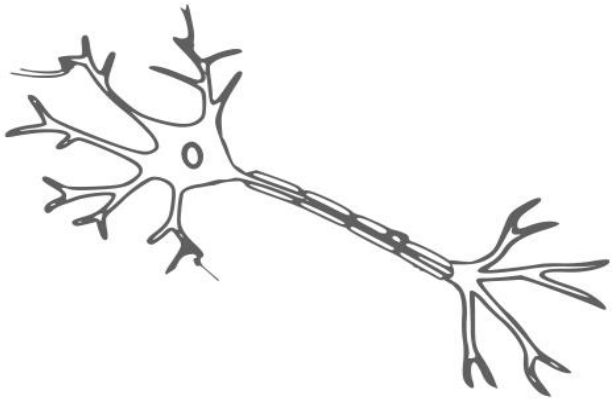
Physiology



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ANS

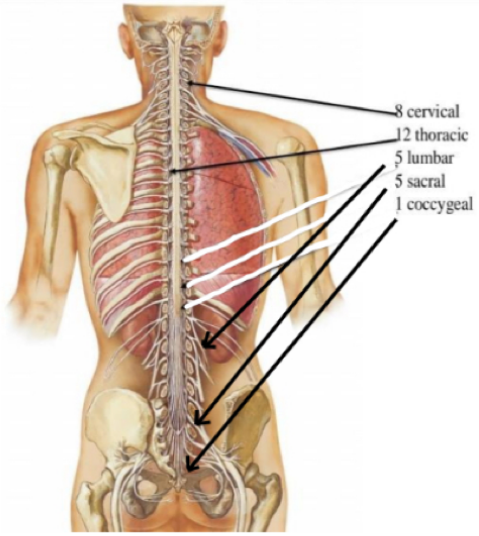
AUTONOMIC NERVOUS SYSTEM

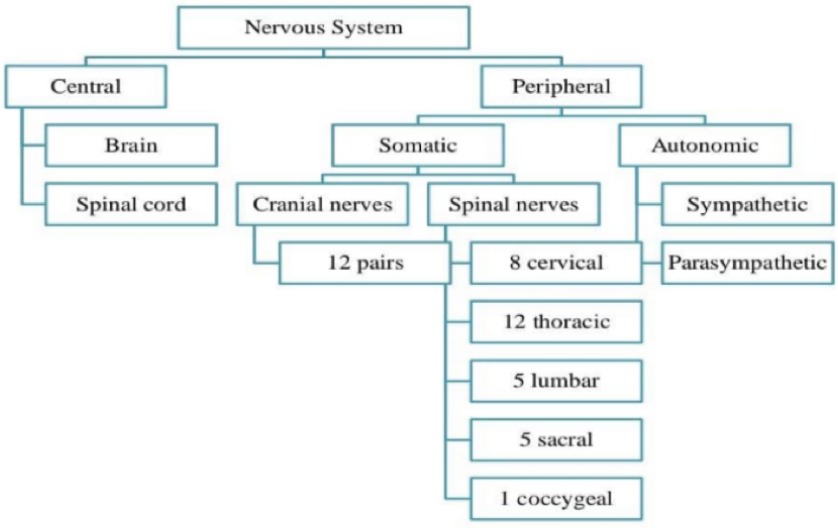
LECTURES 8 & 14

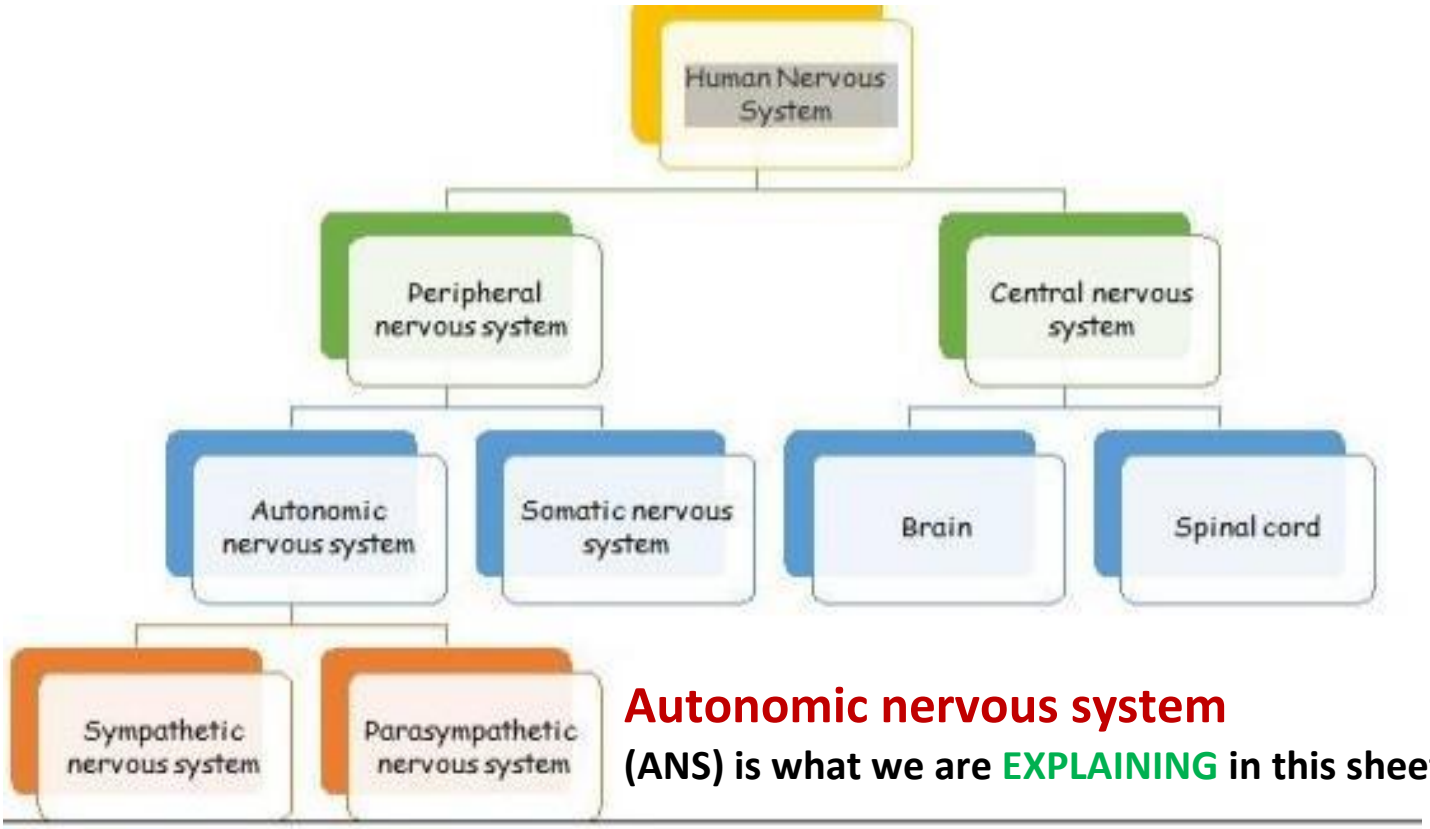
READ ONLY ///

What is the nervous system?

