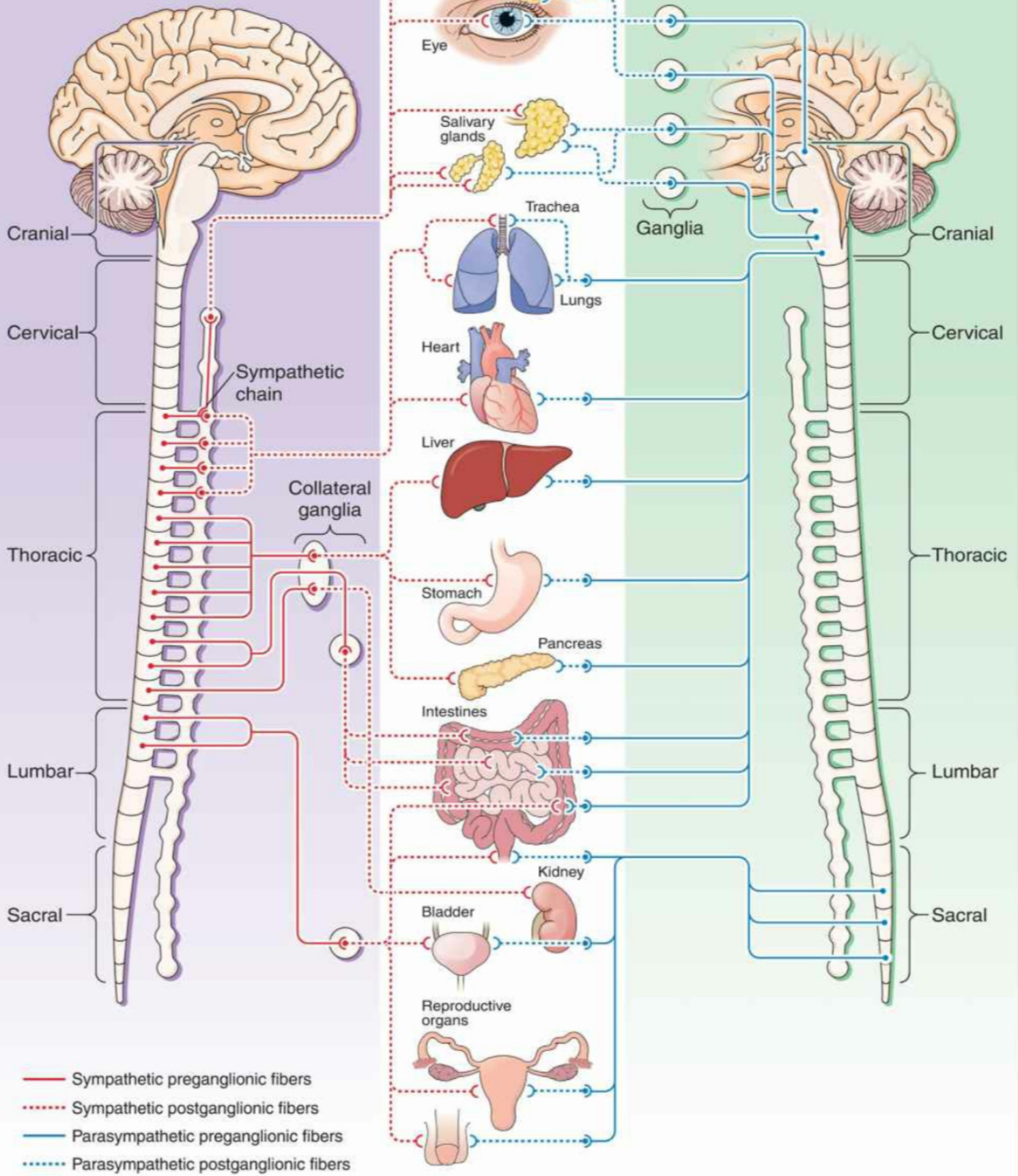
SYMPATHETIC DIVISION

Brain, brain stem, and spinal cord

EFFECTORS

PARASYMPATHETIC DIVISION

Brain, brain stem, and spinal cord



- Sympathetic preganglionic fibers
- Sympathetic postganglionic fibers
- Parasympathetic preganglionic fibers
- Parasympathetic postganglionic fibers

