PHARMACOLOGY

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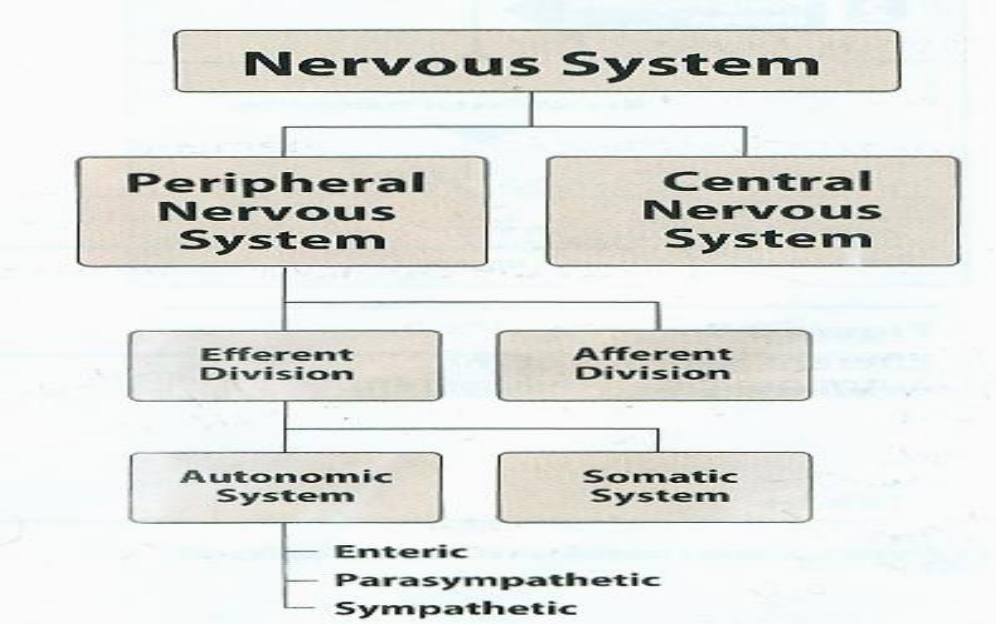
Lecture 11

Second year –passion batch

التفريغ شامل السلايدز

Pharmacology of ANS:



- Nervous system is divided into two types of systems
- ✓ Central nervous system which includes the brain and the spinal cord
- ✓ Peripheral nervous system which divided into

١. Afferent neuron

- ✓ The neurons of which bring information from the periphery to the CNS. (transport the sense impulses to the brain and spinal cord)
- ✓ Afferent neurons provide sensory input to modulate the function of the efferent division through reflex arcs.

٢. Efferent neurons

Which divided into voluntary (somatic) and involuntary (autonomic)

The autonomic nervous system is divided into three types :

- ✓ Enteric (plexus that is found in GIT, pancreas, and gallbladder)

ليش ال GIT مرتبط بال enteric ANS؟ لانه بعض الأوامر بتحتاج استجابة سريعة يعني اتخاذ قرار سريع دون الرجوع للدماغ .

- ✓ Parasympathetic
- ✓ Sympathetic

In Glands, Smooth Muscle & Cardiac Muscle (Involuntary control)

- ✓ The function of efferent neuron: carries nerve impulses from the CNS to the effector organs by way of two types of efferent neurons (the preganglionic neuron and the postganglionic neuron).
- ✓ In pharmacology the drug is either agonist or antagonist so the drug will act mostly on post synaptic cleft (which is between the neuron and the receptor on the target organ) see the fig. below.

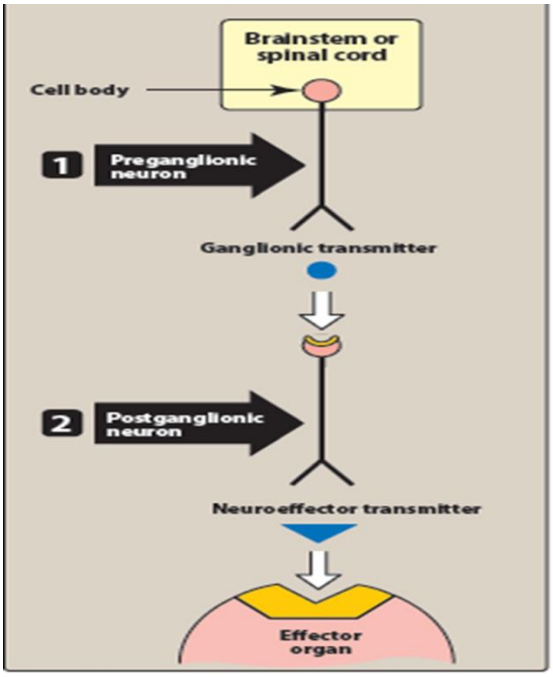


Figure 3.2
Efferent neurons of the autonomic nervous system.