Your nervous system guides almost everything you do, think, say or feel. It controls complicated processes like movement, thought and memory. It also plays an essential role in the things your body does without thinking, such as breathing. The nervous system is the major controlling, regulatory, and communicating system in the body. Together with the endocrine system, the nervous system is responsible for regulating and maintaining homeostasi .In vertebrates it consists of two main parts, the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS consists of the brain and spinal cord. The PNS consists mainly of nerves, that connect the CNS to every other part of the body. The PNS is divided into the somatic, and autonomic nervous systems. The various activities of the nervous system can be grouped together as general, overlapping functions: Sensory & Motor. At the most basic level, the function of the nervous system is to send signals from one cell to others, or from one part of the body to others. Nerves that transmit signals from the brain are called motor nerves , while those nerves that transmit information from the body to the CNS are called sensory nerves .







Autonomic nervous system
(ANS) is what we are EXPLAINING in this sheet

Autonomic nervous system: Portion of the nervous system that controls most of the visceral functions of the body.
examples of functions under ANS control in general:
- Heart rate - Arterial blood pressure - Emptying of urinary bladder
- Digestion, intestinal motility, secretions (these functions are controlled in conjunction with hormones).
- 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).

The body tries to adapt and control the changes that happen and affect the homeostasis (either internal or external) most of these changes are controlled by ANS, for example:
- 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.

All of these adaptations (deals with changes) in our body are controlled through the ANS.

Autonomic system

Sympathetic

(SNS) (fight or flight)

The origin is the thoracic and lumbar region "**thoracolumbar**" T1-L3

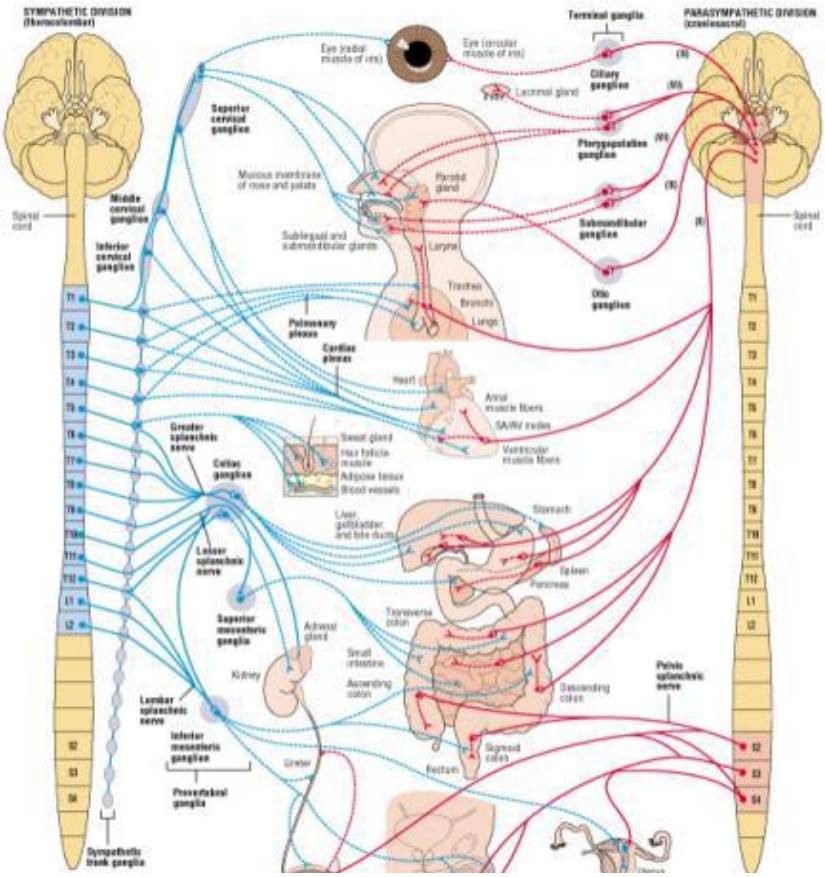
Parasympathetic

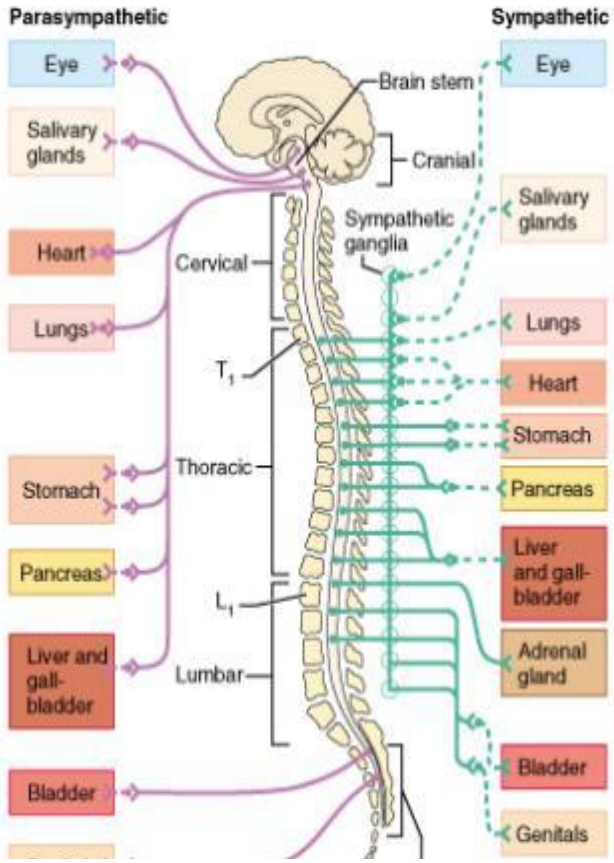
(PSNS) (rest and digest)

The origin is the brain and sacral region"craniosacral"

Cranial 3,7,9,10

Sacral 3,4 (sometimes 2,5)





There are **different origins** for both divisions to provide a huge control for a lot of systems and allow the body to adapt with internal and external changes.

