Physiology | Lecture 8

Autonomic Nervous System (ANS)

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Nervous system:

1-CNS (Central nervous system)

2-PNS (Peripheral nervous system):

A-Somatic nervous system (SNS): voluntary

B-Autonomic nervous system (ANS): involuntary

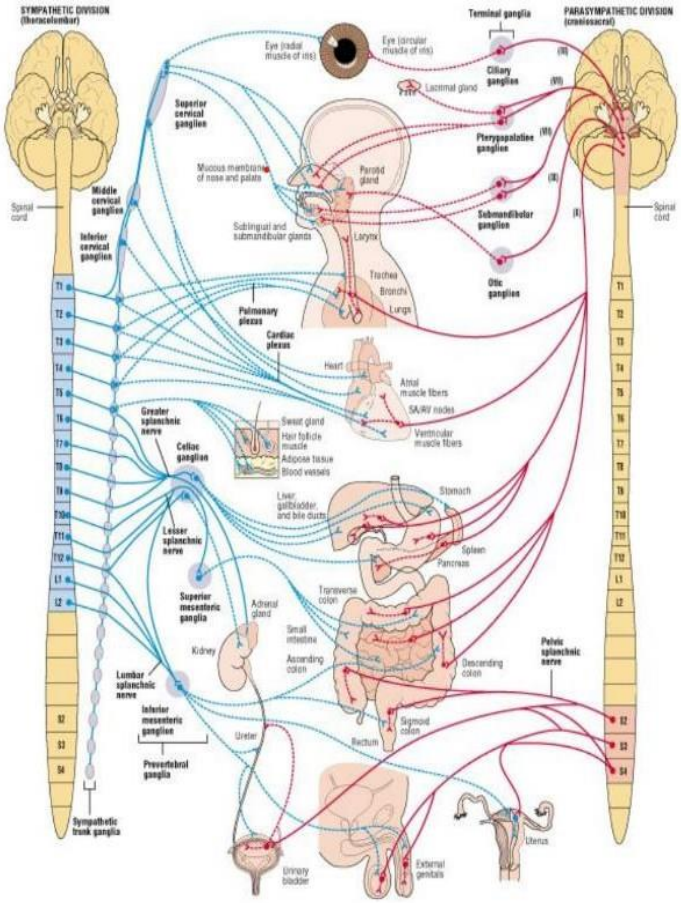
ANS division is anatomically distinct from the motor somatic nervous system, which innervates skeletal muscle. This group of efferent paths originates from the central nervous system and innervates heart, smooth muscle, glandular tissue, and enteric nervous system.

AUTONOMIC NERVOUS SYSTEM (ANS)

We have two divisions for the autonomic nervous system, what we see in red is called the parasympathetic division and what we see in blue is the sympathetic division.

-By the fibers of the autonomic nervous system we are innervating a lot of organs in our body.

As we can see : the origin of parasympathetic division is **craniosacral** , the origin for sympathetic division is **thoracolumbar** or the **spinal cord** .



The functions of the Autonomic nervous system:

The general function of the **ANS** is control and adaptation of body, some functions:

1. regulation of the activity of visceral organ system such as:

-heart rate -blood pressure -emptying of urinary bladder

- Our bodies are exposed to many internal and external changes, the autonomic nervous system is involved in the adaptation of our bodies with these changes that are taking place to get finally in its involvement in the control of the body, and by regulation these functions, ANS plays a major rule in homeostasis.

1-respones to specific environmental stimuli such as:

-Light: dilation of pupil to low light (mydriasis), constriction of pupil to bright light (miosis)

-Temperature: vasodilation in hot T, vasoconstriction in cold T

T: temperatures

-Stress: The ANS (mainly by sympathetic and adrenal medulla) mediates the immediate response (fight or flight), what exactly happens when we feel stress? let's talk about this example in details:

Example of adaptation to external stimuli (stress): fight or flight

-For either to fight or to flight away we need the activity of our muscles and once we need the activity of our muscle that muscle needs a higher oxygenation, nutrition and so on. So, we have a group of reactions that take place in our bodies to adapt them with these new changes and some of these reactions are:

1-Increased heart rate and force of contraction:

Why do we need this? simply we need it to deliver more blood toward muscle and tissue and by delivering more blood we are getting more oxygen for those muscle.

2-Widely dilated pupils:

There is a dilate of pupils because we have smooth muscle cells in it. There will be some relaxation of the smooth muscle cell which result in dilation of pupils, it's important because you try to see all details about that dangerous object by getting wide dilated pupils.

3-Pallor (pole of fear) as blood is directed to the skeletal muscle:

What we mean by pallor? It is the white discoloration of the skin, why that happened?

We need to supply our main muscles with blood , so we are reducing blood supply to unnecessary tissue like skin and we are increasing blood supply to muscles, and by vasoconstriction of vessels that supply skin this adaptation is developed.

Vasodilation: توسع الأوعية الدموية

Vasoconstriction: تضيق الأوعية الدموية

1-Goose pimples:

Actually, this reaction happens because of the contraction of the hair erector muscle (arrestor pili muscle) at hair follicles they are smooth muscle cells which are contracting, by that contracting this reaction will take place, the hair on the head and on the skin stand.

2-Cold sweat:

Simply these people are sweating by activation of sweat gland but why is it cold?

because we reduced blood supply towards the skin so there is no heating for that sweat which is coming out of the skin.

3-Dry mouth:

As we said the body will shut down all unnecessary tissue like ***salivary glands***, for example there will be a *decrease in salivation*, by activation of all fight and flight reaction that causes the vasoconstriction of vessels which supply these salivary glands leading to less secretion of saliva and as a result that person will have a dry mouth.

Its like when we say :

نشفت ريقي! بمعنى خوّفتني

Physiological characteristics for both divisions of ANS:

1. **high speed of onset**: for example, during fight of flight reaction heart rate increase immediately within few seconds (3-5 seconds).

2. **Autonomic nature**: it is not under your voluntary control (without your conscious).

The reflex responses of ANS are sensitive to emotional states (stress,fear,euphoria,etc).

*NOTE: some functions are brought under voluntary control such as urination and defecation through the participation of voluntary muscles.

3. **Tonic activity**: all the time we have specific levels of sympathetic activity and specific levels of parasympathetic.

The ANS fires continuous impulses to target organs at a very low rate. The basal rate of firing is called (sympathetic tone) and (parasympathetic tone) These tones establish basal rate of contractile activity in smooth muscle cells, and secretory activity of glandular tissues, The activity of these effector cells can be changed because of an increase or a decrease in the activity of any divisions of the ANS by increasing or decreasing the number of action potentials per unit time.

Anatomical characteristics and synaptic organization of ANS

Two neurons carry impulses of the ANS from the CNS to the effector organs. The first is known as **preganglionic neuron**, the cell body is located in the CNS (in appropriate nucleus in the brain or in the lateral gray of the spinal cord) as seen in the below picture. The fibers of preganglionic are small and myelinated, and usually end within a (ganglion) where they synapse with the second neuron called **postsynaptic neuron** . The second neuron (postsynaptic) carries impulses to the target organ.

-Axon of 1st (**preganglionic**) neuron leaves CNS to synapse with the 2nd (ganglionic) neuron.

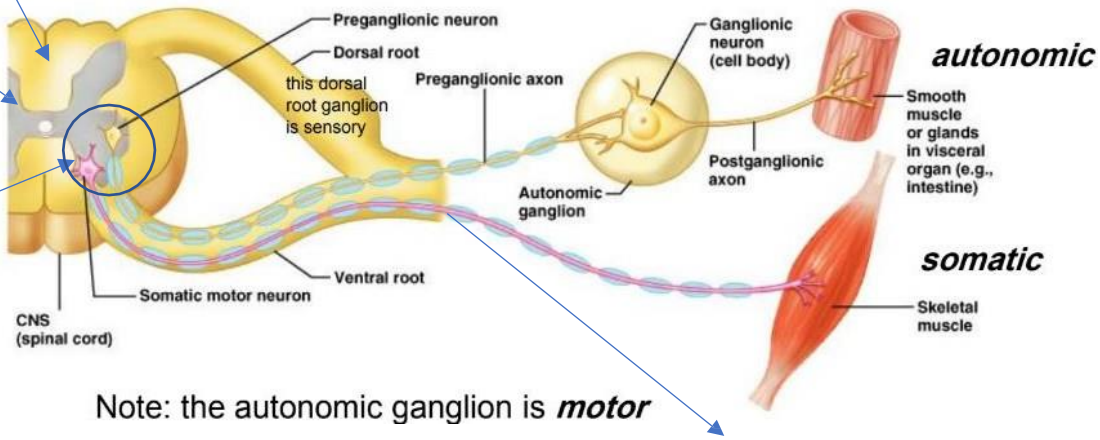
Ganglion: a collection of cell bodies of neurons outside the CNS.