Somatic N.S

Take one motor neuron that come to effector

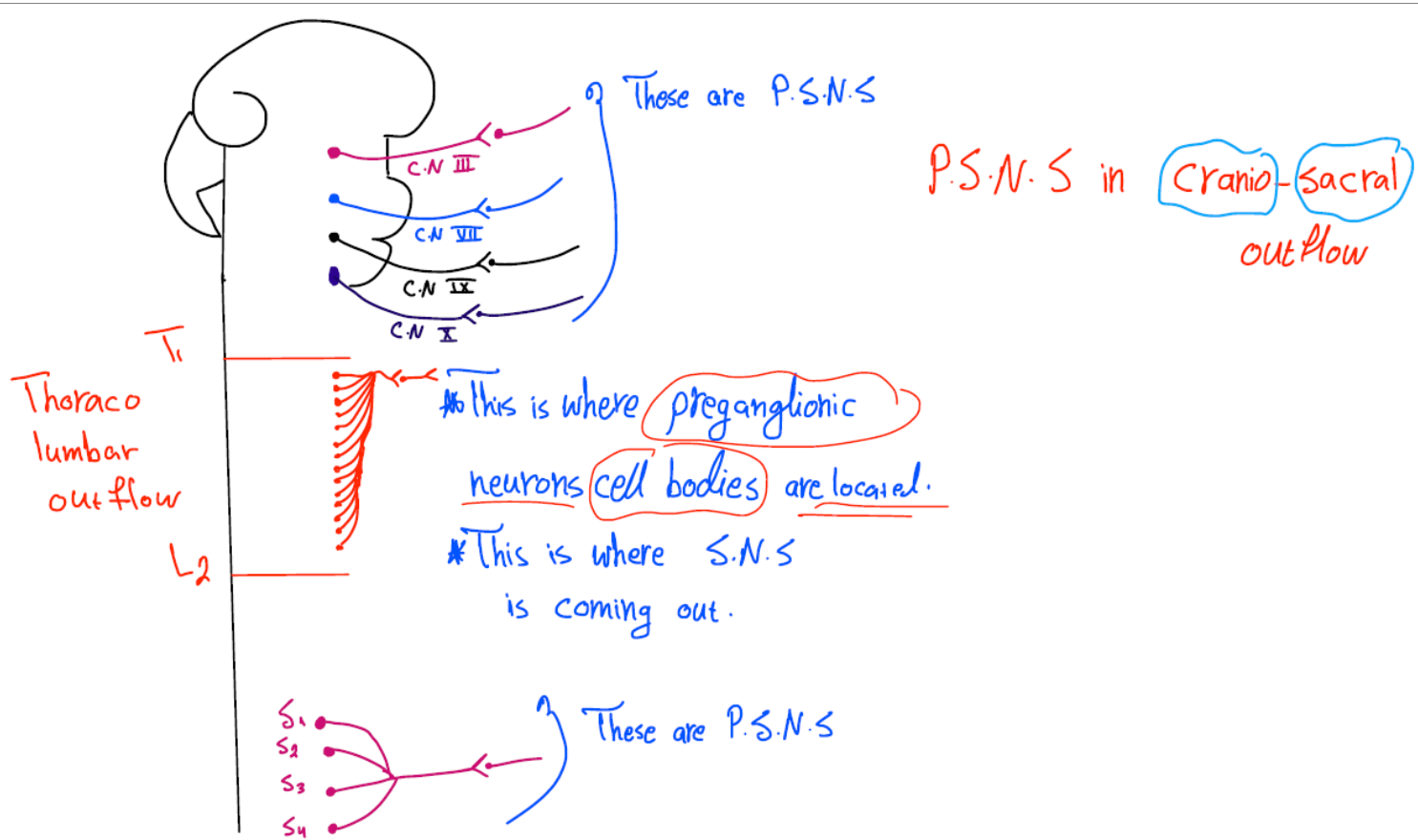
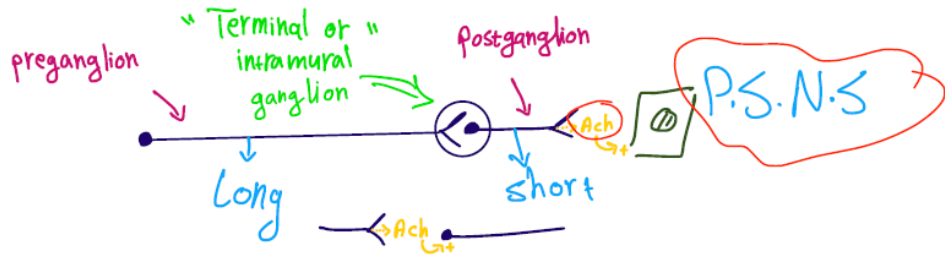
Autonomic N.S