There are some charecteristics for both sympathetic and parasympathetic nervous systems:

1- Speed of onset: ANS can make changes in the activity of the organs it innervates within seconds (3-5), because you must respond in a fast way if you are facing a danger.

2- Automatic nature: you cann't control the activity of the organs that are innervated by the ANS, they are being controlled without your consciuos using involuntary muscles, but the urination process is an exeption, because it has some voluntary muscles.

3- Tonic activity: Increasing or decreasing generation of action potential

Tonic = generation of action potential

That means we haven't zero activity in any time but the level of activity can increase or decrease , so we have certain level for (PSNS) and (SNS)

EXAMPLE OF ADAPTING WITH CHANGES IN EXTERNAL ENVIRONMENT:

Imagine that you are in a forest and you face a bear, so you have two choices: fight or run (flight). In the previous scenario, the body is going to increase **the breathing** to supply the muscles (heightening the rate of **CO2 and O2 exchange**). Also speeds up **metabolic reactions** to generate more nutrients to supply the whole body. (carbs and other energy-rich macromolecules breakdown will increase). Generally, **"fight or flight"** reactions are group of reactions that take place in body response to face the terrifying things or for getting stressed (harmful stimulus), in addition they push the body to speed up its metabolic processes, as well as the following reactions:

******Sympathetic (fight or flight) Example of adaptation to external stimuli (Fight and Flight Reaction)******

1– increasing heart rate and force of contractions; to deliver more blood to cells.

2 – mydriasis, (dilation of pupils).

3 – pallor (pale of fear): paling of the face or the skin; happens as a result of decreasing the amount of blood that goes to the skin. In "fight and flight" reactions the blood circulation is redistributed (higher amount of blood is directed to muscles, lower amount is directed to skin and unnecessary tissues in the response. (vasodilation for muscles blood vessels and vasoconstriction for unnecessary tissues' vessels).

4 – goose pimpling: contraction of the smooth muscles that are found in the root of the hair which causes hair erection.

5 – cold sweat (it is cold because of the low amount of blood that is delievered to the skin)

6 – dry mouth: inactivation of salivary glands THE BODY is trying to shut down all unnecessary tissues by vasoconstriction the blood vessels that supplies these tissues.

Briefly - Increases cardiac output - Accelerates respiratory rate - Releases stored energy and dilates pupils – Inhibits body processes that are less important in emergencies such as digestion and urination.

Important terminology:

1 – **Ganglion**: Nerve cell cluster, where neurons are typically linked by synapses. Also, it`s the border line between preganglionic and postganglionic and where they synapse.

2 – **Preganglionic = presynaptic = first neuron**: the neuron which extends from Central nervous system to its synapse with second neuron.

3 – **Postganglionic = postsynaptic= second neuron**: the neuron that extends from the ganglion to the effectors (usually organs) .

4 – **Paravertebral ganglion**: ganglion that presents near the vertebral column, found in sympathetic nervous system only.

5 – **Prevertebral ganglion**: ganglion that presents apart from the vertebral column near the effectors (usually organs in abdomin), found in sympathetic nervous system only, and they are only three: - celiac ganglion. - superior mesenteric ganglion. - inferior mesenteric ganglion

6 – **Terminal ganglion**: ganglia that are found in the effected organ, only found in parasympathetic nervous system.

NOW LETS START WITH Anatomical characteristics and Synaptic organization of ANS .

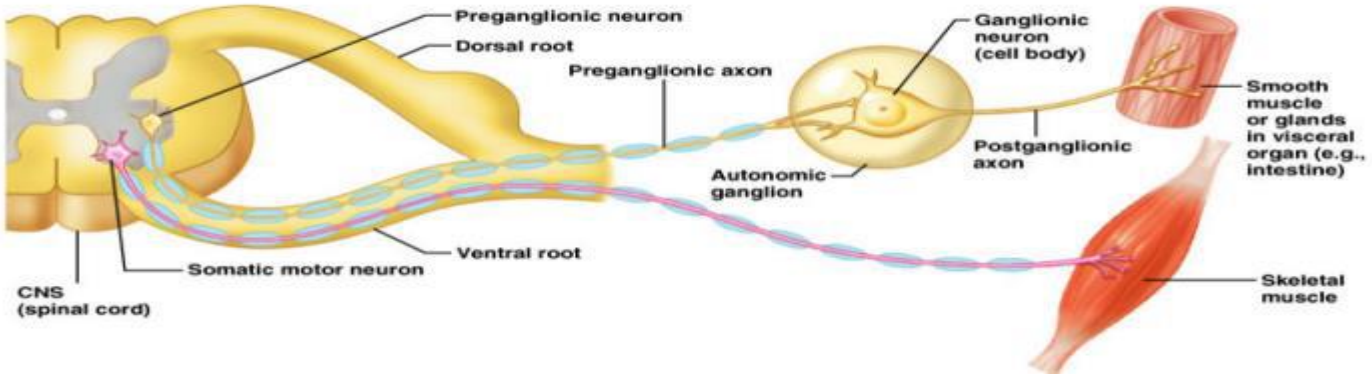
The axon from the origin until the effective structure is composed of two neurons:

1. **First neuron**: come from the spinal cord and ends in the ganglia.

2. **Second neuron**: innervates the functional organ of our body, starts from the ganglia until it reaches the organ.

And we have synapses of 1stneuron with 2nd neuron, located at the gangliaV

NOTE // Ganglia : It is a cluster of the cell bodies of neurons.