-Axon of 2nd (**ganglionic**) neuron extends to the organ it serves.

White matter

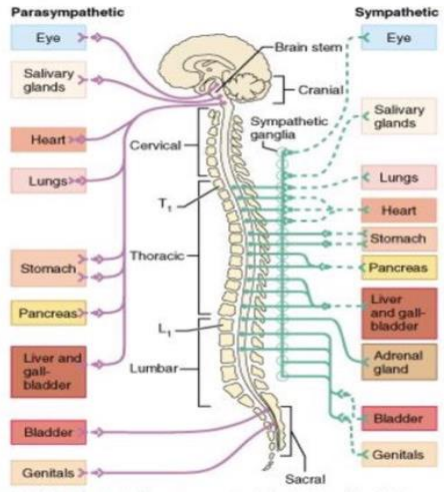
Gray matter

Lateral grey of the spinal cord



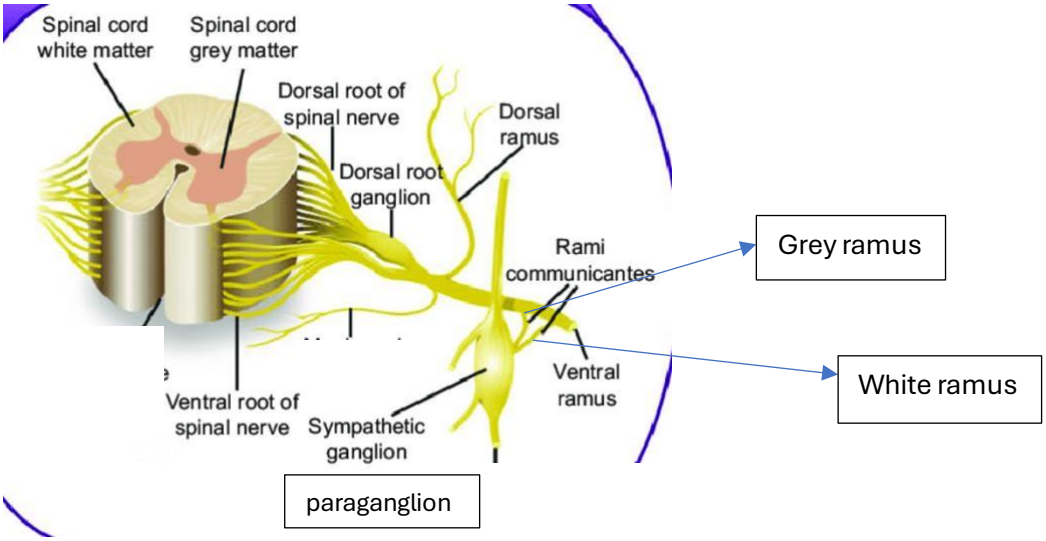
SNS has only one neuron

-Each segment of spinal cord contains gray (in middle) and white matters, spinal cord is subdivided into **cervical region** (8 pairs of spinal nerves)**, thoracic region** (12 pairs)**, lumbar region** (5 pairs)**, sacral region** (5 pairs)**,** and **coccygeal region** (1 pair)**.** 31 pairs of spinal nerves together.



-dorsal root and ventral root fuse to give one spinal cord which is divided to ventral and dorsal rami.

-There are two types of ganglia: 1-Paravertebral ganglia: beside spinal cord (are connected to ventral rami by two channels A-white ramus B-gray ramus)
2-Prevertebral ganglia



I think you have understood the anatomy of spinal cord, Let's talk about SNS and PSNS:

SNS (sympathetic ANS) **(flight or fight)**

As we mentioned before, the cell bodies of preganglionic neurons lie in lateral gray of spinal cord at segmental levels of T1 through L3, so it's origin Thoracolumbar (thoracic and lumbar).

Axons leave spnial cord via ventral roots, then leave ventral root via white rami communicans to enter a vertebral ganglion of the sympathetic chain at the same segmental level.

- ***There are 4 possibilities:***

1-preganlionic neurons synapse with postganglionic neurons at the segmental level.

2-preganlionic neurons turn **cranial(up)** or **caudal(down)** and synapse with sympathetic postganglionic neuron at higher or lower segmental level. (Synapse may occur at more than one postganglionic neuron)

***(After 1 or 2)** By the way that chain of ganglia is called "**paravertebral ganglia**" they are near the spinal cord and near the vertebral column. After synapse with neurons at paravertebral ganglia, axons of second neurons leave ganglia via gray rami communicans to return to the corresponding spinal nerve.

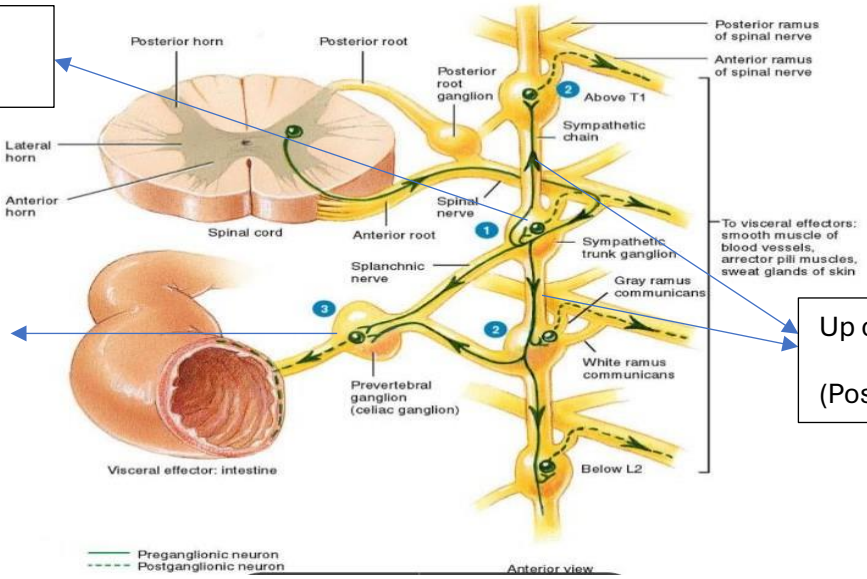
3- Some preganglionic fibers that enter ganglia pass without any synapse at the paravertebral ganglia and continue to some ganglia located in the abdomen known as **prevertebral ganglia**(far away from the vertebral column), where they have the synapse with the second neuron. There are three unpaired prevertebral ganglia: celiac, superior mesenteric and inferior mesenteric ganglia.

4-Some preganglionic fibers pass without synapse in paravertebral ganglia and prevertebral ganglion. These fibers continue to **adrenal gland** where they synapse onto chromaffin cells. These cells liberate epinephrine into blood stream. (next page)

Possible number

Possible number 3

(Prevertebral

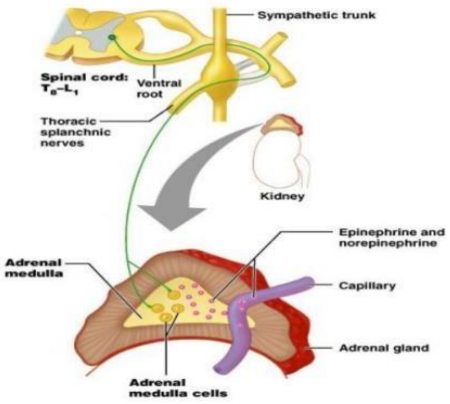


Up or down

(Possible number 2)

-Adrenal gland (possible number 4)

- Synapse in gland
- Can cause body-wide release of epinephrine



Synaptic Organization of sympathetic ganglia:

-Short preganglionic fibers and long postganglionic fibers.

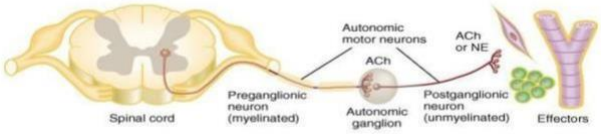
- Individual postsynaptic neurons in vertebral ganglia can receive signals from many preganglionic fibers (convergence) and one preganglionic neuron can relay impulse to many postganglionic neurons at different segmental levels (divergence).

convergence: many neurons synapse with one neuron.

