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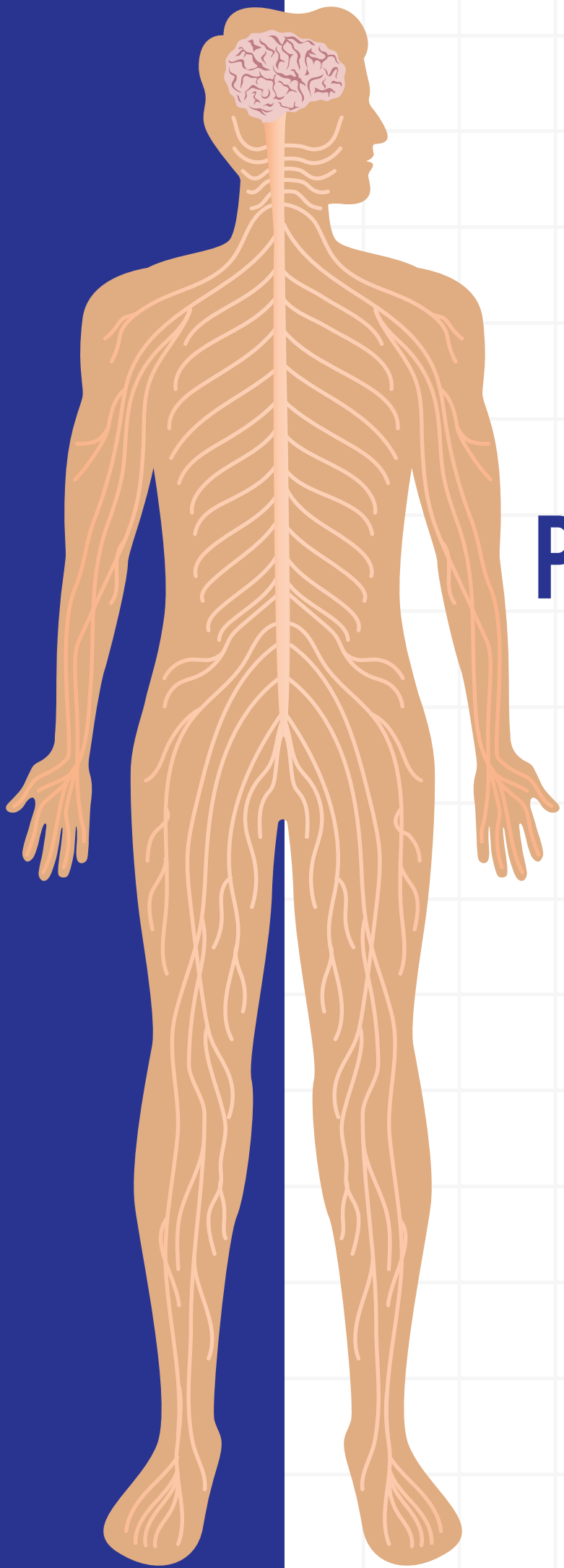
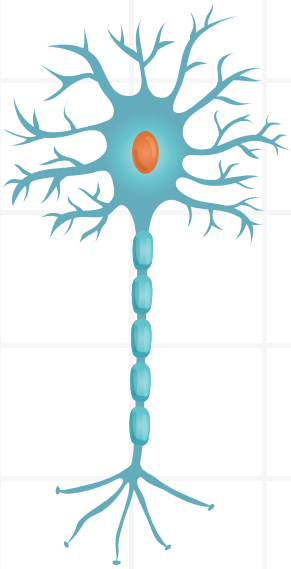


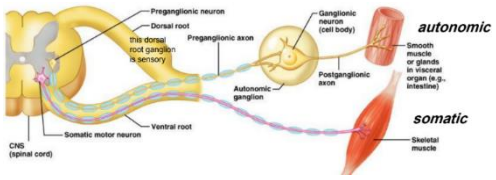
# PHYSIOLOGY

# 2024



DR. AHMAD AL-QAWASMI

- Nervous system is divided into ***central*** and ***peripheral*** Nervous system (CNS & PNS)
- PNS is divided into ***Somatic*** and ***Autonomic*** Nervous system
- The difference between somatic & autonomic nervous systems:
  - The somatic nervous system involves 1 neuron from the control center to the effector, but ANS requires 2 neurons
  - Somatic is voluntary but ANS is unvoluntary