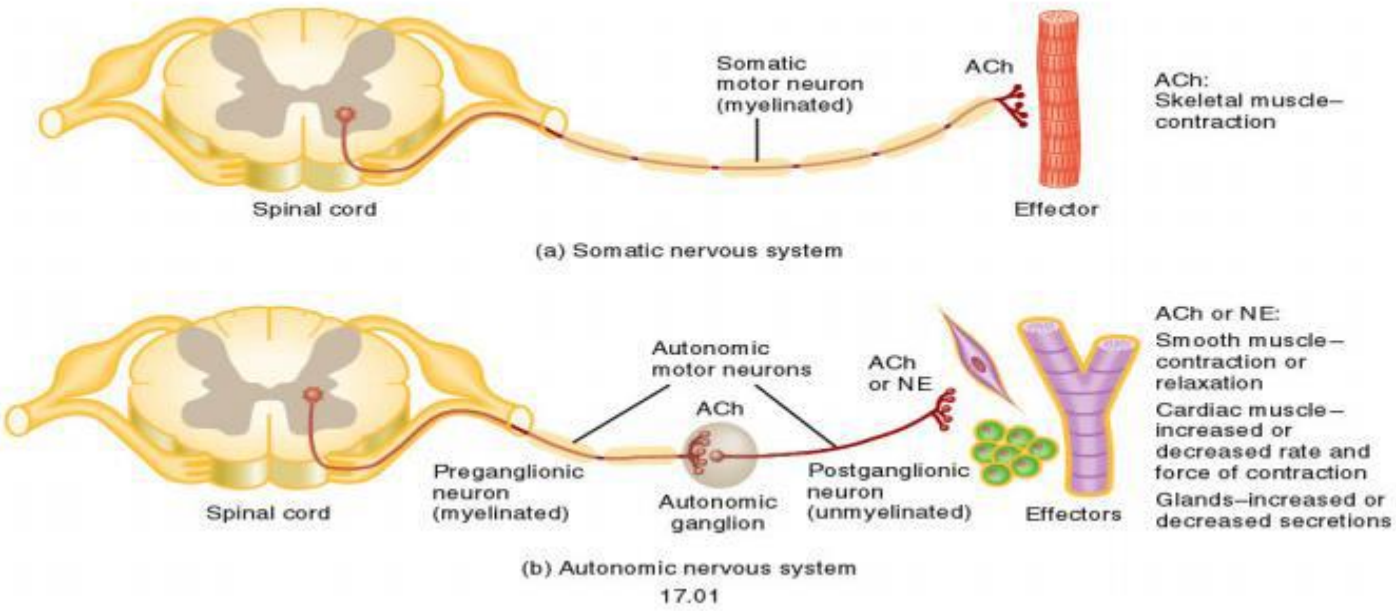
We can see the difference between the somatic neuron and the ANS nuron In the picture above, the somatic is composed of only one fiber, but the autonomic has two fibers, preganglionic and postganglionic.

Parasympathetic (rest and digest) Some difference between SNS and PSNS :

-In SNS, the preganglionic nerve fiber is short and the postganglionic one is long, and this makes the divergence and convergence processes easier.

-In PSNS, the preganglionc nerve fiber is long, and the postganglionic one is short, and this is why we don't have divergence or convergence here.

-remember that the origin is another different between them.



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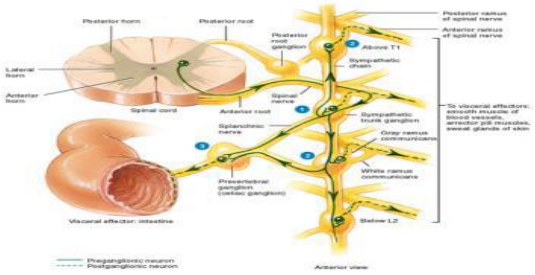
This represent ganglion where we have the synapses between the postganglionic and preganglionic neurons (in autonomic), and the cell bodies of the postganglionic neurons are located in ganglion which is different from the somatic system .
The somatic system is having cell body at the level of spinal cord (like the motor neuron), long axon towards the effector structure, which is skeletal muscles, and the synapse between the terminal of somatic neuron and effected structure (nuoro-muscular junction).
We don't have ganglion along the somatic nerve system but we have along autonomic.

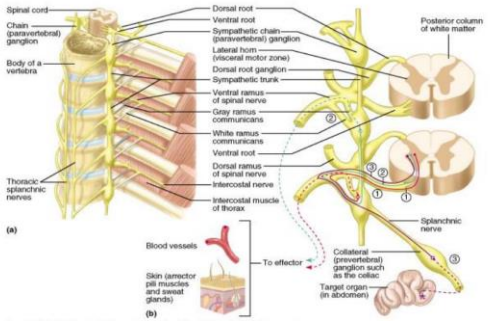
Convergence and divergence in sympathetic:

In **convergence**: the cell body of the postganglionic neuron can receive signals from more than one preganglionic neuron. In **divergence** the preganglionic neuron can synapse with more than one postganglionic neuron.

NOTE / ***The question is why we want to have one preganglionic synapses with more than one postganglionic, and vice versa? Because in "fight or flight" reactions the body wants to accelerate the reactions of the targeted effectors, and they give a push to these reactions . In parasympathetic preganglionic and post ganglionic are 1:1 or maximum 2:1 because each change in PANS is localized and specified to a targeted organ, not like SANS.***

The axon of the preganglionic neuron does not have only one terminal, it can have many terminals, some of them will synapse with the postgangilionic neurons at the same segmental level, or it may curve downward or upward to synapse with a postganglionic neuron from a lower or hugher segmental level.





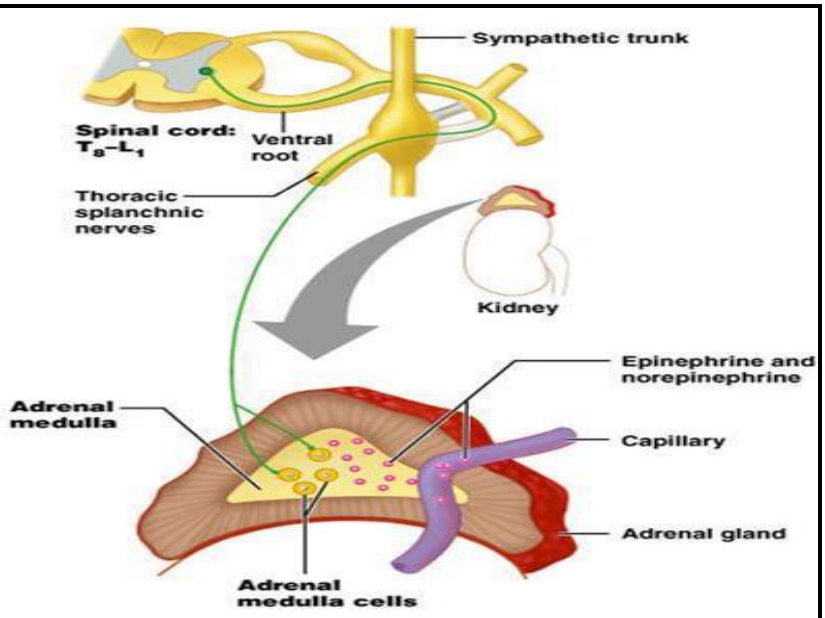
This neuron can have some neurons from this significant level so we have a lot of convergence while in parasympathetic you have long axon tour

The responses to parasympathetic stimulation are localized responses while to sympathetic are more generalize responses .
This because of the origination of the fiber , we have more divergence and convergence in the sympathetic system which are depend more diffuse in the responsible stimulation , while for the parasympathetic stimulation you have more drifted responses and related to organ themselves .
Ex. When the food retching to the small intestines, you are getting more activity in the small intestines and reducing the activity in the stomach , so we have limited responsible to parasympathetic system .