Efferent neurons divisions

The body is controlled by brain this controlling as we said is divided into two parts:

- Somatic nervous system (skeletal muscles) :
  - ✓ Carries nerve impulse to skeletal muscle (voluntary control)
  - ✓ A single myelinated motor neuron (The somatic neuron is a single long neuron with no ganglia and doesn't need a gap junction).
  - ✓ Faster response
  - ✓ Controlled by synaptic cleft that has acetylcholine. (
  - ✓ So the substance which is responsible for impulse transmission to the muscles is acetylcholine→ it causes contraction or relaxation of our muscles (voluntary).
  - ✓ Here we are talking about neuromuscular junction acetylcholine not the acetylcholine which is found in parasympathetic system.
  - ✓ When we need to inhibit or encourage acetylcholine receptors?
  - ✓ When we inhibit this receptors ➔ this leads to relaxation➔ so that means we can use it for anesthesia which has ٤ rules :

١. No pain
٢. Muscle relaxation
٣. No reflex
٤. Unconsciousness

  - ✓ When we increase acetylcholine ➔ we increase contraction ➔ so that means we can use it in myasthenia gravis.

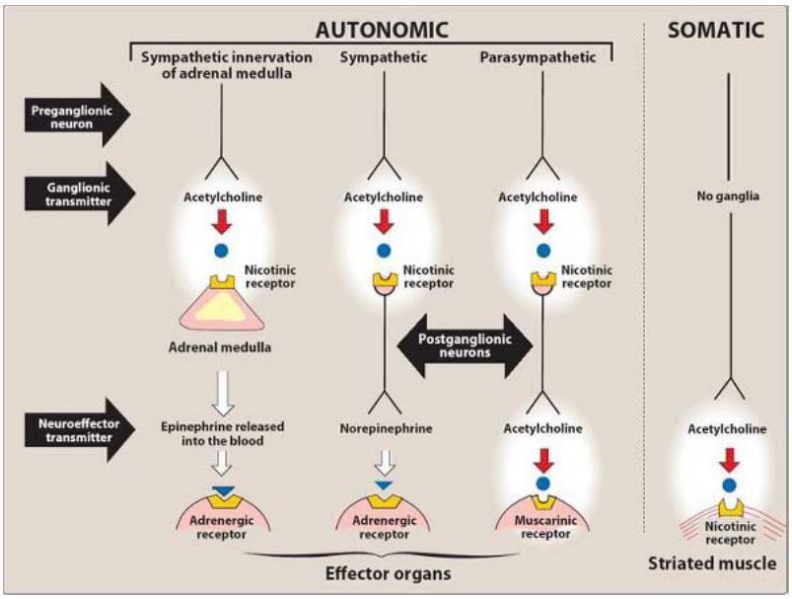
Autonomic nervous system:

Divided into sympatahtic and parasympathatic

- In this system there is ganglia which has acetylcholin (note the fig. below) and it will not be inhibitid by the acetylcholin in somatic system becouse they have diffirent receptors (M١,M٢,M٣) receptors.
- The post gnglic in parasympathatic has acetylcholin but in sympathatic it's norepinephrine. What is the target?
- Every organ in our body has two innervation ➔ one by sympathatic and the other one by parasympathatic and we call this **Dual innervation**

  يعني اذا بنزيد ال sympathatic بنقلل ال parasympathatic والعكس

- Receptors for sympathatic system are alpha and beta.
- Receptors for parasympathatic are nicotinic muscarinic.