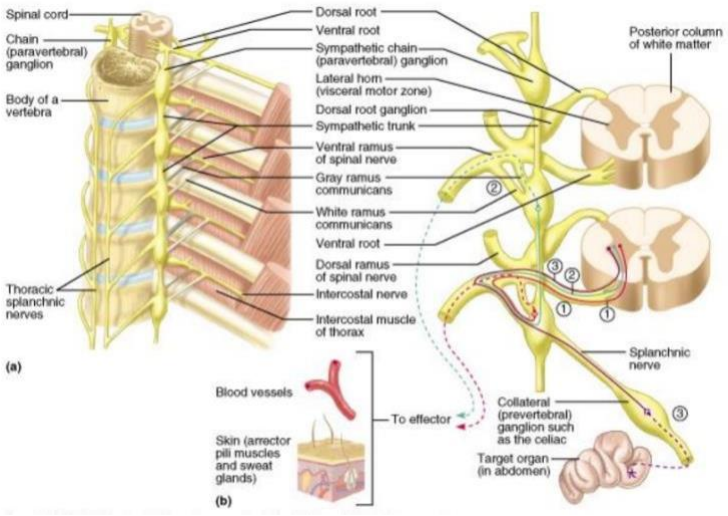
divergence: one neuron with many terminal synapses with many postsynaptic neurons.

This organization of the sympathetic system induces widespread effects on target cells innervated by sympathetic postganglionic fibers.

Basic Anatomy of ANS



- **Preganglionic neuron**
  - cell body in brain or spinal cord
  - axon is myelinated type B fiber that extends to autonomic ganglion
- **Postganglionic neuron**
  - cell body lies outside the CNS in an autonomic ganglion
  - axon is unmyelinated type C fiber that terminates in a visceral effector



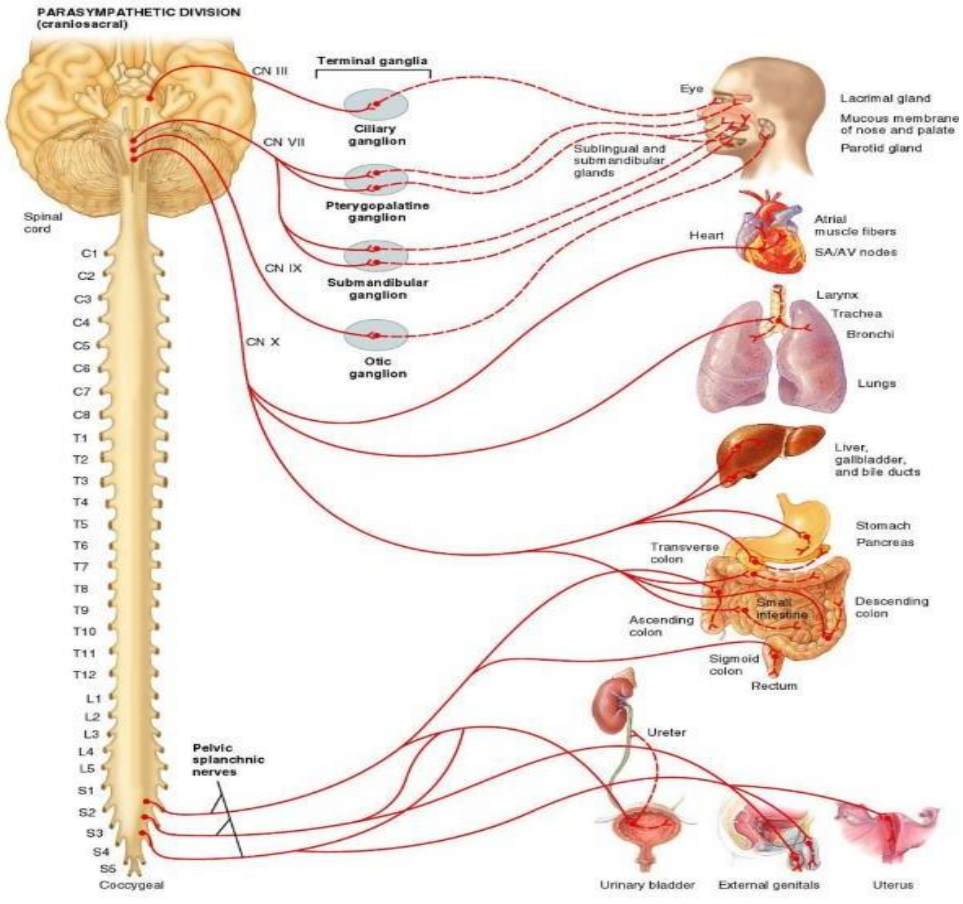
PSNS (Parasympathetic) **(rest or digest)**

The preganglionic fibers arise in appropriate cranial nuclei and in segments S3 and S4 (sometimes S2, S5 also) SO, it's origin is Craniosacral. These fibers leave the CNS in the III, VII, IX, and X **(vagus) nerves for fibers of cranial origin** and in **pelvic nerves for fibers of sacral origin**. The preganglionic fibers are long and go all the way to the effector organ where they synapse with the second postganglionic neuron located within the tissue of the effector organ or to a ganglion located very close to the effector organ. The axons of postsynaptic neurons are short.

-cranial origin: vagus nerves -sacral origin: pelvic nerves

Synaptic Organization of parasympathetic ganglia:

In parasympathetic there is no or little branching of preganglionic fibers (divergence). The ratio of pre to post ganglionic neurons is 1:1 or 1:2. As a result of this arrangement, the parasympathetic actions tend to be more discrete and confined to the innervated organ.



If we analyze the parasympathetic as you see, we have long preganglionic fibers synapse with one neuron (a few amount) located at the effector organ, so we do not have high divergence and convergence in parasympathetic, but we have in sympathetic.

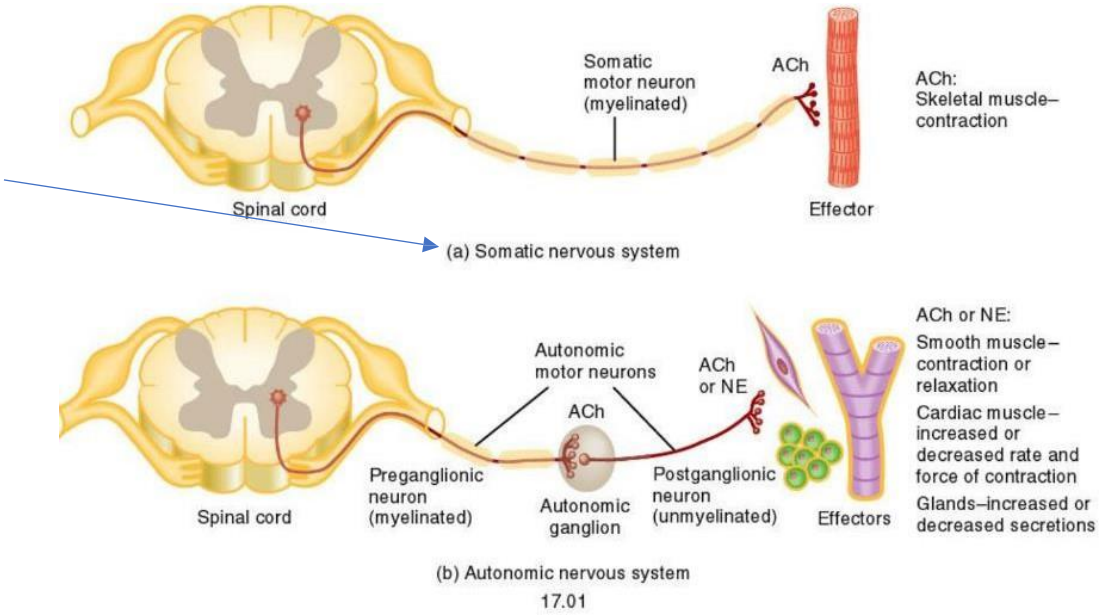
/	Sympathetic (fight or flight)	Parasympathetic (rest and digest)
Origin	**Thoracolumbar (thoracic and lumbar)**	**Craniosacral (cranial and sacral)**

The somatic nervous system

We have a cell body of 1 neuron at the spinal cord going directly toward organs(muscles) and innervated it.