Adrenal medulla=
adrenal gland =
suprarenal gland:

mainly secretes epinephrine (adrenaline).And norepinephrine (noradrenaline)

*****one neuron passes to the effector without any synapse (Synapse in gland)*****



Effects of sympathetic stimulation :

NOTE// we have some tissue in our body which are widely distributed tissue such as (vessels and sweat glands) .

These widely distributed tissues are need a systemic which can diffuse effect .
these structure innervation only by sympathetic system .
we don't have parasympathetic control over these function structure .

1. **Blood pressure** , There are many things involved in regulating blood pressure (vessels , hormones, function of the heart itself and the body fluid) We'll focus on diameter of vessels … Sympathetic is the major in the control of the diameter of vessels by cause of vessels friction which lead to decrease of blood pressure , so the tissue are widely distributed tissue .

2. **Body temperature** , by the sympathetic effects on cutaneous blood vessels and sweat glands appears as a result of vasodilation and vasoconstriction
Dilation—losing temperature—sweating (cold sweat)
Constriction—fixing temperature—no sweating.

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** , by increasing heart rate , causing more powerful contraction (increasing the force of contraction) which lead to more blood distributed to our tissue , more oxidation of these tissues and increasing "cardiac output" : is the amount that can be measured (volume of blood pumped per minute)

5. **Respiratory system** ,causes relaxation of bronchial muscle which result in bronchodilation,getting more oxygen to the smooth muscles ,we needing more air flow .

6. **Digestive system** , inhibition of motility and secretion, one of the aspect is dry mouth .

7. **Metabolic effects** , metabolic simply is break down of glycogen to more glucose become available in body fluid , by (SNS) : mobilization of glucose , Increased lipolysis and Increased metabolic rate .

Effects of Parasympathetic stimulation :

1.**Gastrointestinal system** , increases motility and secretory activity.

2.**Glands** , increases secretory activity (but remember sweat glands are under sympathetic control).

3. **Heart** , decrease rate of contraction (bradycardia). At conductive tissue ! We have slow depolarization contraction potential by increasing parasympathetic stimulation , the rate of slow depolarization become more slow , so in this case the number of action potential generation per minute will be less in this by the parasympathetic stimulation. While by sympathetic stimulation we have increasing the rate of slow depolarization and we got more frequent generation of action potential.

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

5.Accommodation of the **lens** for near vision.

6.Voiding the **urinary bladder** (micturition)

MOLECULAR BASIS OF PHYSIOLOGICAL ACTIONS OF THE ANS:

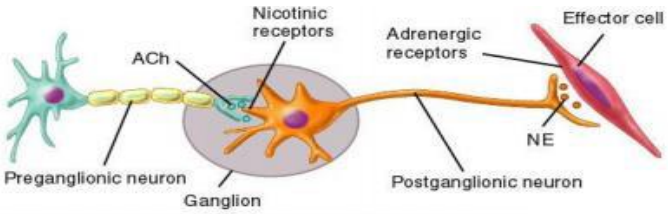
• We know now that the preganglionic neurons synapse with the postganglionic neurons in the ganglia, and then the postganglionic neurons interact with different effectors to induce different actions in the body.

So, what type of neurotransmitters that these neurons release?

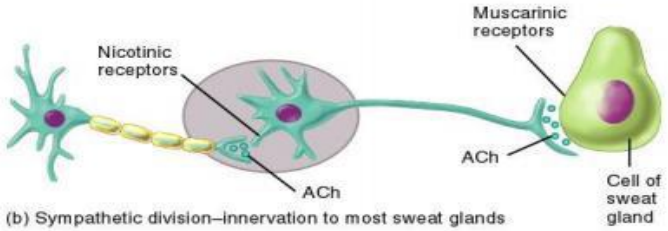
First, at ganglion: preganglionic neurons of **both *sympathetic and parasympathetic*** release **Acetylcholine (Ach)** and causing activation of the second neuron (the postganglionic neuron).

Now, while the second neuron is active….the ***parasympathetic postganglionic neurons*** release also **Acetylcholine** to the effector cells.

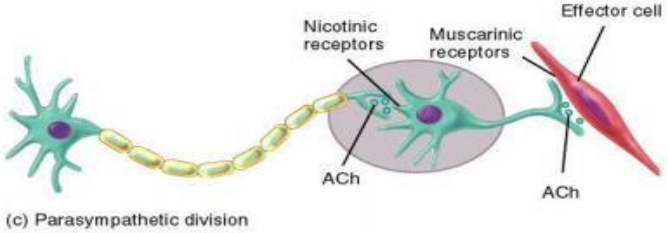
While the ***postganglionic neurons of sympathetic*** release **norepinephrine** to the effector cells ***except*** the postganglionic neurons that innervates sweat glands and piloerector muscles (small muscles attached to hair follicles), they release **Ach** Instead **of norepinephrine.**