	SYMPATHETIC	PARASYMPATHETIC
Sites of origin	Thoracic and lumbar region of the spinal cord (thoracolumbar)	Brain and sacral area of spinal cord (craniosacral)
Length of fibers	Short preganglionic Long postganglionic	Long preganglionic Short postganglionic
Location of ganglia	Close to spinal cord	Within or near effector organs
Preganglionic fiber branching	Extensive	Minimal
Distribution	Wide	Limited
Type of response	Diffuse	Discrete

Sympatahatic :

- Its function: adjusting in response to stressful situations, such as trauma, fear, hypoglycemia, cold, and exercise
- It is a temporarry action happen to our body when we are under stress or fight or something ubnormal.
- All glands are controlled by sympathatic nervous system.

١. **Effects of stimulation of the sympathetic division:**

- Increase heart rate(arythmia) and blood pressure
- To mobilize energy stores of the body
- Increase blood flow to skeletal muscles and the heart while diverting flow from the skin and internal organs.
- Dilation of the pupils(mydriasis) and the bronchioles
- Decrease GI motility
- Increase blood flow to skeletal muscles.
- constipation

٢. **Fight or flight response**

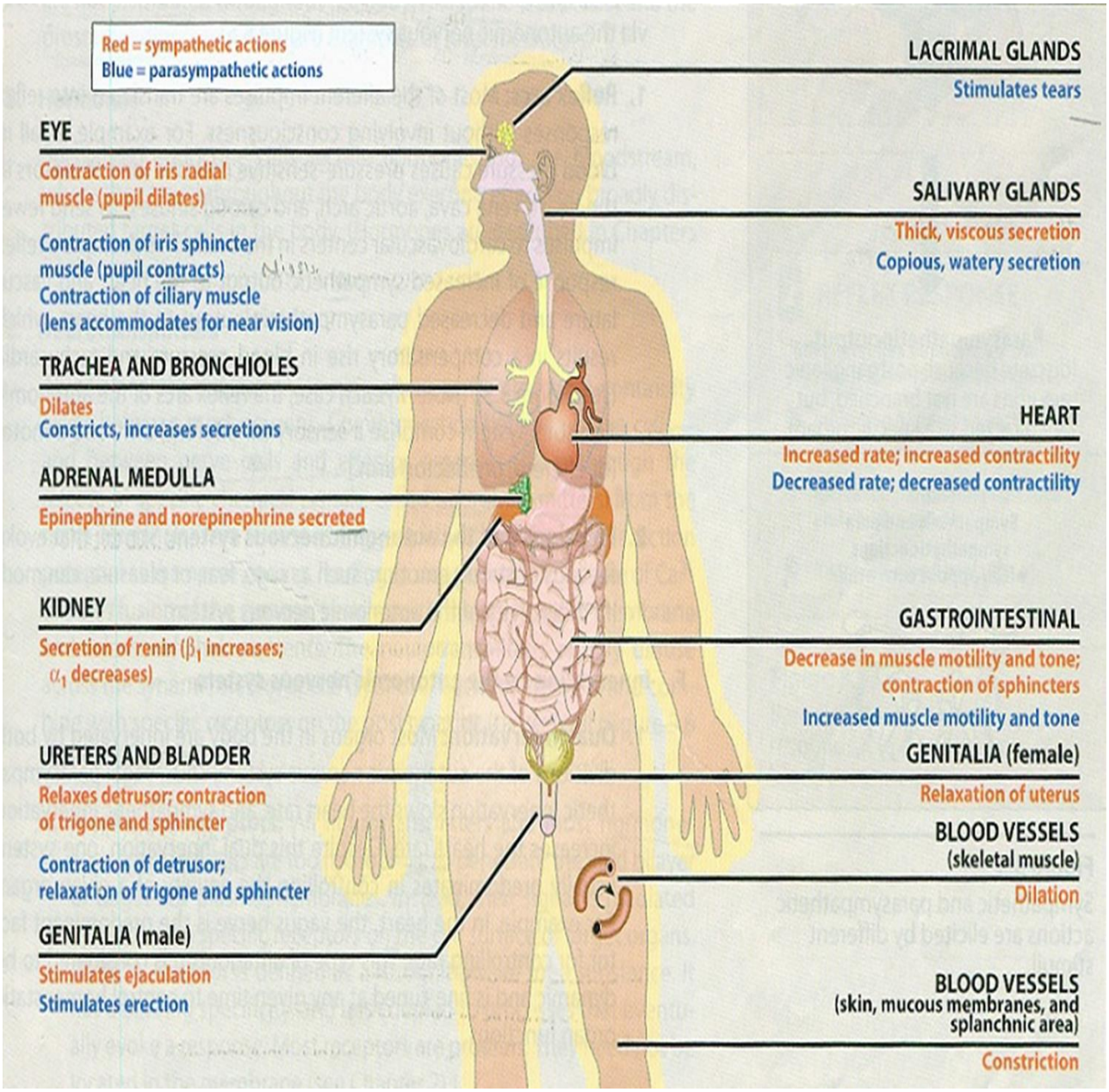
- The changes experienced by the body during emergencies have been referred to as the “fight or flight”