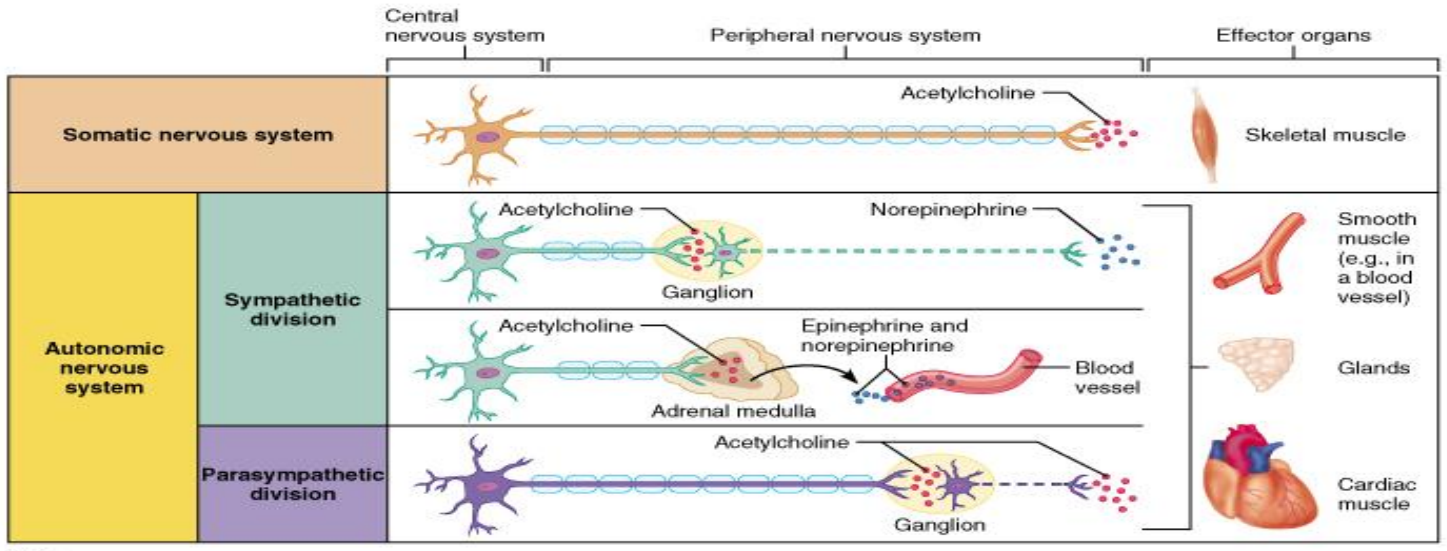
Come from spinal cord or brain stem.



Take 2 motor neuron to reach to effector.

ACh: Acetylcholine





Key:
 — = Preganglionic axons (sympathetic) - - - = Postganglionic axons (sympathetic) ⊖ = Myelination — = Preganglionic axons (parasympathetic) - - - = Postganglionic axons (parasympathetic)









VC:vasoconstriction
 VD:vasodilation
 MM:mucous membranes

	Sympathetic action	Parasympathetic action
CVS Heart	Increase all cardiac properties	Decrease all cardiac properties <u>except</u> <u>atrial conduction</u>
Blood vessels	* <u>VC</u> of <u>skin</u> and <u>mm</u> * <u>VD</u> of <u>skeletal</u> and <u>coronary blood vessels</u>	* <u>Non innervated</u>
Blood pressure	ارتفاع الضغط <u>Hypertension</u>	انخفاض الضغط <u>Hypotension</u>

SMF	<i>Pupil widening</i> Active mydriasis <i>المترقة pupill</i>	Miosis <i>Pupil Constriction</i>
Eye		
Bronchi	Bronchodilatation	Bronchocnstriction
GIT	<i>يمنع حركة الأمعاء ويوقف الإفراج</i> Inhibit motility of wall Contract sphincter	<i>يجعل الأمعاء وتوسع بعملية الإفراج</i> Contract wall Relax sphincter
Urinary tract	Inhibit motility of wall Contract sphincter	Contract wall Relax sphincter
Sex organ	* Ejaculation in males * Relax uterine wall in female	* Erection in male
Exocrine glands		<i>In night acts, by releasing secretes, so when you woke up cough to excrete these secretins</i>
Salivary glands	Thick viscid secretion	Profuse watery secretion * No effect
Sweet glands	Increase	

Exocrine glands has duct that release their secretions in it.
Endocrine glands secretes their secretions in blood.

Sympathetic and Parasympathetic Effects on Body Tissues

BODY TISSUE/ORGAN	SYMPATHETIC RESPONSE*	PARASYMPATHETIC RESPONSE*
Eye 	Dilates pupils	Constricts pupils
Lungs 	Dilates bronchioles	Constricts bronchioles and increases secretions
Heart 	Increases heart rate	Decreases heart rate
Blood vessels 	Constricts blood vessels	Dilates blood vessels
Gastrointestinal 	Relaxes smooth muscles of gastrointestinal tract	Increases peristalsis
Bladder 	Relaxes bladder muscle	Constricts bladder
Uterus 	Relaxes uterine muscle	
Salivary gland 		Increases salivation

*The sympathetic and parasympathetic nervous systems have opposite responses on body tissues and organs.