-we only have one neuron (very long axon).

*__NOTE__: The terminals of autonomic nerve fibers are unlike terminals of the somatic motor fibers (skeletal neuromuscular junction). The autonomic terminals are highly branched forming extensive network of fibers beaded with small swellings or varicosities. These varicosities are sites from where transmitter is released.



Effects of sympathetic stimulation

Sympathetic system innervates widely distributed tissues. These include, sweat glands, smooth muscle cells of blood vessels supplying skeletal muscle, skin, etc, smooth muscle cells of hair follicles. This innervation is consistent with diffuse

projections of the sympathetic postganglionic fibers that originate in vertebral ganglia and distribute with the spinal nerves.

Both divergence and diffuse projections contribute to the broad, coordinated activation of the sympathetic system. Divergence allows a single preganglionic neuron to influence multiple postganglionic neurons, and those postganglionic neurons then spread out to affect many tissues, which we describe as diffuse projections.

the sympathetic which has excitatory effects on these tissues regulates:

1-Blood pressure: (blood vessels supplying skeletal muscles are major players). In addition to that the effect on heart also contributes in regulation of blood pressure.

2-Body temperature: by the sympathetic effects on cutaneous blood vessels and sweat glands.

Body temperature can be controlled by controlling the vascular tone (dilation / restriction) of cutaneous blood vessels .

The sympathetic nervous system also controls sweat gland activity (When body temperature rises, sweat production increases, leading to more evaporation and greater cooling) .

Blood vessels and sweat glands are innervated only by the sympathetic nervous system (an exception to the general rule of the dual autonomic innervation)

3-Cardiovascular system: effects on vessels will result in redistribution of blood by enhancing blood flow to skeletal muscle and reducing blood flow to skin and mesentery.

4- Effects on heart: increasing cardiac output (volume of blood pumped per minute).

Increased cardiac output is necessary because it enhances oxygen delivery to muscles and other tissues during the fight or flight response .

5-Respiratory system: causes relaxation of bronchial muscle which results in bronchodilation.

It allows more air flow towards the lungs and more exchange of gases.

6-Digestive system: inhibition of motility and secretion.

7-Metabolic effects:

- Mobilization of glucose.
- Increased lipolysis.
- Increased metabolic rate

Effects of the two branches of the ANS

Organ	Sympathetic Effect	Parasympathetic Effect
Pupil	dilation	constriction
Lens	Far focus (lower curvature)	Near focus (increased curvature)
Salivary Gland secretion	High in viscosity	serous
Heart	Increased rate and pressure	Lower rate and pressure
Lungs	Dilation of respiratory passages	Constriction of respiratory passages
Gastrointestinal	Decreased motility	Increased motility
Kidneys	Decreased filtration rate	Increased filtration rate
Male genitalia	Ejaculation	Erection
Vascular smooth muscle	Variable depending on the neurotransmitter	Relaxation
Sweat glands	Increased activity	No innervation
Arteries to skeletal muscle	dilation	No innervation
Veins	Variable depending on the neurotransmitter	No innervation

Effects of parasympathetic stimulation

1) **Gastrointestinal system**: increases motility and secretory activity.

Note:

- The parasympathetic, in contrast to sympathetic system is viewed as regulator of activities involved in replenishment of energy supply and general maintenance of the organism. The control provided by parasympathetic system is discrete and selectively directed to individual organs.

- **SNS** is acting over the cardiac muscle to increase the force of contraction while the

2) **Glands**: increases secretory activity (**remember sweat glands are under sympathetic control**).
3) **Heart**: decrease rate of contraction (**bradycardia**).

For example, at conductive tissue we have slow depolarization contraction potential by increasing parasympathetic stimulation, the rate of **slow** depolarization become **slower**, in this case the number of action potential generated per minute will be less. While by sympathetic stimulation we are **increasing** the rate of slow depolarization and we got more frequent generation of action potential.

- للتوضيح: التحفيزالودي يزيد من فعالية مضخة القلب وهذا الذي نحتاجه أثناء حدوث الجهد العالي، أما التحفيز اللاودي يقلل من فعالية ضخ القلب للدم وهذا الذي يؤدي إلى إراحة القلب مثلًا بعد رياضة شديدة او بعد صعود درج الكلية

4) **Pupil**: control pupil diameter by papillary light reflex (**miosis, regulates the amount of light falling on retina**).

Functions of the pupillary parasympathetic control :

1. regulates light entry
2. enhances near vision
3. opposes sympathetic dilation.

- لكل من التحفيزان الودي و اللاودي اثره على العين)تمدد وانقباض حدقة العين للتكيف مع الضوء(، لكن التحفيز اللاودي يعتبر المسؤول الأساسي عنها وهنا خاصة للرؤية القريبة.

5) Accommodation of the lens for **near** vision (by changing the convexity of the lens by contraction of smooth muscle cells)
6) Voiding the **urinary bladder** (**micturition**).

- In this sheet we will use:

SNS → Sympathetic Nerve System

PSNS → Parasympathetic Nerve

NOTE :

Pupil constriction = myosis
Pupil dilation = mydriasis

Sympathetic nervous system -- urine storage
Para-sympathetic nervous system – urine voiding

MOLECULAR BASIS OF PHYSIOLOGICAL ACTIONS OF THE ANS

Remember that the preganglionic neurons synapse with the postganglionic neurons in the ganglia (releasing neurotransmitters) and then postganglionic neurons interact with effectors to induce actions.

Transmitters:

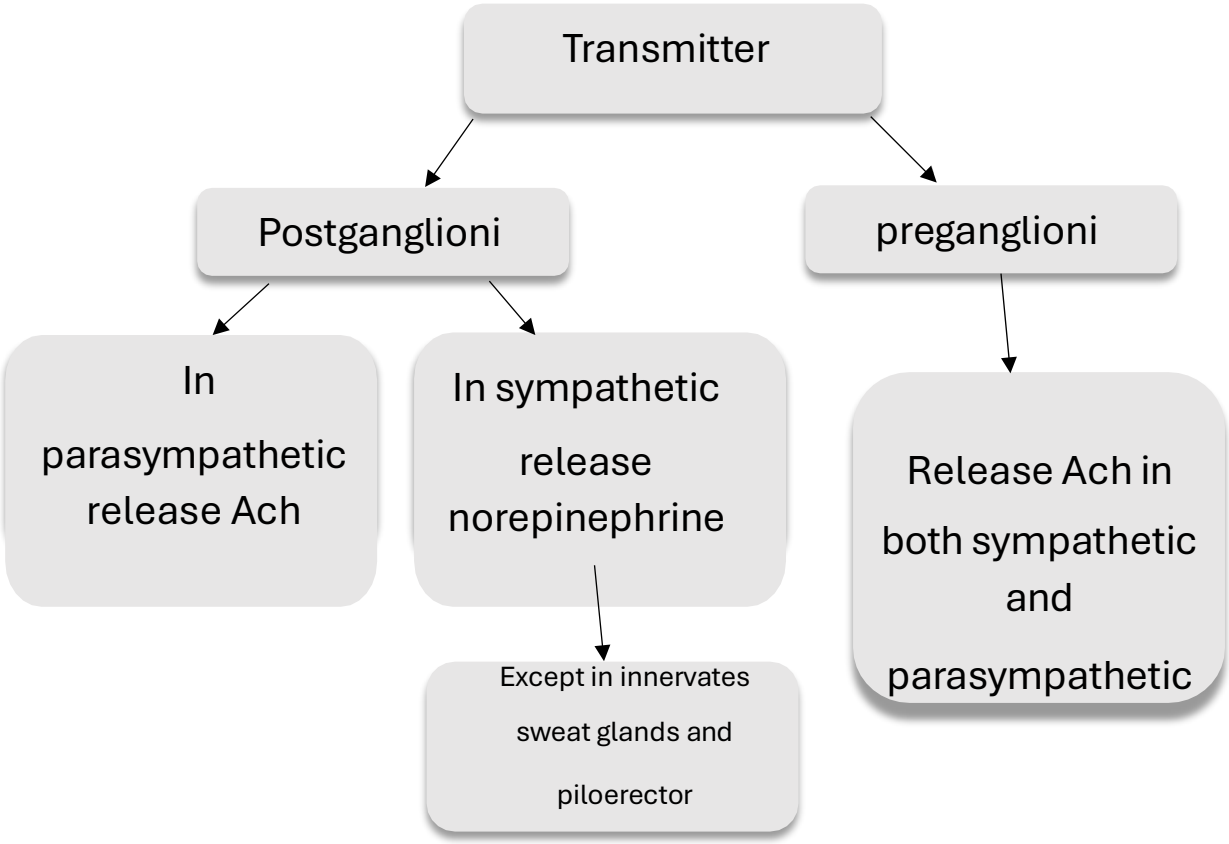
At ganglion: **pre**ganglionic neurons of both sympathetic (**SNS**) and parasympathetic (**PNS**) release **acetylcholine (Ach)** and activation of the second neuron "**postganglionic neuron**".