Parasympathatic:

- is involved with maintaining homeostasis within the body.
- it maintains essential bodily functions, such as digestive processes and elimination of wastes
- “rest and digest” situations.
- In this case pupil contract (meiosis).
- Causing diarrhea.

Enteric NS :

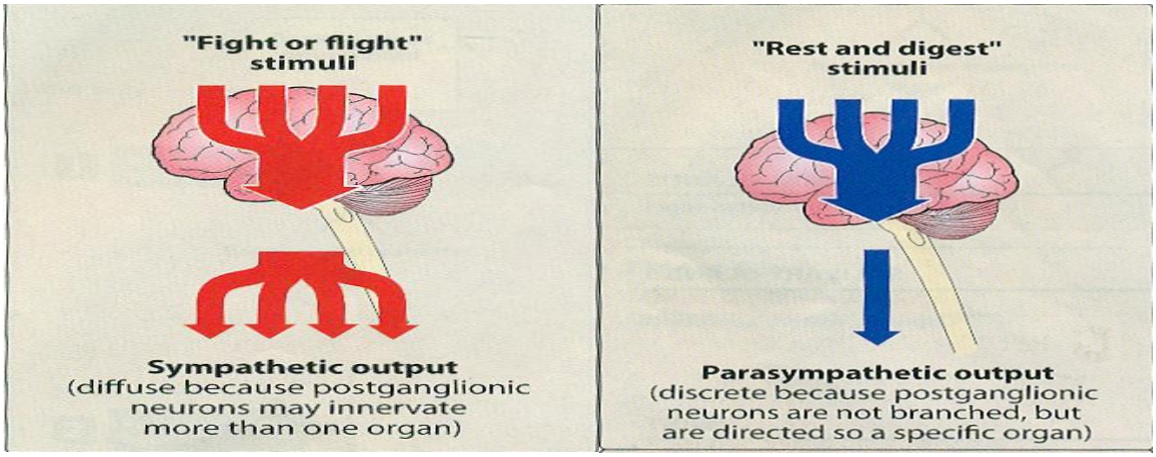
- collection of nerve fibers that innervate the gastrointestinal (GI) tract, pancreas, and gallbladder,
- This system functions independently of the CNS and controls the motility, exocrine and endocrine secretions, and microcirculation of the GI tract.
- It is modulated by both the sympathetic and parasympathetic nervous systems.



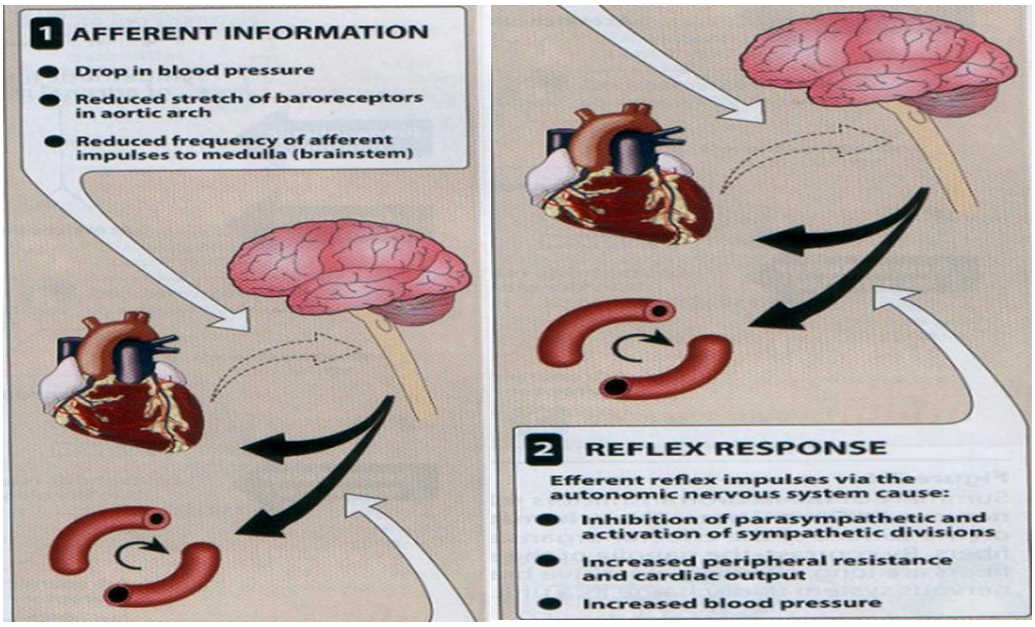
Important notes about the fig. above:

- No innervation by sympathetic in lacrimal glands.
- In the kidney (sympathetic): when you have hypotension the sympathetic system increase renin concentration ➔ leading to increase the pressure

- In the heart (sympathetic) : increase the heart rate (chronotropic) and increase the heart contractility (inotropic) leads to increase the pressure. ➔ in emergency cases such as a patient with a low heart rate (less than ٤٠-٥٠) you give him adrenalin which is a sympathetic.
- Blood vessels :
  ✓ There are two types of blood vessels… blood vessels going to :
  Skeletal muscles: the sympathetic cause them to dilation → more blood flow
  Smooth muscles → constriction → <u>increase the blood pressure.</u>
  ✓ Why we need to increase the blood pressure?
  ١. To increase the heart rate
  ٢. To increase the heart contractility
  ٣. Increase secretion of renin, aldosterone and angiotensin٢.
  ✓ Angiotensin٢ causes vasoconstriction so <u>increase the blood pressure.</u>
  ✓ Aldosterone causes sodium and water retention (increase the blood volume). → This increase cardiac output then <u>increases the blood pressure</u>.
  ✓ Blood pressure= ٢*heart rate *cardiac output.
  لهيك معظم أدوية الضغط رح تكون sympathetic <u>antagonist</u>
- Lung (parasympathetic): causes bronchoconstriction .
  So that asthmas drugs are two types :
  ١. For lung (sympathetic agonist) such as salbutamol (beta ٢ agonist)
  ٢. For lung (parasympathetic antagonist)



Reflax arcs :



Reflax arcs are found in some organs like the heart

- When the blood pressure is decreased there are a sensitive receptors on the heart (paro receptor)➔ they are sensitive to blood pressure ➔ they send impulses to the brain ➔ the brain activate the sympathatic to secrete more adrinaline.

في ملاحظة مهمة انه الادرينالين بكون صنع وجاهز ومخزن داخل vessels بالتالي الأمر الي بيعمله ال sympathatic انه بحفز ال excreation للأدرينالين مشان هيك ما بتاخد وقت طويل.

عملية ال excreation تحتاج وجود ال CA^{+2} لانه بتتم من خلال ال exocytosis

CHEMICAL SIGNALING BETWEEN CELLS:

- Hormones : chemicals released by glands into the bloodstream ⇒ physiological effects on tissues - specific hormone receptors.
- Local mediators : Most cells in the body secrete chemicals that act locally, and they don't enter blood. E.g, histamine and prostaglandins .
  It's available any where for allargic reaction (inflammotary reaction) and it's transmitted from one cell to another such as (prostaglandins , interleukins)
- Neurotransmitters: A specific chemical signals, released from the nerve terminals only.(found in neurosynaptic cleft of nerve).

- **Neurotransmitters**

- Norepinephrine and epinephrine – ANS (sympathatic) on the post synaptic cleft (on the organ) and they have alpha and beta receptors.
- Norepinephrine (NE) and epinephrine (E) (adrenergic) Transmission from the postganglionic nerves to the effector organs in sympathetic system

- Acetylcholine – ANS
  mediates the transmission of nerve impulses across:
  ١. Transmission of nerve impulses from the postganglionic nerves to the effector organs in parasympathetic system

  Parasympathatic acetylcholin (muscarinic receptor)