SYMPATHATIC

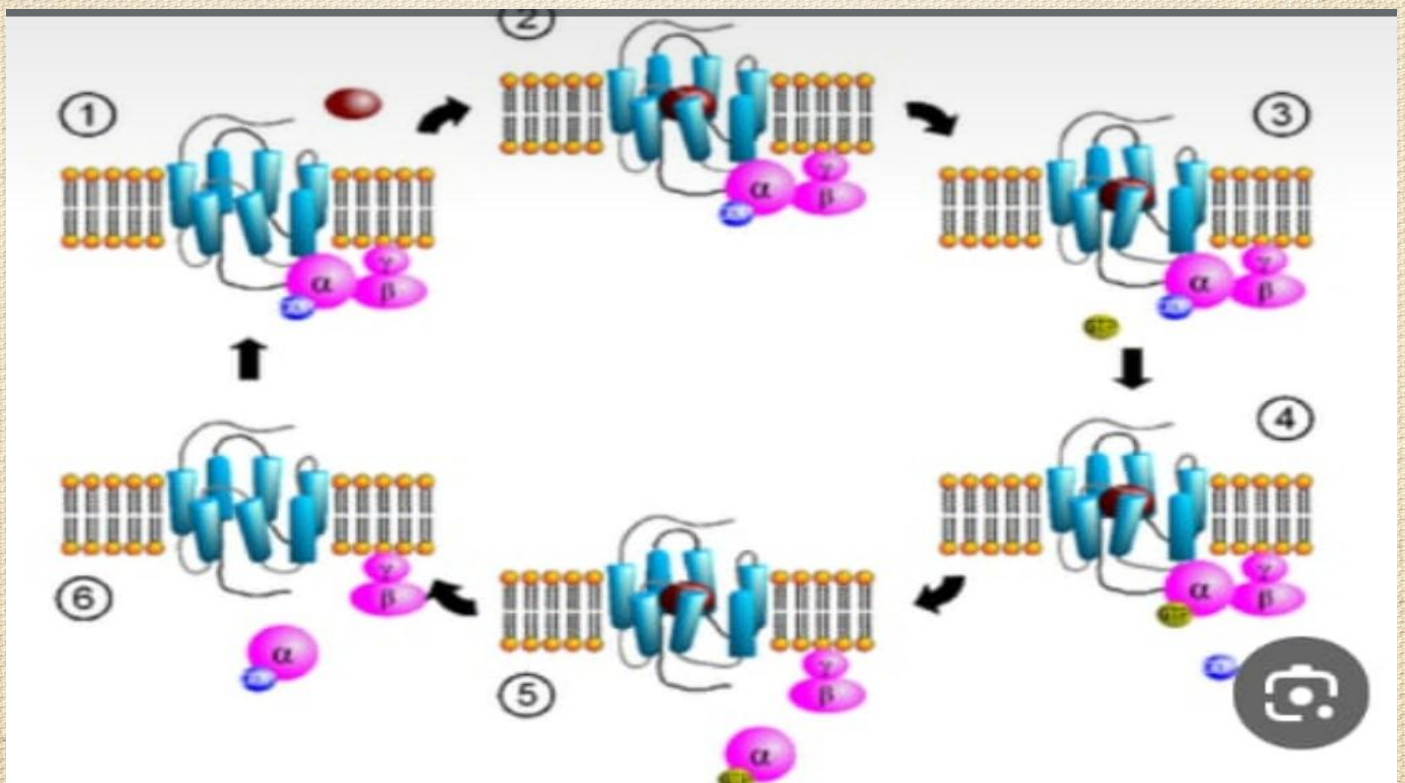
- ****Chemical transmitter**
- ****Types of adrenergic receptors: $\alpha - \beta$**
Sympathetic receptors known as Adrenergic receptors, because in many cases the neurotransmitter that secreted from postganglionic neuron is adrenaline and neurons known as adrenergic neurons
- ****Mechanism of actions of adrenergic receptors:**
- **They are G protein coupled receptors**
- **1-Alpha 1: Gq proteins: stimulate**
- **Phospholipase C \rightarrow \uparrow IP3 and DAG \rightarrow \uparrow intracellular ca**
- **2-Alpha 2: Gi proteins: decrease adenyl cyclase \rightarrow \downarrow CAMP**
- **3-Beta receptors: Gs proteins: stimulate adenyl cyclase \rightarrow \uparrow CAMP**

Molecular Mechanism of Action of Sympathomimetics

Very important

Table 6-3. Characteristics of some important adrenoceptors in the ANS.

Receptor	Location	G Protein	Second Messenger	Major Functions
α_1	Effector tissues: smooth muscle, glands	G_q	\uparrow IP ₃ , DAG	\uparrow Ca ²⁺ , causes contraction, secretion
α_2	Nerve endings, some smooth muscle	G_i	\downarrow cAMP	\downarrow Transmitter release, causes contraction
β_1	Cardiac muscle, juxtaglomerular apparatus	G_s	\uparrow cAMP	\uparrow Heart rate, \uparrow force; \uparrow renin release
β_2	Smooth muscle, cardiac muscle	G_s	\uparrow cAMP	Relax smooth muscle; \uparrow glycogenolysis; \uparrow heart rate, force
β_3	Adipose cells	G_s	\uparrow cAMP	\uparrow Lipolysis
D ₁	Smooth muscle	G_s	\uparrow cAMP	Relax renal vascular smooth muscle



to biological response

When alpha subunit dissociated from G protein it will be activated

Types of coupled receptors:

1. Alpha 1 receptors:

It has Gq protein...when its activated this leads to stimulate C phospholipase and increase IP3 and DAG and leads to increase intracellular Ca^{++} , this release mediators and contract muscles

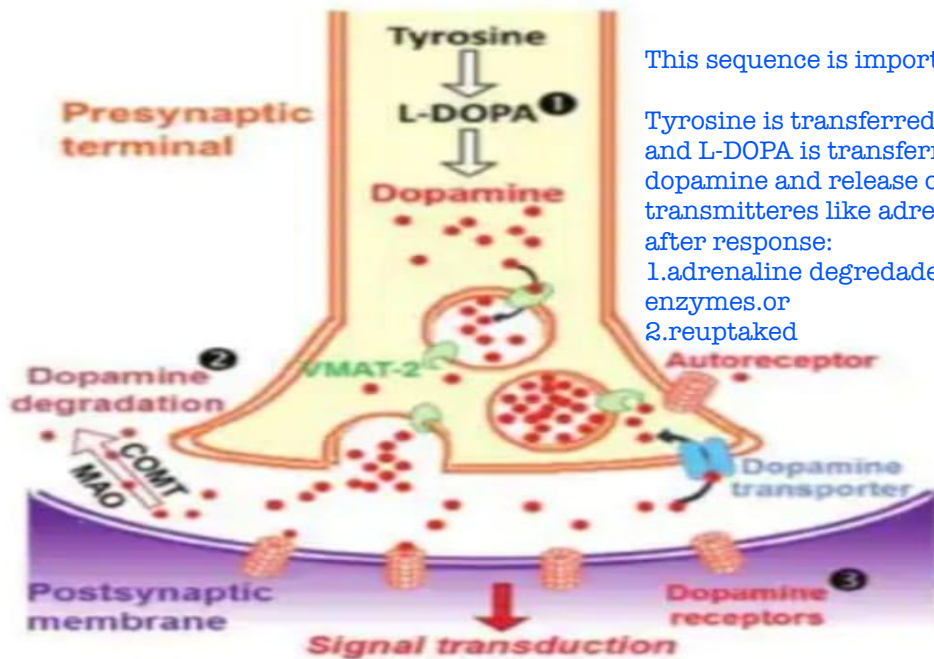
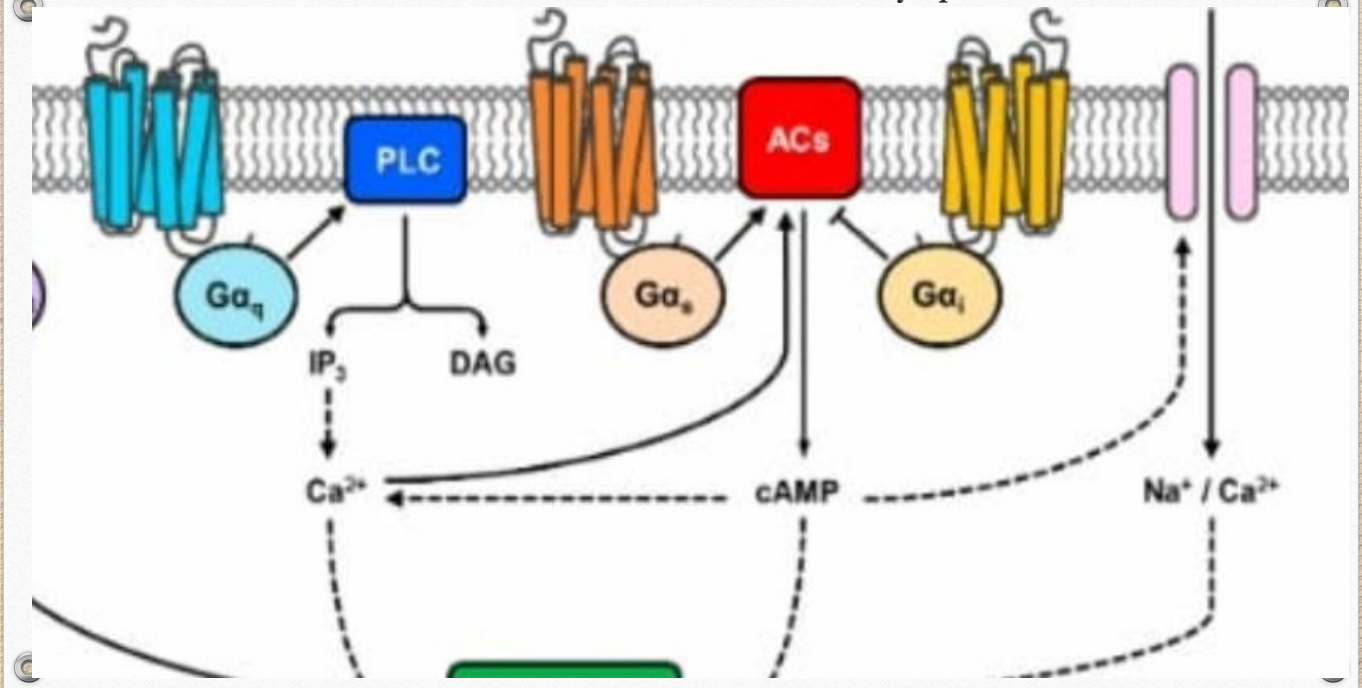
2. Alpha 2 receptors

it has Gi protein...when its activated leads to inhibits adenylyl cyclase and inhibits CAMP