At effector organs: when the second neuron is activating, the **parasympathetic** **post**ganglionic neurons release **acetylcholine** to the effector cells, while the **post**ganglionic neurons of **sympathetic** release **norepinephrine** to the effector cells except the **post**ganglionic neurons that innervates sweat glands and piloerector muscles "**small muscles attached to hair follicles**", they release Ach Instead of norepinephrine.

Important note: the released **Ach** by **parasympathetic** system is **inactivated** by breakdown by acetylcholinesterase (**an enzyme that breaks down Ach**).

Also, **norepinephrine** is inactivated by recapture by postganglionic nerve varicosities.

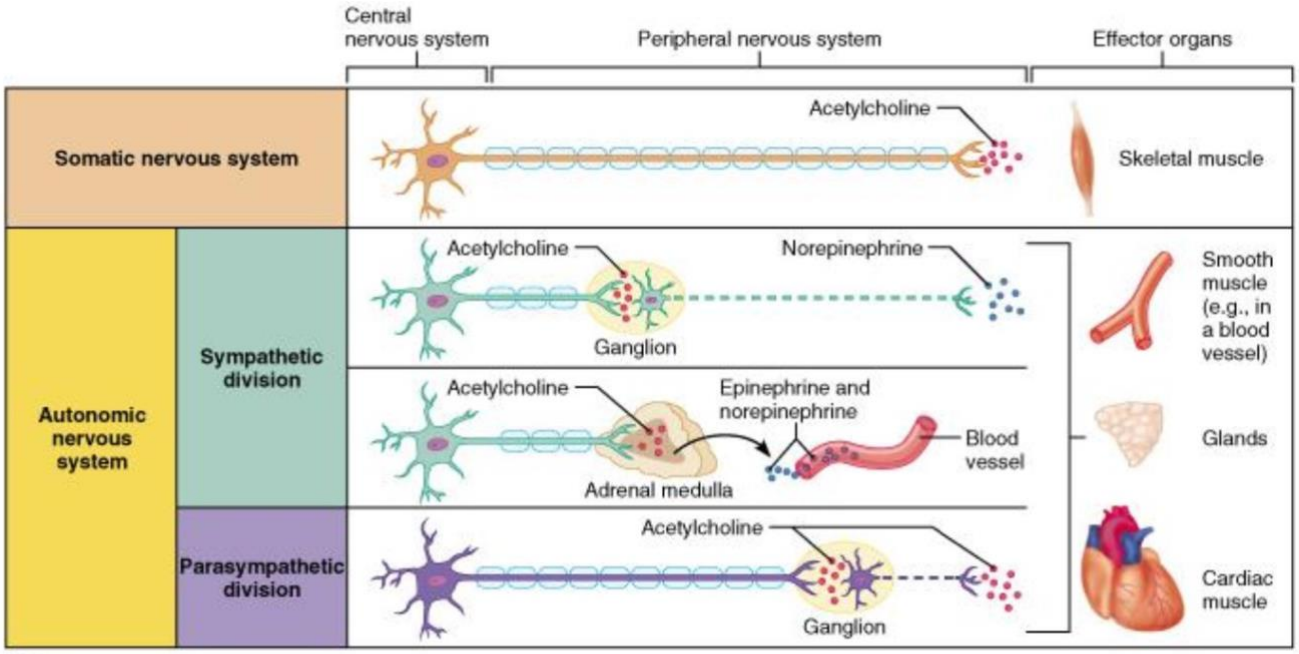
ملخص سريع يوضح ما كان أعلاه : 😊

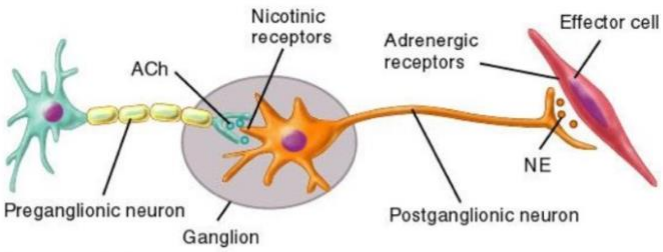


The images you will see bellow summarize the above information with some additions that we will mention now:

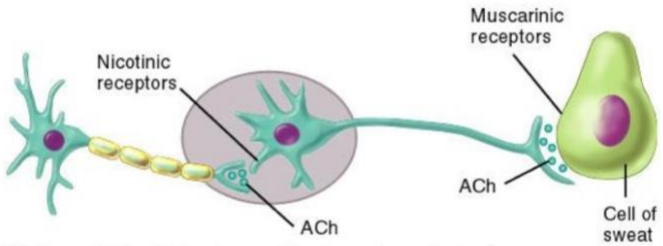
1) The **somatic** fibers release **Acetylcholine**.
2) The **sympathetic** fibers that innervate the adrenal gland release **Acetylcholine**, notice the fibers that innervate adrenal gland don't pass throw any ganglia, so there are no postganglionic fibers.

Note: adrenal gland releases **high** concentration of **epinephrine** and **low** concentration of **norepinephrine** to the blood stream.

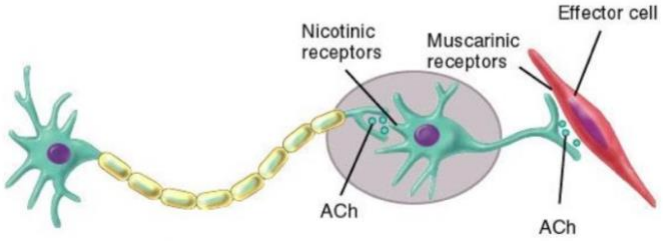




(a) Sympathetic division–innervation to most effector tissues



(b) Sympathetic division–innervation to most sweat glands



(c) Parasympathetic division

Receptors and signal transduction mechanisms

- Receptors are found at postsynaptic or post junctional membranes and they interact with transmitters released from the nerve terminals.
- These receptors function as coding system and they have **high** degree of specificity.
- The nature of response elicited in a particular tissue to a given transmitter is very precise and depends on the properties of receptor and the signaling mechanisms employed in that tissue.

Receptors on effector cells **(different type on each target):**

1) Receptors at ganglion (**parasympathetic and sympathetic**)
2) Muscarinic receptors: receptors on effector cells (**parasympathetic**)
3) Adrenergic receptors: receptors on effector cells (**sympathetic**).

Now we will talk about each one of them in detail (**FOCUS HERE**)

1) **At ganglia:** On **post synaptic (postganglionic)** membrane of sympathetic and parasympathetic there are (**nicotinic**) receptors.

- mentioned in These receptors are excited by **acetylcholine**.
- The drug **nicotine** can also stimulate these receptors.
- This receptor is similar but not identical (**they have different subunit structures**) to nicotinic receptor of the neuromuscular junction.
- This receptor gates ligand gated **Na^+ channel**, Activation of this receptor will cause **depolarization** on postsynaptic membrane, so when the ligand (Ach) binds to it, it opens Na^+ channels and causes depolarization of the post synaptic membrane and action potential is generated.

2) Muscarinic receptors (M1–M5):

- These **cholinergic** receptors lie on effector cells of **parasympathetic** neuro-effector junctions.
- They differ from nicotinic receptors found on ganglia and neuromuscular junction.
- Many muscarinic receptors have been known (M1-M5) at these junctions.
- All these receptors are **coupled to G protein**.

For example**,** the inhibitory receptor that is found in the heart **(M2)** is coupled to **Gi protein**, which **inhibits adenylyl cyclase activity**, which in turn **decreases cyclic AMP** and slows the heart rate.

This Gi protein is also linked to **K^+ channels**, activation of this receptor will **slow** the rate of **depolarization**, so it **decreases** heart rate.