## ❖ Autonomic nervous system (ANS)

- Functions of the ANS:
  - ***Controls most of the visceral functions*** of the body such as Heart rate, Arterial blood pressure, digestion, intestinal motility, secretions, emptying of urinary bladder, secretory activity of respiratory tract and airways resistance (by regulation of diameter of bronchioles)
    - ✓ ANS plays an important role in maintaining constancy of internal environment (**homeostasis**)
  - ***Adaption and Rapid responses (Reflexes)*** to internal or external stimuli, including:
    - ✓ **Light:** Constriction of the pupil to bright light (*miosis*) and its dilation to low light (*mydriases*)
    - ✓ **Temperature:** Cutaneous vasodilation and sweating during warmth, vasoconstriction in cold
    - ✓ **Stress:** The sympathetic branch mediates *fight or flight response* to threatening stimuli

- 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, blood pressure can take place within seconds (3-5 sec)

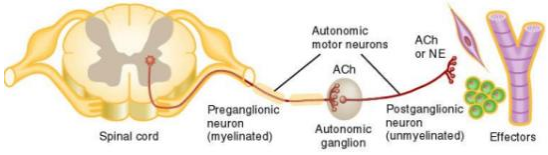
### 2) Automatic nature

- Regulation of visceral functions occurs **without conscious control**
- The impulses in ANS to target organs are set up **reflexively** in response to specific type of sensations

### 3) Tonic activity

- The ANS fires **continuous impulses (will never be zero)** to target organs at very low rate
- The basal rate of firing is called sympathetic tone and parasympathetic tone
- Activity of effector cells can be changed by the increase or decrease in the activity of ANS divisions

- In the ANS, the signal is carried from the CNS into the effector organ by **2 neurons**
  - ***Preganglionic neuron:*** The ***first*** neuron, where its cell body is located in a *nucleus* in the gray matter of the CNS, its fibers are usually *small & myelinated* (type B)
  - ***Postganglionic neuron:*** The ***second*** neuron, where its cell body is located in a *ganglion* out of the CNS, it carries the impulses to the target organ
  - ***Ganglion:*** A collection of cell bodies ***out of the CNS***, where the pre- & post- ganglionic neurons synapse
  - ***Nucleus:*** A collection of cell bodies ***in the CNS***




- ANS is divided into:
  1) *Sympathetic Nervous System: Fight or flight*, has a *thoracolumbar* [T1-L3] origin
  2) *Parasympathetic Nervous System: Rest and digest*, has a *craniosacral* origin (C3,7,9,10 + S2,3,4,5)

## ❖ Sympathetic Nervous System

- The preganglionic neuron synapse in 3 positions:
  - *Paravertebral ganglion:* A ganglion that presents ***near the vertebral*** column
  - *Prevertebral ganglion:* A ganglion that presents ***apart from*** the vertebral column in the abdomen including celiac ganglion, superior mesenteric ganglion, inferior mesenteric ganglion
  - *Adrenal (Suprarenal) gland*, where the terminals synapse with the chromaffin cells in the cortex

- Example of adaptation to external stimuli (Fight or Flight, Stress Response):
  - ***Redistribution of circulation***, where *higher* amount of blood (vasodilation) is directed to skeletal muscles, *lower* (vasoconstriction) amount is directed to skin and unnecessary tissues
  - ***Tachycardia*** *(Increasing heart rate, force of contraction and cardiac output)*
    - ✓ They cause an increase in blood pressure
  - ***Mydriasis*** (dilation of pupils) to increase the light reaching the retina
  - ***Pallor*** (pale of fear): happens as a result of decreasing the amount of blood that goes to the skin
  - ***Cold sweat*** due to the low amount of blood delivered to the skin
  - ***Goose pimples***: hair erection by the contraction of piloerector muscles
  - ***Dry mouth*** due to the inactivation of salivary glands → the body is trying to shut down all unnecessary tissues by vasoconstriction the blood vessels that supplies these tissues
  - ***Bronchodilation*** by the relaxation of the bronchial muscles which enhances the respiration
  - Digestive, urinary and secretory functions are ***inhibited***
  - *Metabolic rate is increased* where mobilization (utilization) of glucose, lipolysis