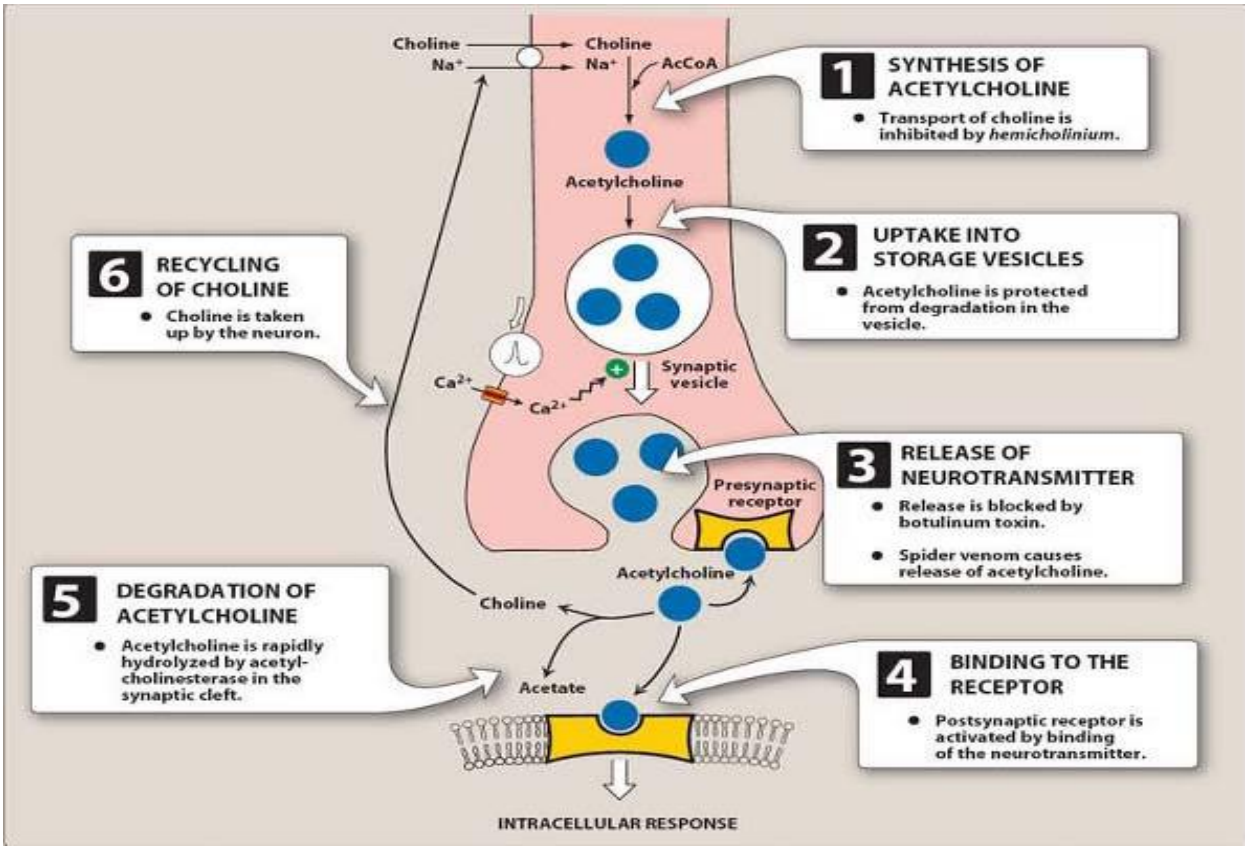
  ٢. Ganglia (autonomic ganglia in both sympathetic and parasympathetic NS.)
  ٣. Neuromuscular junction
  ٤. at adrenal medulla
  ٥. A few sympathetic fibers, such as those involved in sweating, are cholinergic

  They have the same substance but different receptors.

- Dopamine – CNS(responsible for depression and parkinson disease)
- Serotonin - CNS (responsible for depression)
- Histamine - CNS (H_1 receptors in the brain) → allergic
- γ-aminobutyric acid (GABA)- CNS

- **Co-transmitters,** such as adenosine, often accompany neurotransmitter on nerve stimulation and modulate the transmission process.

Neurotransmission in cholinergic neurons involves six steps:



Acetylcholin is storeged normally , but when we need to secret it we need calcium.