Once Ach binds to M2 receptor it activates a K^+ channel and inhabitation of (T-Ca^{+2}), it will slow the depolarization of the conductive tissue of the heart, that's mean we are decreasing the number of beats per minute .

Note: Other inhibitory muscarinic receptors are negatively coupled via Gi protein to adenylyl cyclase and decrease production of c-AMP.

- The excitatory receptors (**M1, M3, M5**) found on smooth muscle and glands are coupled via Gq protein to phospholipase C. This enzyme increases production of inositol-1,4,5-trisphosphate (IP3), IP3 causes release of Ca^{+2} from internal stores in muscle or glands, causing contraction or secretion.

للاختصار :

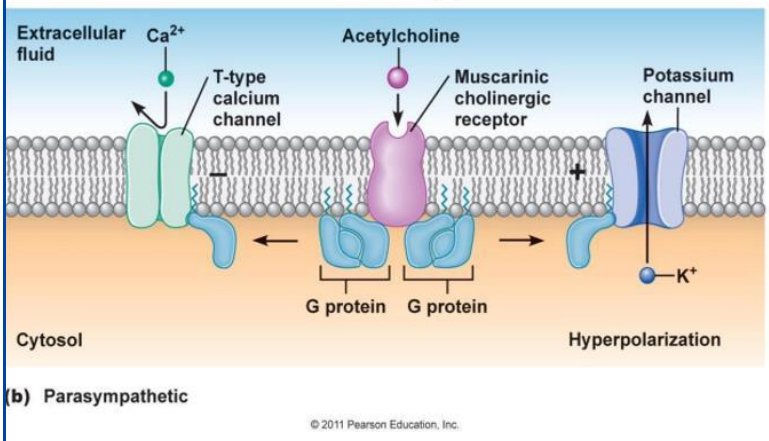
Smooth muscle and glands: Gq protein → stimulation of phospholipase C, increase in IP3 and intracellular (Ca^{+2}).

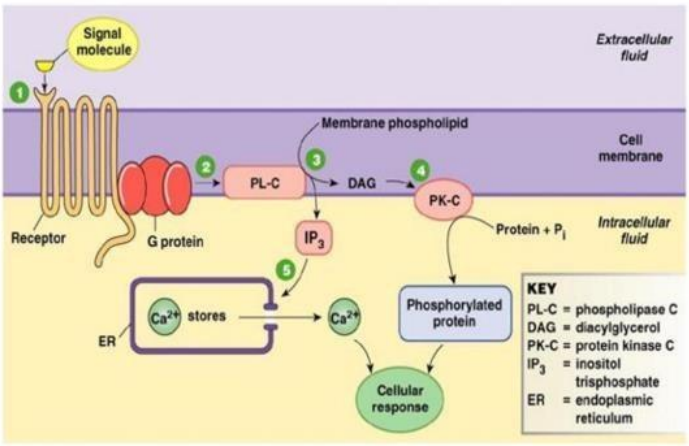
Gq proteins: a family of G-protein that activates phospholipase C.

Phospholipase C: membrane associated enzyme responsible for the cleavage of phospholipids and convert it to DAG and IP3.

The increase of Ca^{+2} causes various response.

Gi→adenylate Cyclase→ reduces cAMP





Note: Nicotinic receptors are stimulated by Nicotine, muscarinic receptors are activated by muscarine which is found in a type of toxic mushroom, if someone has been ingested with it, all muscarinic receptors will be activated.

"Muscarinic receptors" are activated by muscarine and inhibited by atropine.

Agonist: is a chemical substance that binds to a receptor and activates it to produce a biological response (**muscarine and nicotine are agonists for Acetylcholine, but for different receptors**), so when someone gets ingested with muscarine the receptors will be activated and he will develop obvious symptoms.

- The targets of muscarinic receptors' stimulation are illustrated by muscarine poisoning.

These effects include (**activation of muscarinic receptors**):

1) Stimulation of secretory activity: salivation, tearing, sweating, nasal and bronchial secretion.
2) Increase gastrointestinal tract motility: vomiting and diarrhea.
3) Contraction of urinary bladder: urination.
4) Slowing of the heart: Bradycardia.

- These receptors are blocked by atropine from a plant.
  Atropa belladonna which induces reversal effects of muscarinic poisoning.

Effects of atropine include:

1) Inhibition of glandular secretions: dry mouth, dry eyes, and dry nasal passages.

2) Tachycardia (increase heart rate).

3) Loss of pupillary light reflex.

4) Loss of ability to focus the lens for near vision.

Summery :

- Muscarine is an agonist for muscarinic receptors and leads to parasympathetic effects like slowing the heart rate and stimulating glands.
- Nicotine is an agonist for nicotinic receptors and leads to stimulating effects such as increased heart rate, blood pressure, and dopamine release, contributing to its addictive properties. Both muscarine and nicotine mimic acetylcholine's actions, but they affect different types of receptors and produce opposite physiological outcomes.

3) Adrenergic receptors: These receptors respond to catecholamines (epinephrine "EP" and norepinephrine "NE").

- Two types of receptors are known: alpha (**α**) and beta (β) receptors.

Alpha receptors:

The alpha receptors are subdivided into α_1 and α_2 receptors.

- **The alpha 1 (α_1) receptor**: is widely distributed on **smooth muscles** with the exception of **bronchial muscle**.
  NE and EPI are about equally effective on these receptors. Stimulation of this receptor produces **excitation** → This effect involves IP3 production and release of Ca^{+2} from intracellular stores. Some (**α_1 are coupled to Ca^{+2} gated channels**).

- **The alpha 1 (α_1):**
  Excitatory: PLC → IP3

- **Alpha2 receptors:**
  Nerve Adrenergic terminals → reduce NE release.

- **Alpha 2 Heteroreceptors:**
  Non Adrenergic-Gi → Adenylyl

- **Alpha2 receptors**: found on **sympathetic postganglionic nerve** terminals. These receptors are important for self-inhibition of NE release, similar receptors are found on non-adrenergic terminals we call it **"Alpha2 heteroreceptors"**.

- These receptors are negatively coupled to adenylyl cyclase via Gi protein and decrease c-AMP production.

Beta receptors:

These receptors are subdivided into beta1 (β1) and beta 2 (β2) receptors. Both of them are more sensitive to catecholamines than alpha receptors.

- Catecholamines stimulate these receptors at much lower concentration than stimulation of alpha receptors.

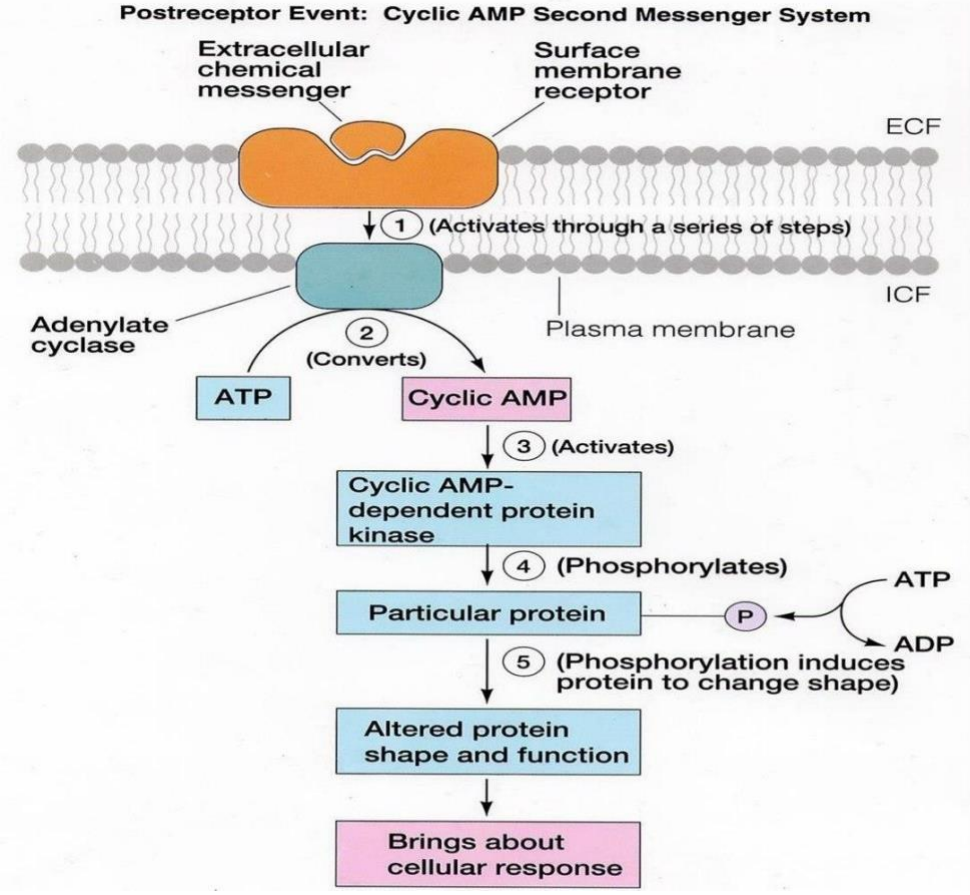
- **Beta 1 (β_1) receptors**: found on heart and produces excitation in the heart.
- **Beta 2 (β_2) receptors**: found on tracheal and bronchial smooth muscle, in the gastrointestinal tract, and on smooth muscles of blood vessels supplying skeletal muscles (**occurs along with alpha 1 receptors**).