- The widely distributed tissues are innervated only by sympathetic system (no parasympathetic system)
  - They include **sweat glands,** smooth muscles of the **blood vessels** & **hair follicles**

## ❖ Parasympathetic Nervous System

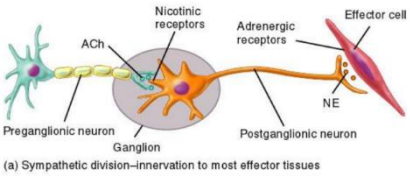
- The ganglion is ***terminal ganglion*** which is found ***in the effector*** **(**or ***very close to it*****)**
- Parasympathetic works as a regulator of activities involved in replenishment of energy supply and general maintenance of the organism
- Its control is discrete and selectively directed to individual organs
- The effects of the parasympathetic stimulation on each of the following:
  - ***Gastrointestinal system is activated***
    - ✓ Increases motility and secretory activity
  - ***Increases secretory*** activity of glands
    - ✓ Except sweat glands (sympathetic only)
  - ***Bradycardia*** where heart rate is decreased
  - ***Miosis*** (constrict the pupil)
  - Accommodation of the ***lens*** for near vision
  - *Voiding the* urinary bladder *(**micturition**, **Urination**)*

## ❖ Difference between Sympathetic & Parasympathetic

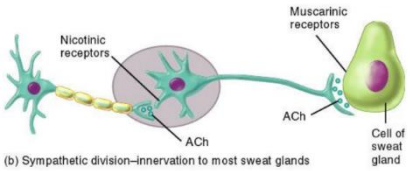
- In sympathetic, the preganglionic is ***short***, that makes the ***divergence*** and ***convergence*** easier
- In parasympathetic, the preganglionic is ***long***, that is why there are ***no divergence*** or ***convergence***
  - Parasympathetic response is localized while sympathetic is more generalize responses
- Synapse can occur in the same segmental level, or can curve downward or upward to synapse with a postganglionic neuron from a lower or higher segmental level

## ❖ Molecular basis of physiological action of the ANS

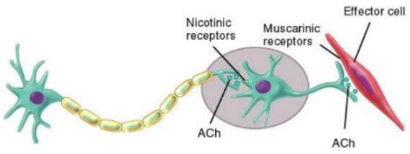
- In ganglion ***pre**ganglionic* neurons of *both sympathetic and parasympathetic* release Acetylcholine (**Ach**) *into the ganglion* causing activation of the postganglionic neuron
- While the ***post**synaptic* neuron releases the following *into the effector*:
  - **Norepinephrine** to the effector cells in the *sympathetic*
  - **Ach** by:
    - ✓ *Parasympathetic*
    - ✓ Sympathetic innervating *sweat glands and piloerector muscles*



(a) Sympathetic division–innervation to most effector tissues

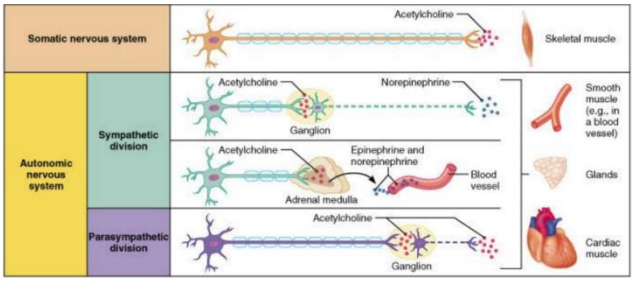


(b) Sympathetic division–innervation to most sweat glands




- The **somatic** fibers & the sympathetic fibers that innervates the **suprarenal gland** release **Ach**
  - Adrenal gland (suprarenal) Secretes Epinephrine (EPI) and Norepinephrine (NE) but EPI is more dominant
- The released Ach by parasympathetic system is inactivated by breakdown by acetylcholinesterase
- Epinephrine is inactivated by recapture by postganglionic nerve