(a) Sympathetic division–innervation to most effector tissues



(b) Sympathetic division–innervation to most sweat glands



(c) Parasympathetic division

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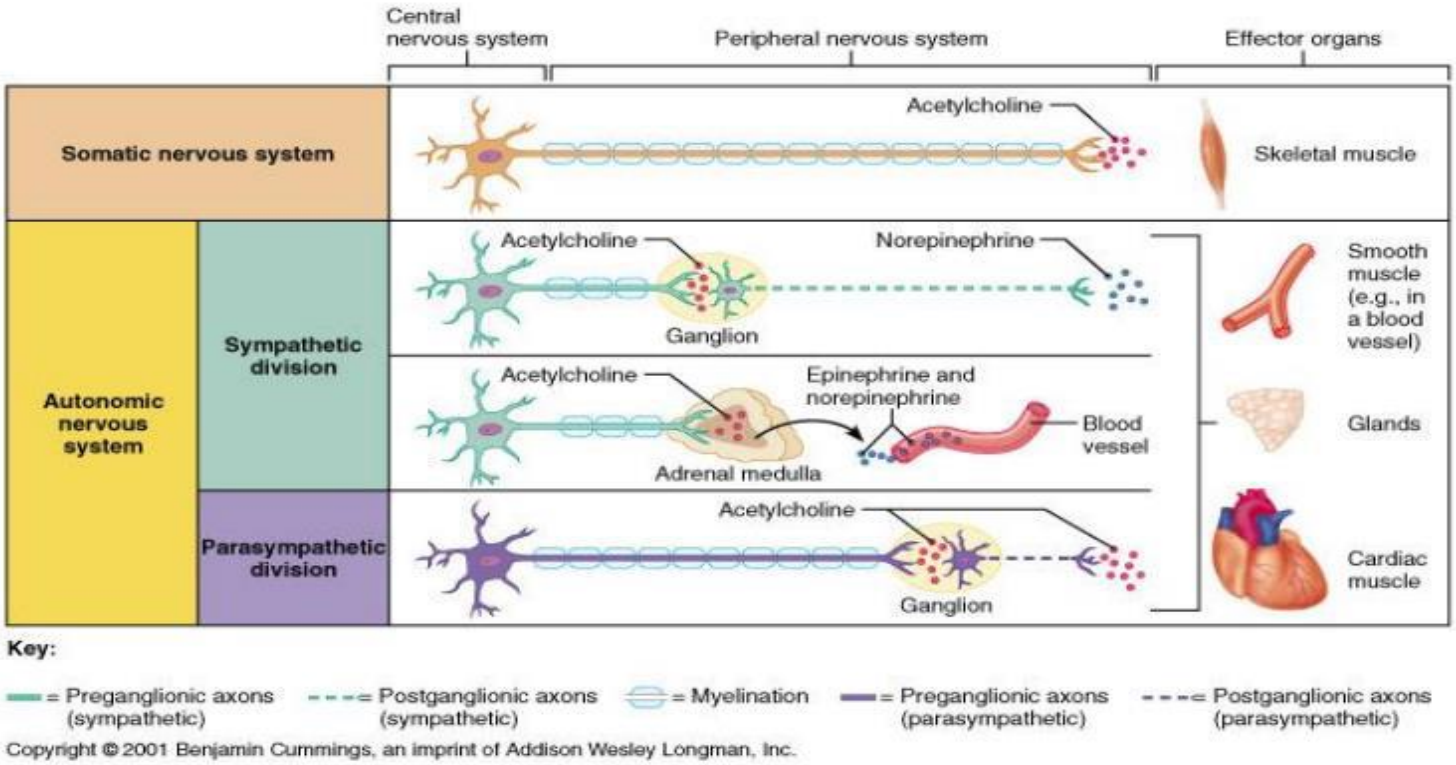


•Note from this picture that the somatic fibers also release Acetylcholine like the parasympathetic fibers, and the sympathetic fibers that innervates the suprarenal gland (adrenal gland) release Acetylcholine.

The fibers that innervate adrenal gland don't pass throw any ganglia….so there are no postganglionic fibers.

Keep in mind that adrenal gland is an endocrine gland that releases high concentration of epinephrine and low concentration of norepinephrine to the blood stream.

These neurotransmitters must have receptors located on their targets, these **receptors** are:

1) Receptors on the postganglionic neurons (at ganglia) are called nicotinic receptors.
2) Receptors on the parasympathetic targets are called muscarinic receptors.
3) Receptors on the sympathetic targets are called adrenergic receptors.

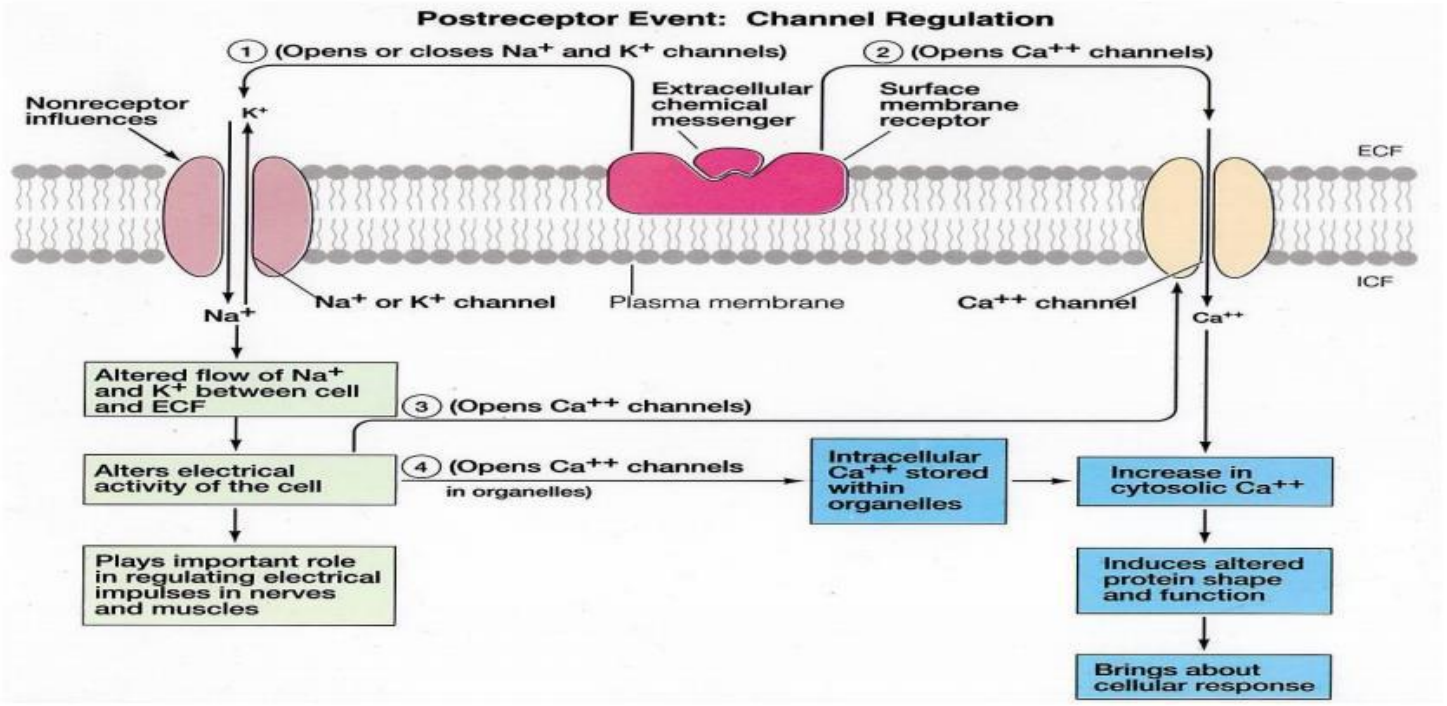
RECEPTORS AND SIGNAL TERANSDUCTION MECHANISMS