3. Beta receptors

It has Gs protein...when its activated leads to induce adenylyl cyclase and activate CAMP

Molecular Mechanism of Action of Sympathomimetics



This sequence is important

Tyrosine is transferred to L-DOPA and L-DOPA is transferred to dopamine and release of transmitters like adrenaline and after response:
 1. adrenaline degraded by enzymes. or
 2. reuptaked

Due to activation of phospholipase c and release Ca⁺⁺ and cause contraction

VC of mm blood vessels leads to feel of

$\alpha 1$ • coldness in your hands

- **1-CVS: V.C of skin and mm membrane blood vessels**
- **2-SMF: - Eye : Iris ms (dilator pupillae → mydriasis)**
- **3-Salivary glands**

$\alpha 2$ • Alpha 2 Causes balance to decrease effect of alpha 1

(inhibitory) •

- **1-CNS: inhibit sympathetic centres → ↓ sympathetic outflow**

- **2-Presynaptic → It decrease NA release**

→ In presynaptic ganglion to decrease noradrenaline release

Beta 1 •

- **1-CVS: Heart: Increase all cardiac properties (Contractility-Conductivity-Excitability-Heart rate) and C.O.P -O₂ consumption**
- **2-SMF: - Eye : Cilary epithelium → ↑ aqueous secretion (↑IOP) Intraocular pressure**
- **3-Other actions:**
 - Kidney: Renin secretion** • Increase blood pressure
 - CNS: ↑ sympathetic outflow**

كثير الدكتوراة نبهت عالفرق بينهم
Differ between alpha 1
and beta 1 effect on CVS

Beta 2

- **1-CVS:** VD of skeletal and coronary blood vessels
- **2-SMF:** - **Eye:** Cilary epithelium → ↑ aqueous secretion (↑IOP)
- - **Bronchi:** relaxation
- - **GIT and urinary wall:** relaxation
- - **Uterus:** relaxation

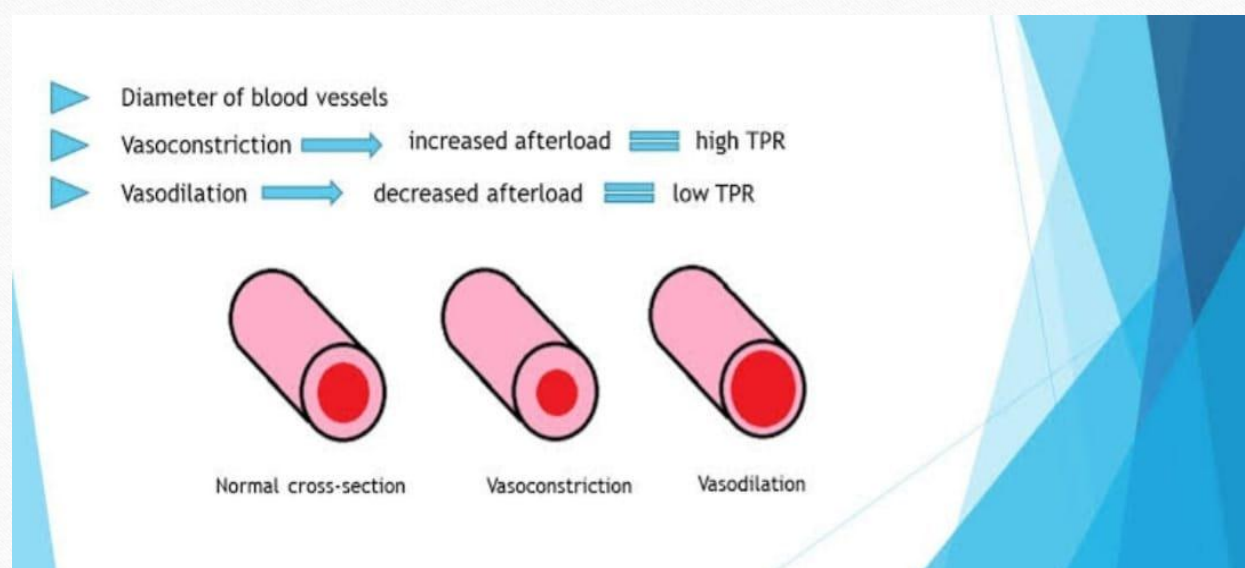
3-Other actions:

- - **Liver:** Glycogenlysis → ↑ glucose
- - **Skeletal muscles:** - Muscles tremors • To cause muscle contraction
- - ↑uptake of K by skeletal muscles → Hypokalemia

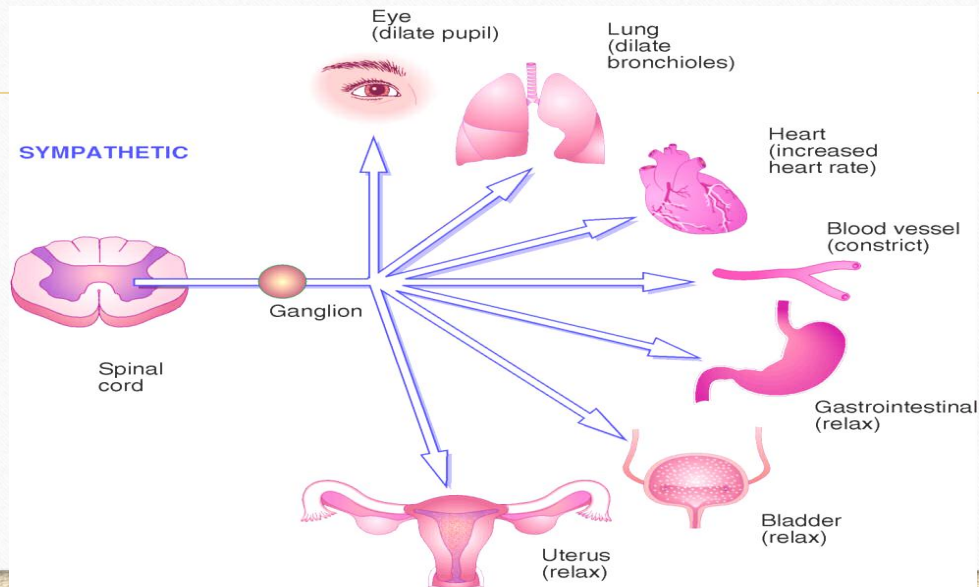
مثلا لما تكون تركض بدك طاقة عشان هيك الكبد يكسر الجلايوجين ويرفع جلوكوز الدم

Beta 3

- **Fat cells:** ↑ lipolysis



SYMPATHETIC RESPONSES



Drugs that activates S.N.S

- **Sympathomimetics**

- Drugs that produce actions similar to sympathetic nerve stimulation.

- **Classifications:**

- *1-According to Chemistry:*

- *2. According to Mechanism of Action:*

This classification according to catechol ring

Catecholamines	Non-catecholamine
- Contain catechol nucleus	-Don't contain catechol nucleus
- Not absorbed orally	-Well absorbed orally
-Rapid onset, short duration	-Slow onset, long duration
- can not pass BBB	can pass BBB
- Metabolized by MAO and COMT.	- Not metabolized by MAO or COMT
-Adrenaline, noradrenaline Dopamine, Isoprenaline, Dobutamine.	- Ephedrine, Amphetamine

Direct action: go and bind with receptor and activates it

Indirect action: release neurotransmitters from vesicles and activates receptor

This classification according to action on receptors

Direct	Indirect	Dual
-Direct stimulation of the receptor include:	Release Nor-adrenaline from vesicles	- Dual mechanism
Effect increased after Sympathectomy (supersensitivity)	Absent	Present Present
- No Tachyphylaxis	Present	
Adrenaline, Noradrenaline Isoprenaline Dopamine Dobutamine	Amphetamine Tyramine	Ephedrine

Catecholamine

**Adrenaline - Noradrenaline -
Dopamine - Isoprenaline, Dobutamine.**

Adrenaline=Epinephrine (α +B)

Routes of administration: •

local on eye- inhalation- ^{In emergency} intracardiac- SC- not oral •

• **Pharmacological actions:**

• **Systemic effects**

- **local effects:**

Just act at site of administration

- Systemic effects:

- **- Cardiovascular system:**
- **-heart:** adrenaline increase all properties of the cardiac muscle through action on (B 1).
- Increase (↑) heart rate - (↑) contractility- (↑) conductivity
- (↑) excitability and automaticity of the heart - (↑) cardiac output (C.O.P.) and cardiac work
-
- **-Blood vessels:** VC of blood vessels of skin, mucous membrane ($\alpha 1$)
- VD of coronary and skeletal blood vessels (B2)
-
- **- Blood pressure (BP):**
- -adrenaline increase C.O.P, so increase systolic BP with slight variation in diastolic BP
-

• 2- Eye:

- **A- pupil size: mydriasis ($\alpha 1$) and decongestion**
- **B- intraocular pressure (IOP) : decrease IOP (in open angle glaucoma)**

وانت بتركض يكون الهوا اللي بقابل وجهك بعمل ضغط على العين فعشان هيك
بقل الضغط داخل العين كنوع من balance

- **3-Respiratory system:**
- Bronchodilation :B2
- Decongestion due to $\alpha 1$ stimulation of mucous membrane blood vessels
- **4-GIT**
-
- Relax wall (B2) - Contraction of sphincters ($\alpha 1$)
-
- **5-Urinary**
- Relax wall (B2)- Contraction of sphincters ($\alpha 1$)
-
- **6-Sex organs**
-
- Males : ejaculation ($\alpha 1$)
- Females: relaxation of pregnant human uterus (B2).