هون بنستنتج انه لو ما بدنا ال acetylcholin يطلع بنستخدم دواء يقلل من الكالسيوم

Botulinum toxin ➔ it's a bacteria and its toxin is used as a drug

سمومها تمنع ال acetylcholin releasing بالتالي يحدث muscles relaxation

هذا الدواء يسمى botox يستخدم لبعض الحالات المرضية مثل :

١. Migrane
٢. Muscle strain in the neck

Now … what is the fate of acetylcholin ? it associate with the receptor(GPCR)and do the action ➔ after the action ends it inhibited and dissociated by enzyme located in the gab junction called acetylcholinestrase enzyme ➔ this enzyme destroys it into acetyl and cholin to reuse it later.

يمكن إعطاء دواء يقوم بتحطيم الانزيم وبالتالي يبقى ال acetylcholin لوقت أطول وبيعمل ال action تبعه و كإنه عمل ك agonist

الدكتورة : رائع ☺

هاد الدواء يستخدم للي عندهم مرض ال dysthemia gravis

Cholinergic receptors (CHOLINOCEPTORS):

A) Muscarinic receptors

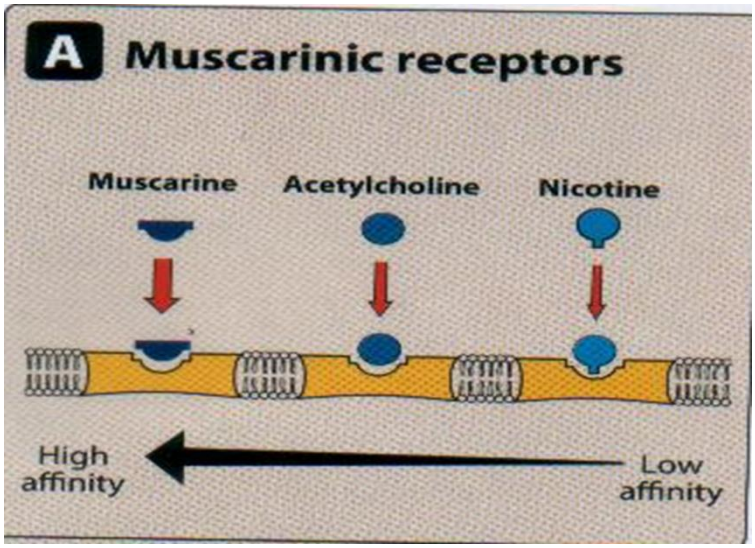
- G protein–coupled receptors.
- Recognize muscarine, ACh, and weak affinity to nicotine NT.
- five subclasses of muscarinic receptors:

  M١, M٢, M٣, M٤, and M٥.

- Found on the effector organs of parasympathetic such as the gastric (M١) , heart and smooth muscle (M٢), bladder and exocrine glands and smooth muscle (M٣)

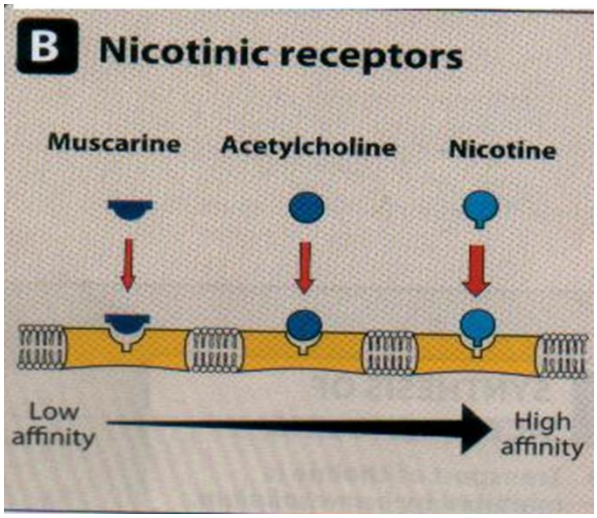
  These receptors have three neurotransmitters that can associate with it

  ١. Mascarin
  ٢. Nicotin
  ٣. Acetylcholin (has a moderate affinity) and most of these receptors depend on it.
- When M receptor activated – G-protein – IP٣ and DAG - intracelluar Ca^{2+} - cause hyperpolarization, secretion, or contraction



B) Nicotinic receptors

- ligand-gated ion channel
- Recognize nicotine, ACh, and weak affinity to muscarine NT.
- Two types : Nm(neuromuscular junction) and Nn(nicotinic)
- Located in the CNS, adrenal medulla, autonomic
- ganglia (called Nn), and the neuromuscular junction (NMJ) called Nm



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