- The receptors of the released neurotransmitters:
  - Receptors on the body of the postganglionic neurons (at ganglia) are ***nicotinic receptors***
  - Receptors on the sweet glands, piloerector and parasympathetic effector are ***muscarinic receptors***
  - Receptors on the sympathetic effector are ***adrenergic receptors***




### ♦ Nicotinic receptor

- They are **cholinergic** receptors excited by Acetylcholine
- The drug **nicotine** can also stimulate these receptors
- Activation of nicotinic receptors causes activation of $Na^+$ channels, depolarization of the postsynaptic membrane which can generate action Potential

### ♦ Muscarinic receptors

- These cholinergic receptors can be stimulated by **Muscarine** (found in a type of *toxic mushroom*)
- All muscarinic receptors (M1-M5) are GPCRs (linked to G-proteins)
  - ***M2** receptor in the heart*
    - ✓ It is an ***inhibitory*** receptor coupled to $G_i$ protein which inhibits adenylyl cyclase activity so decreasing cAMP and slowing the heart rate
    - ✓ Can cause activation of potassium channels so slow the rate of depolarization
  - ***M1, M3, M5** in smooth muscle cells and glands*
    - ✓ They are ***excitatory*** receptors linked to $G_q$ proteins in the smooth muscles and glands
    - ✓ Activates phospholipase C (PLC) causing cleavage of $PIP_2$ and convert it to DAG and $IP_3$
    - ✓ $IP_3$ releases $Ca^{+2}$ from its stores (SER) causing many responses such as contraction and secretion
- Muscarinic poisoning causes:
  - ***Stimulation of secretory*** activity, such as: salivation, tearing, sweating nasal and bronchial secretions
  - Contraction of urinary bladder causing ***urination***

- Increase in the gastrointestinal tract motility, which causes ***vomiting and diarrhea***
- Slowing of the heart (***Bradycardia***)

- If a patient ate a toxic mushroom, how to reverse the effects of intoxication by muscarine?
  - We use a drug (antagonist) to block the muscarinic receptors which is called ***Atropine***
- What happens if the patient was given an overdose of Atropine?
  - Inhibition of glandular secretions, causes dry mouth, dry eyes and dry nasal passage
  - Increases heart rate (Tachycardia)
  - Loss of pupillary light flex, pupil dilation [Mydriasis]
  - Loss of ability to focus lens for near vision

## ♦ Adrenergic receptors

- Respond to catecholamines (epinephrine EPI, norepinephrine NE)

### ❁ *Alpha receptors*

- ***Alpha 1*** *in smooth muscles of blood vessels that innervate the skin*
  - Activation of PLC activates $Ca^{+2}$ gated channels of SER causing vasoconstriction (excitatory)

- ***Alpha 2*** *in sympathetic postganglionic nerve terminals*
  - These receptors are important for **self-inhibition** of NE release (negative feedback)

- ***Alpha 2 heteroreceptor***
  - Heteroreceptor found in non-adrenergic neurons
  - Work through $G_i$ proteins, reduce the synthesis of c-AMP and inactivate these neurons

### ❁ *Beta receptors*

- They are **more sensitive** to EP& NE than alpha (less concentration needed for a response to occur)
- ***Beta 1*** *in the heart*
  - An ***excitatory*** receptor
- ***Beta 2*** *in the smooth muscle cells like in the bronchial, tracheal, blood vessels supplying skeletal muscles and GI tract*
  - An ***inhibitory*** receptor causing dilation of these muscles
  - They are preferentially activated by **EPI** rather than NE

- Both receptors are positively coupled to adenylyl cyclase via $G_s$ protein, and increase c-AMP, results in subsequent activation of protein kinase and phosphorylation of one or more proteins
  - The response elicited depends on the role of phosphorylated proteins & the tissue type

- All subclasses of adrenergic receptors can be blocked by specific blocking agents (antagonists)
  - Beta 1 blockers are useful as ***anti-arrhythmic*** drugs
  - Beta 2 selective agonist (produce more activation of Beta 2 receptor) will dilate bronchi
    - ✓ This agonist is useful in ***asthma***