1) Receptors at ganglion (nicotinic receptor)

❖ On postganglionic 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 binds to ligand gated Na+ channel. Activation of this receptor will cause depolarization on postganglionic membrane.



In the ganglion, the nicotinic receptors are linked -via G-proteins- to the sodium channels.

So the signal transduction mechanism here:

Activation of nicotinic receptors

→ ***activation of the Na+ channels***

→ ***Depolarization of the postsynaptic membrane***

→ ***Action potential***

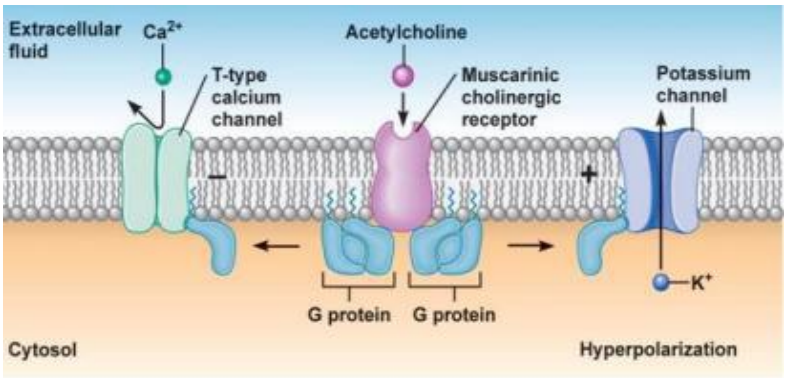
2) muscarinic receptors

These cholinergic receptors lie on the 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 so decreasing cyclic AMP and slowing the heart rate (we will talk about the mechanism of that later on) this Gi protein is also linked to K+ channels, activation of this receptor will slow the rate of depolarization.

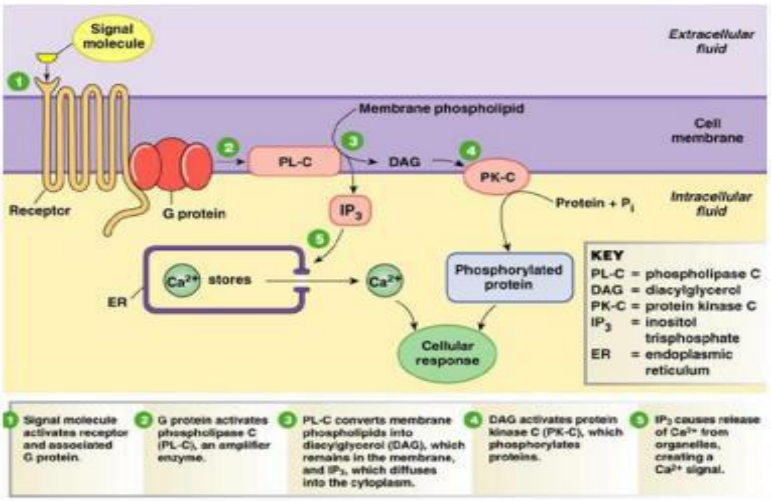
This is a muscarinic receptor(M2), once ACH bind to the receptor, it can cause activation of potassium channels and inhibition of the T-type calcium channels, so the slow depolarization of the heart conducive tissue becomes even slower (we have less number of beats per minute), which leads to decrease in the heart rate



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

Gq proteins: a family of the heterotrimeric G-protein alpha subunits.

While we have M2 receptor that is considered as inhibitory receptors, we have also another sub-types that are excitatory receptors which are (M1,M3,M5) receptors that are found on smooth muscle cells and glands, these receptors are linked to Gq proteins to activate phospholipase C



❖ ❖ ***Due to the activation of phospholipase C, the concentration of the IP3 in the cytosol increases, which causes the release of Ca2+ from its stores and the ER.***

❖ ***The increase in Ca+2 causes various responses, like muscle contraction.***

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

****** Remember: Agonist is a chemical that binds to a receptor and activates the receptor to produce a biological response. (muscarine and nicotine are agonists for Acetylcholine but for different receptors)***

• **This type of toxic mushroom is rich in muscarine, and ingesting it causes activation of all muscarinic receptors, and patients will develop a lot of obvious signs and symptoms like:**

1) Stimulation of secretory activity→ salivation, tearing, sweating nasal and bronchial secretions, pupil constriction [Miosis].

2) Contraction of urinary bladder → urination

3) Increase in the gastrointestinal tract motility, which causes vomiting and diarrhea.

4) Slowing of the heart, which is called Bradycardia.

****** Always remember that muscarine is an agonist for Acetylcholine that is responsible for the parasympathetic activity, so when muscarine is ingested in the body… we expect to see the same signs of parasympathetic activity + the activity of sweat glands even if they are sympathetic because they are activated by ACH (look at the signs above)***

So how to reverse the effects of intoxication by muscarine?