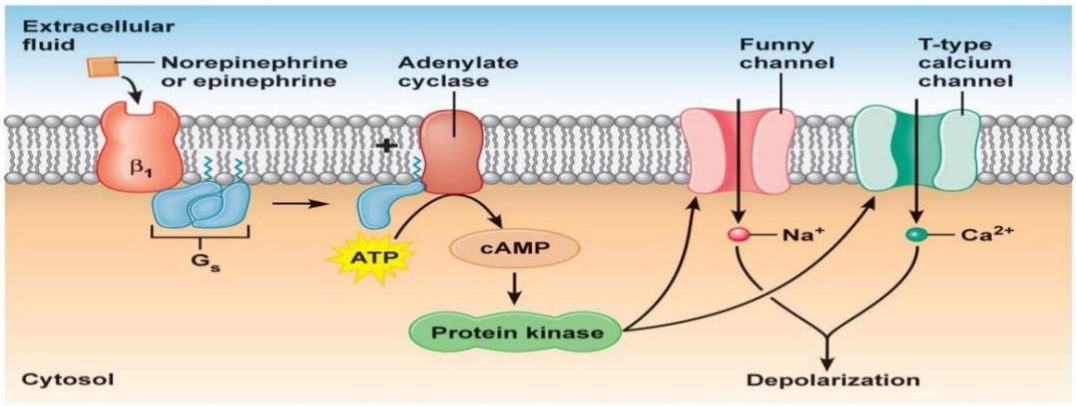
- The β_2 receptors are preferentially activated by EPI rather than NE.

Important note 1: Both receptors are positively coupled to adenylyl cyclase via Gs protein and increase c-AMP, this will result in subsequent activation of protein kinase and phosphorylation of one or more proteins. The response elicited depends on the role of phosphorylated proteins.

Important note 2: All subclasses of adrenergic receptors can be blocked by specific blocking agents (**antagonists**).

- β_1 blockers are useful as antiarrhythmic drugs.
- β_2 selective agonist (**produce activation of β2 receptor**) will dilate bronchi, this agonist is useful in asthma.





(a) Sympathetic

THE END OF SHEET #10

GOOD LUCK :)

Please check on the professor's handout,
Very Important ..

University of Jordan
Faculty of Medicine
Department of Physiology & Biochemistry

Medical and Dental 1st year students**. Introduction to Physiology**

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Textbook of Medical Physiology, Guyton, 14th Ed: 763-773, 13th ed: 773-784, 12th ed: 729-738, and 11th ed. P748-760.

AUTONOMIC NERVOUS SYSTEM (ANS):

This nervous division is anatomically distinct from the motor somatic nervous system, which innervates skeletal muscle. This group of efferent paths originates from the central nervous system and innervates heart, smooth muscle, glandular tissue and enteric nervous system. ANS has two subdivisions, sympathetic and parasympathetic, which together perform the following functions on effector tissues they innervate.

1. Regulation of the activity of visceral organ systems:
   examples of functions under ANS control include:
   - heart rate
   - arterial blood pressure
   - digestion, intestinal motility, secretions (these functions are controlled in conjunction with hormones.
   - emptying of urinary bladder
   - secretory activity of respiratory tract and airways resistance (by regulation of diameter of bronchioles).

By regulation of these functions, ANS plays an important role in maintaining constancy of internal environment (homeostasis).

2. Rapid responses to specific environmental stimuli,
   these include:
   - Light: constriction of the pupil to bright light (miosis), and dilation of pupil to low light (mydriases).
   - Temperature: cutaneous vasodilation and sweating in a warm environment, and vasoconstriction in cold.
   - Stress: The ANS (mainly the sympathetic and the adrenal medulla) mediates the immediate response (fight or flight response) to threatening stimuli. This involves a series of well coordinated responses to meet the metabolic demands for severe physical exertion. The features of this response include:

- increase heart rate and force of contraction.
- Widely dilated pupils.
- Pallor (pale of fear) as blood is directed to the skeletal muscle.
- Goose pimple.
- Cold sweat.
- Dry mouth.

Characteristics of autonomic responses:

1. Speed of onset: ANS can produce dramatic changes in the level of activity of organs they innervate within seconds. Changes in heart rate, sweating, goose pimples, and rise or fall in blood pressure can take place within few seconds (3-5 sec).

2. Automatic nature: regulation of visceral functions occurs **without conscious control**. Some functions are brought under voluntary control such as urination and defecation through the participation of voluntary muscles. The impulses in ANS to target organs are set up **reflexively** in response to specific type of sensory information. The reflex responses are sensitive to emotional states of the body. Stress, excitements, euphoria, fear, anxiety or anger can influence reflexes and induce a variety of symptoms, such as sweating, palpitation, or digestive disturbances.

3. Tonic activity: The ANS fires continuous impulses to target organs at very low rate. The basal rate of firing is called "sympathetic tone" and "parasympathetic tone". These tones establish basal rate of contractile activity in smooth muscle cells, and secretory activity of glandular tissues. The activity of these effector cells can be changed as a result of an increase or a decrease in the activity of any divisions of the ANS.

Physiological anatomy:

Two neurons carry impulses of the ANS from the CNS to the effector organs. The first is known as **preganglionic neuron**, the cell

body is located in the CNS (in appropriate nucleus in the brain or in the lateral gray of the spinal cord). The fibers of preganglionic are small and myelinated, and usually end within a ganglion where they synapse with the second neuron called **postsynaptic neuron**. The second neuron (postsynaptic) carries impulses to target organ.

DIVISIONS OF ANS:

There are two divisions of the ANS sympathetic and parasympathetic autonomic nervous systems.

Sympathetic nervous system:

The cell bodies of preganglionic neurons lie in lateral gray of spinal cord at segmental levels of T1 through L3. Axons leaves spinal cord via ventral roots, then leave ventral root via white rami communicans to enter a vertebral ganglion of the sympathetic chain at the same segmental level. The preganglionic axon then can:

* Synapse with postganglionic cells at the **same segmental level**.

* Turn cranial or caudal and synapse with sympathetic postganglionic neuron at **higher or lower segmental level.** Synapse may occur at more than one postganglionic neuron.

After synapse with neurons at paravertebral ganglia, axons of second neurons leave ganglia via gray rami communicans to return to the corresponding spinal nerve.

* Some preganglionic fibers that enter ganglia **pass without any synapse** at the paravertebral ganglia and continue to some ganglia located in the abdomen known as **prevertebral ganglia**, where they have the synapse with the second neuron. There are three unpaired prevertebral ganglia: celiac, superior mesenteric and inferior mesenteric ganglia.

* Some preganglionic fibers pass without synapse in paravertebral ganglia and celiac ganglion. These fibers continue to adrenal gland where they synapse onto chromaffin cells. These cells liberate epinephrine into blood stream.

Synaptic organization of sympathetic ganglia:

Individual postsynaptic neuron in vertebral ganglia can receive signals from many preganglionic fibers (**convergence**) and one preganglionic neuron can relay impulse to many postganglionic neurons at different segmental levels (**divergence**). This organization of the sympathetic system induces widespread effects on target cells innervated by sympathetic postganglionic fibers.

Parasympathetic nervous system:

The preganglionic fibers arise in appropriate cranial nuclei and in segments S3 and S4 (sometimes S2, S5 also). These fibers leave the CNS in the III, VII, IX, and X (vagus) nerves for fibers of cranial origin and in pelvic nerve for fibers of sacral origin. The preganglionic fibers are long and go all the way to the effector organ where they synapse with the second postganglionic neuron located within the tissue of the effector organ or to a ganglion located very close to the effector organ. The axons of postsynaptic neurons are short.