هون حكمة ربنا انو الرحم برتخي لما يصير stress
او مثلا البنات اللي عندهم trunk contraction بوخذوا دواء بشتغل على B2 reseptors

- **7-Other actions:**
- 1-Kidney: Renin secretion \uparrow (B1)
- 2-Liver: Glycogenolysis \rightarrow \uparrow glucose (B2)
- 3-Sk. ms: -Muscles tremor(B2)
- \uparrow uptake of K by sk.ms (B2)
- - Facilate NM(neuromuscular) Transmission ($\alpha 1$)
- 4-Fat cells: Lipolysis(B3)
- -CNS: affect sympathetic flow
-
- **8- antiallergic action:**
- Adrenaline is the physiological antagonist of histamine.
-

• **- local effects:**

- 1- Vasoconstriction (VC) of cutaneous blood vessels ($\alpha 1$) : used to prolong action of local anesthetics
- 2- VC of mucous membrane blood vessels of the nose ($\alpha 1$) : used as nasal pack for hemostasis in epistaxis **لعلاج رعاف الانف**
- 3- VC of conjunctival blood vessels ($\alpha 1$) **In severe inflammation adrenaline used locally**
- 4- VC of mucous membrane blood vessels of the bronchi ($\alpha 1$) and bronchodilator (B2) :inhalation in acute bronchial asthma

١. يقلل احتقان bronchi وهذا يؤدي الى توسع bronchi
٢. يتأخذ استنشاق ويرخي smooth muscle of bronchi

• **Therapeutic use:**

• **A- local uses:**

- 1- With local anaesthetics to prolong its effect.
- 2- local hemostatic in epistaxis and bleeding surfaces
- 3- Decongestion of m.m of nose and eye
- 4- acute bronchial asthma :inhalation

Here as first aid procedure give to patient adrenaline for cardiac resuscitation انعاش القلب

- **B- systemic uses:**

- 1-Cardiac resuscitation: intracardiac .
- 2-Acute attack of bronchial asthma: SC .
- 3-Contraction ring during labour to relax the uterus
- 4- Allergic reactions e.g. anaphylactic shock.
- 5- Hypoglycemic coma (SC)
-



Relaxation of constriction ring to facility delivery

Constriction ring

Contraindications: a condition or circumstance that suggests or indicates that a particular technique or drug should not be used in the case in question.

يعني ادوية تنعطاش في حالة وجود حالة معينة

Side effects	Contraindications
Tachycardia, palpitation arrhythmia.	Arrhythmia
Hypertension and cerebral haemorrhage	Hypertension
If used with local anaesthesia in region of end arteries (Finger, toe, penis) → gangrene.	with local anaesthesia in region of end arteries (Finger, toe, penis)
If used with general anaesthesia → ventricular fibrillation	with general anaesthesia

- **Noradrenaline (NA)= Norepinephrine**

- **(α +weak B1+No β 2)**

- **Therapeutic uses:**

- **In hypotensive states to elevate BP.**

Isoprenaline (Beta only)

-
-
- Therapeutic uses:

- **1-Heart block**

- **2-Bronchial asthma**

Heart block, also called AV block, is when the electrical signal that controls your heartbeat is partially or completely blocked.

يعني استخدمو كانهاش للقلب

Increase blood supply particularly to kidney • Dopamine (Dopaminergic receptors+B1+ α)

- Therapeutic uses:

- 1-Different types of shock (Cardiogenic, hemorrhagic & Septic shock) due to: * VD of renal blood vessels \rightarrow \uparrow renal blood flow

- * increase of C.O.P and systolic blood pressure.

- 2-Heart failure, hypotension

- **Dobutamine**

- (Selective β_1 + weak α)

-

- **Therapeutic uses:**

- 1-Shock due to: increase of C.O.P and systolic blood pressure.

- 2- Heart failure, hypotension

-

-

Non Catecholamines

CNS stimulant: as **Ephedrine** - **Amphetamine**

الشهية فقدان ***Anorexigenics:*** as Fenfluramine- Phenmetrazine

- ***Vasopressors*** as Methoxamine – Midodrine – Metraminol-
Phenyl ephrine (weaker than NA)

للاج احتقان الانف تعمل VD

Nasal decongestant **Old group:** as **Phenylephrine** – **Pseudoephedrine**

Recent group:as **Naphazoline** – **Xylometazoline**

Vasodilators and uterine relaxants as Isoxsuprine- **Ritodrine**

Bronchodilators as Salbutamol- Terbutaline- Salmeterol



Thanks

#النادي_الطبي

#معكم_خطوة_بخطوة