• **we use a drug (antagonist) to block the muscarinic receptors which is called Atropine [from a plant (Atropa Belladonna)]. The doses are given to the patient until we notice a change reversing of the intoxication effects by –mainly- following the patient's heart rate and pupillary light reflex [change in the pupil diameter as a response to light].**

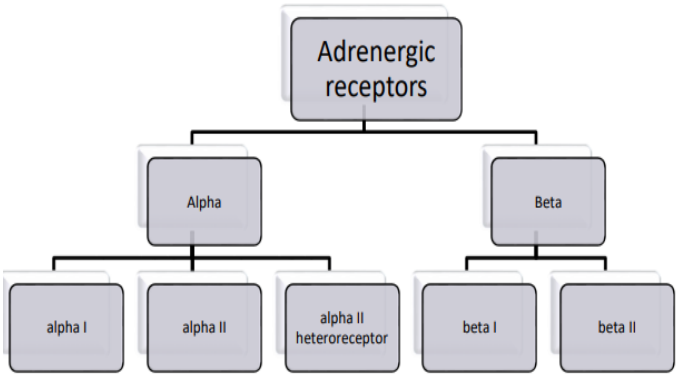
**** What happens if the patient was given an overdose of Atropine?**

1. Inhibition of glandular secretions → causes dry mouth, eyes and nasal passage.

2. Increase in heart rate → which is called Tachycardia.

3. Loss of pupillary light flex, pupil dilation [Mydriasis] and loss of ability to focus lens for near vision.

3) *Adrenergic receptors*



• The stimulation of the sympathetic NS causes the release of norepinephrine and epinephrine [which are also called catecholamines], and in our bodies we have a type of receptors called adrenergic receptors that response to these neurotransmitters.

ALPHA RECEPTORS

1) Alpha I → Excitatory, found in smooth muscle cells of vessels and arteries.

o Here there is an Activation of phospholipase C which cause Vasoconstriction [constriction of blood vessels → raise the blood pressure], this effect involves IP3 production and Ca2+ release since alpha I is coupled with Ca2+ gated channels.

2) Alpha II → are found on sympathetic postganglionic nerve terminals. These receptors are important for self-inhibition of NE release (negative feedback) .

3) Alpha II heteroreceptor → found in non-adrenergic neurons Work through Gi proteins, reduce the synthesis of c-AMP and inactivate these neurons.

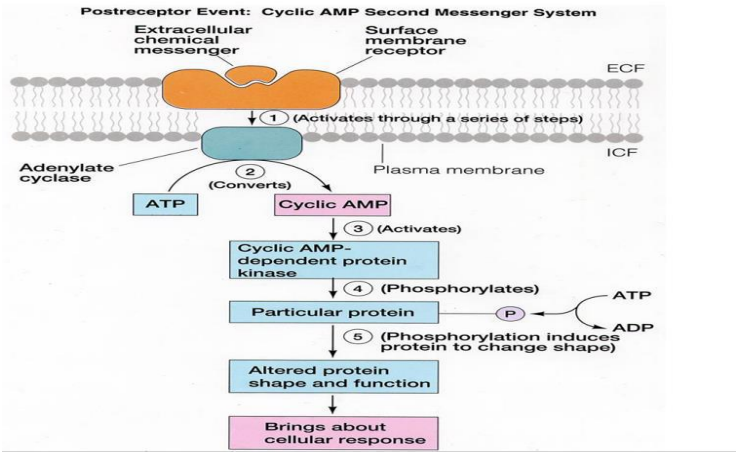
BETA RECEPTORS

• These receptor are more sensitive to EP& NE than alpha, (lesser concentration needed for a response to occur)

1. Beta I → an excitatory receptor in the heart.

2. Beta II → an inhibitory receptors found in smooth muscle cells like in the bronchial muscle cells, the gastrointestinal tract,blood vessels supplying skeletal muscles.

The activation of the receptors increases cAMP concentration which will act in an either excitatory or inhibitory way, depending on beta receptors location [the type of cells they are found in], for example, increasing the cAMP in the smooth muscle cells will lead to relaxation of these muscles, while in the heart increasing the cAMP will increase the heart rate.



This is what really happens in the conductive tissue of the heart due to increase in cAMP :

Activation of adenylyl cyclase → **Increase in cAMP concentration** → **Activation of Na+ & T-type Ca2+ channels** → **Increase the heart rate**

ANS HANDOUT

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 - emptying of urinary bladder
- digestion, intestinal motility, secretions (these functions are controlled in conjunction with hormones.
- 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 (a) and beta (B) receptors. 9
Alpha receptors:
The alpha receptors are subdivided into a_1 and a_2 receptors.
The **alpha 1 (**a_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 **(**a_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.
These receptors are negatively coupled to adenylyl cyclase via Gi protein and decrease c-AMP production.

Beta receptors:

These receptors are subdivided into beta1 (B_1) and beta 2 (B_2) 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 (B_1**) receptors**: found on heart and produces **excitation** in the heart.
Beta 2 (B_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 B_2 receptors are preferentially activated by EPI rather than NE.

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.
All subclasses of adrenergic receptors can be blocked by specific blocking agents (antagonists). B_1 blockers are useful as antiarythmic drugs. B_2 selective agonist (produce activation of B_2 receptor) will dilate bronchi. This agonist is useful in asthma.

ANS BAST PAPERS

All the followings may describe the parasympathetic system EXCEPT:
• A)When stimulated it causes an increase in intestinal movements
• B)Second neurons release a neurotransmitter that binds to muscarinic receptors
• C)It dominates in quiet and relaxed situation
• D)Its postganglionic neurons can also be stimulated by nicotine
• E)When stimulated it is increasing sweating
Ans//E

One of the followings does NOT characterize the sympathetic nervous system:
• A)Has acetylcholine as transmitter in preganglionic neuron
• B)Is always giving excitatory responses
• C)Is a part of the autonomic nervous system
• D)Has short preganglionic and long post ganglionic fibers
• E)Promotes responses for fight or flight reaction
Ans//B

All the following with regard to beta adrenergic receptors are true EXCEPT:
• A)Their stimulation increases heart rate
• B)They are present in the heart
• C)They are stimulated by a neurotransmitter released by SNS
• D)They are blocked by atropine
• E)Their stimulation increases the air flow to the lung
Ans//D

Which type of cholinergic receptor is found at synapses between preganglionic and postganglionic neurons of the sympathetic system?
• A) Muscarinic. • B) Nicotinic. • C) Alpha. • D) Beta-1. • E) Beta-2
Ans//B

Which spinal cord level contains the entire population of preganglionic sympathetic neurons?
• A) C5-T1 • B) C3-C5 • C) S2-S4 • D) T1-L3 • E) T6-L
Ans//D

Cells of the adrenal medulla receive synaptic input from which type of neuron?
• A) Preganglionic sympathetic
• B) Postganglionic sympathetic
• C) Preganglionic parasympathetic
• D) Postsynaptic parasympathetic
• E) Presynaptic parasympathe
Ans//A

The End
Good luck