Synaptic organization of parasympathetic nervous system:

In parasympathetic there is no or little branching of preganglionic fibers (divergence). The ratio of pre to post ganglionic neurons is 1:1 or 1:2. As a result of this arrangement, the parasympathetic actions tend to be more discrete and confined to the innervated organ.

Organization of the autonomic neuroeffector junction:

The terminals of autonomic nerve fibers are unlike terminals of the somatic motor fibers (skeletal neuromuscular junction). The autonomic terminals are highly branched forming extensive network of fibers beaded with small swellings or varicosities. These varicosities are sites from where transmitter is released.

The receptors on effector cells are scattered widely over the innervated organ. Unlike skeletal muscle, there is no specialized receptive region at the effector cell. The effect of ANS on these cells can be stimulatory or inhibitory. This effect depends on transmitter type, receptor subtype and changes in functional proteins induced in cell by binding of transmitter to its receptor.

Effects of sympathetic stimulation:

Sympathetic system innervates widely distributed tissues. These include, *sweat glands, smooth muscle cells of blood vessels* supplying skeletal muscle, skin, etc, *smooth muscle cells of hair follicles*. This innervation is consistent with diffuse projections of the sympathetic postganglionic fibers that originate in vertebral ganglia and distribute with the spinal nerves.

In human, **the previously mentioned target tissues do not have any parasympathetic innervation**. Thus, the sympathetic which has excitatory effects on these tissues regulates:

- Blood pressure (blood vessels supplying skeletal muscle are major players). In addition to that the effect on heart also contributes in regulation of blood pressure.
- Body temperature by the sympathetic effects on cutaneous blood vessels and sweat glands.

In addition to its effect on widely distributed tissues, sympathetic system is involved in handling **stress responses** (fight or flight reaction). Together with adrenal gland, the sympathetic system is designed to promote the production of energy for muscular work and to shut down organs which have nonessential functions in reaction to stressful situations. These effects on the following systems include:

- Cardiovascular system: effects on vessels will result in redistribution of blood by enhancing blood flow to skeletal muscle and reducing blood flow to skin and mesentery.

  Effects on heart: increasing cardiac output (volume of blood pumped per minute).
- Respiratory system: causes relaxation of bronchial muscle which result in bronchodilation.
- Digestive system: inhibition of motility and secretion.
- Metabolic effects:
  - Mobilization of glucose.
  - Increased lipolysis.
  - Increased metabolic rate.

Effects of parasympathetic stimulation:

Overall, the parasympathetic, in contrast to sympathetic system is viewed as regulator of activities involved in replenishment of energy supply and general maintenance of the organism.

The control provided by parasympathetic system is discrete and selectively directed to individual organs.

The types of actions produced by parasympathetic stimulation include:

- Gastrointestinal system: increases motility and secretory activity.
- Glands: increases secretory activity (but remember sweat glands are under sympathetic control).
- Heart: decrease rate of contraction (bradycardia).
- Pupil: control pupil diameter by papillary light reflex (miosis) (regulates the amount of light falling on retina).
- Accommodation of the lens for near vision.
- Voiding the urinary bladder (micturition).

MOLECULAR BASIS OF PHYSIOLOGICAL ACTIONS OF THE ANS:

Transmitters:

At ganglion: preganglionic neurons of both sympathetic and parasympathetic release **acetylcholine** (Ach).

At effector organs:

- Post ganglionic terminals of parasympathetic fibers release **acetylcholine**.

- Post ganglionic terminals of sympathetic fibers release **norepinephrine**. An exception for sympathetic nerves to sweat

glands, which release **acetylcholine** (Ach).

The released Ach by parasympathetic system is inactivated by breakdown by *acetylcholinesterase*. Epinephrine is inactivated by recapture by postganglionic nerve varicosities.

Receptors and signal transduction mechanisms:

Receptors are found at postsynaptic or post junctional membranes and interact with transmitters released from the nerve terminals.

These receptors function as coding system and they have high degree of specificity. The nature of response elicited in a particular tissue to a given transmitter is very precise and depends on the properties of receptor and the signaling mechanisms employed in that tissue.

Receptors at ganglion:

On post synaptic membrane of sympathetic and parasympathetic there are **nicotinic receptors**. These receptors are excited by acetylcholine. The drug nicotine can also stimulate these receptors.

This receptor is similar but not identical (they have different subunit structures) to nicotinic receptor of the neuromuscular junction. This receptor gates ligand gated Na+ channel. Activation of this receptor will cause depolarization on postsynaptic membrane.

Receptors on effector cells:

- Muscarinic receptors:

These cholinergic receptors lie on effector cells of parasympathetic neuro-effector junctions. They differ from nicotinic receptors found on ganglia and neuromuscular junction.

Many muscarinic receptors have been known (M1-M5) at these junctions. All these receptors are coupled to G protein.

- The inhibitory receptor that is found in the heart (M2) is coupled via G protein to K+ channels. Activation of this receptor will slow the rate of depolarization.

- Other inhibitory muscarinic receptors

are negatively coupled via Gi protein to adenylyl cyclase and decrease production of c-AMP.

- The excitatory receptors (M1, M3, M5) found on smooth muscle and glands are coupled via Gq protein to phospholipase C. This enzyme increases production of inositol-1,4,5-trisphosphate (IP3). IP3 causes release of Ca++ from internal stores in muscle or glands, causing contraction or secretion.

These receptors are activated by muscarine and inhibited by atropine.

The targets of muscarinic receptors' stimulation are illustrated by muscarine poisoning. These effects include:

- stimulation of secretory activity: salivation, tearing, sweating, nasal and bronchial secretion.
- Increase gastrointestinal tract motility→ vomiting and diarrhea.
- Contraction of urinary bladder →urination.
- Slowing of the heart →Bradycardia.

These receptors are blocked by **atropine** from a plant *atropa belladona* which induces reversal effects of muscarinic poisoning.
Effects of atropine include:

- Inhibition of glandular secretions→ dry mouth, dry eyes, and dry nasal passages.
- Tachycardia. (increase heart rate).
- Loss of pupillary light reflex.
- Loss of ability to focus the lens for near vision.

- Adrenergic receptors:

These receptors respond to **catecholamines** (epinephrine (EP) and norepinephrine (NE)).

Two types of receptors are known alpha (α) and beta (β) receptors.

Alpha receptors:

The alpha receptors are subdivided into α_1 and α_2 receptors.

The **alpha 1 (α_1)** receptor is widely distributed on smooth muscles with the exception of bronchial muscle. NE and EPI are about equally effective on these receptors.

Stimulation of this receptor produces excitation. This effect involves IP3 production and release of Ca++ from intracellular stores. Some **(α_1** are coupled to Ca++ gated channels).

Alpha2 receptors: are found on sympathetic postganglionic nerve terminals. These receptors are important for self inhibition of NE release.

Similar receptors are found on nonadrenergic terminals are called Alpha2 heteroreceptors.

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Additional Resources

رسالة من الفريق العلمي:

عن أبي ذر ـ رضي الله عنه ـ قال : قال رسول الله ـ صلى الله عليه وسلم ـ: (إني لأعلم آخر أهل الجنة دخولا الجنة، وآخر أهل النار خروجا منها، رجل يؤتى به يوم القيامة، فيقال: اعرضوا عليه صغار ذنوبه، وارفعوا عنه كبارها، فتعرض عليه صغار ذنوبه، فيقال: عملت يوم كذا وكذا، كذا وكذا، وعملت يوم كذا وكذا ، كذا وكذا ، فيقول نعم ، لا يستطيع أن ينكر، وهو مشفق من كبار ذنوبه أن تعرض عليه، فيقال له: فإن لك مكان كل سيئة حسنة، فيقول: رب قد عملت أشياء لا أراها ها هنا، **فلقد رأيت رسول الله!** ـ صلى الله عليه وسلم ـ ضحك حتى بدت نواجذه (أضراسه) رواه مسلم .

صلِّ اللهمّ على حبيبنا وعلى آله ومُنّ علينا برؤيةِ وجهه في جناتِ النعيم

For any feedback, scan or click the code.

Versions	Slide #	Before	After
V0 → V1			
V1 → V2			