AUTONOMIC RECEPTORS

BY Dr Riffat

- The autonomic system is the part of the peripheral nervous system that is responsible for regulating involuntary body functions, such as **heartbeat, blood flow, breathing, and digestion**

Autonomic nervous system receptors

- The act as on**/off buttons that control the various sympathetic and parasympathetic effects in the body**.
- These buttons are turned on or off, effects appear in body.

The types of sympathetic or **adrenergic receptors**

- are alpha, beta-1 and beta-2.
- **Alpha Receptors are located in the arteries vascular smooth muscles and effectors tissue**
- There are two types of Alpha Receptors namely Alpha1 and Alpha2 Receptors

  Epinephrine or norepinephrine, stimulates alpha receptors as a result the arteries constrict.
- This increases the blood pressure and the blood flow returning to the heart.
- The blood vessels in skeletal muscles lack alpha-receptors because they need to stay open to utilize the increased blood pumped by the heart.

if alpha-receptors are blocked?

- Right, the arteries dilate. Thus an alpha-blocker medication causes vasodilation and can be used to treat hypertension.
- Next are the beta receptors.
- Beta-1 receptors are located in the heart.
- When beta-1 receptors are stimulated they increase the heart rate and increase the heart's strength of contraction or contractility

Location of beta-2 receptors

Beta-1 receptors are predominantly found in:

kidney

fat cells

bronchial muscles

uterine muscles

arteries of the skeletal muscles.

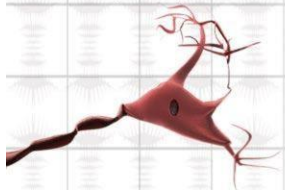
- When these receptors are stimulated, they increase the diameter of the bronchioles to let more air in and out during breathing and they dilate the vessels of the skeletal muscles so they can receive the increased blood flow produced by stimulating the alpha and beta 1 receptors

- The beta-1 adrenergic receptor is a G-protein-coupled receptor communicating through the Gs alpha subunit

neurotransmitter of the sympathetic nervous system

Neurotransmitters and Receptors

- Sympathetic nervous system
  - Primary neurotransmitter—norepinephrine
  - Adrenergic neurons - neurons that release norepinephrine
    - Epinephrine/norepinephrine also released from adrenal medulla
  - To elicit an effect, effector organ must contain receptor for epinephrine/norepinephrine



Adrenergic Receptors

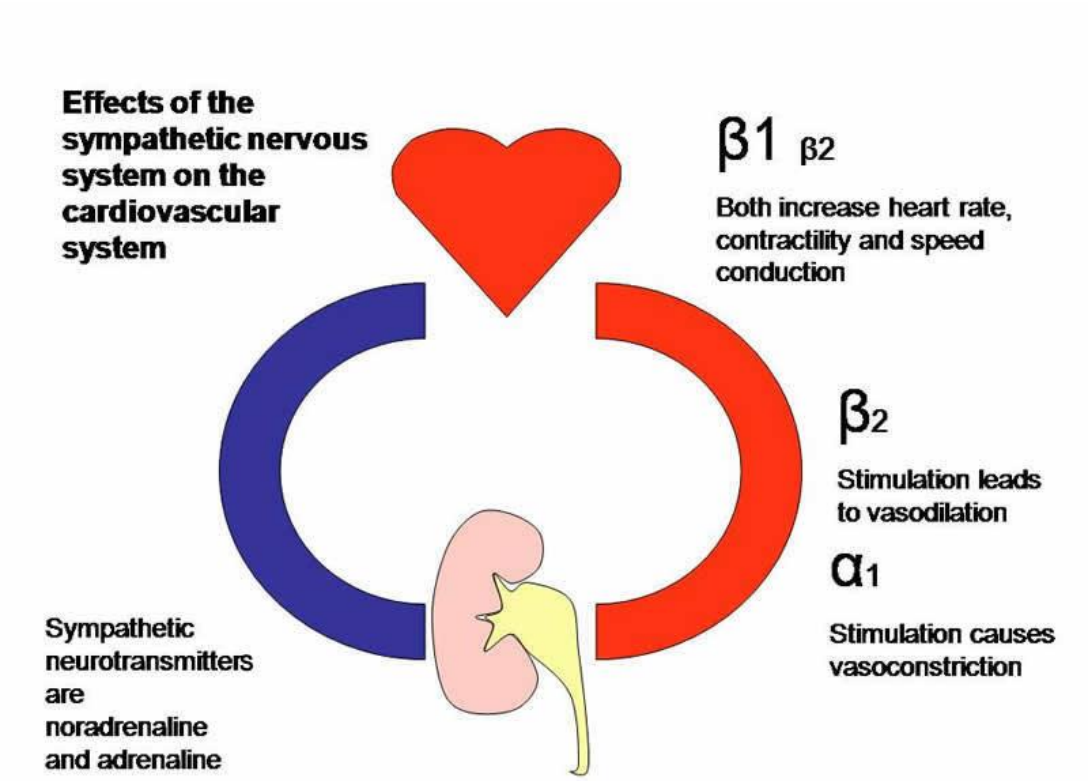
Alpha	Beta
+++ Norepinephrine + Epinephrine	+++ Epinephrine + Norepinephrine
Smooth muscle contraction	Smooth muscle relaxation

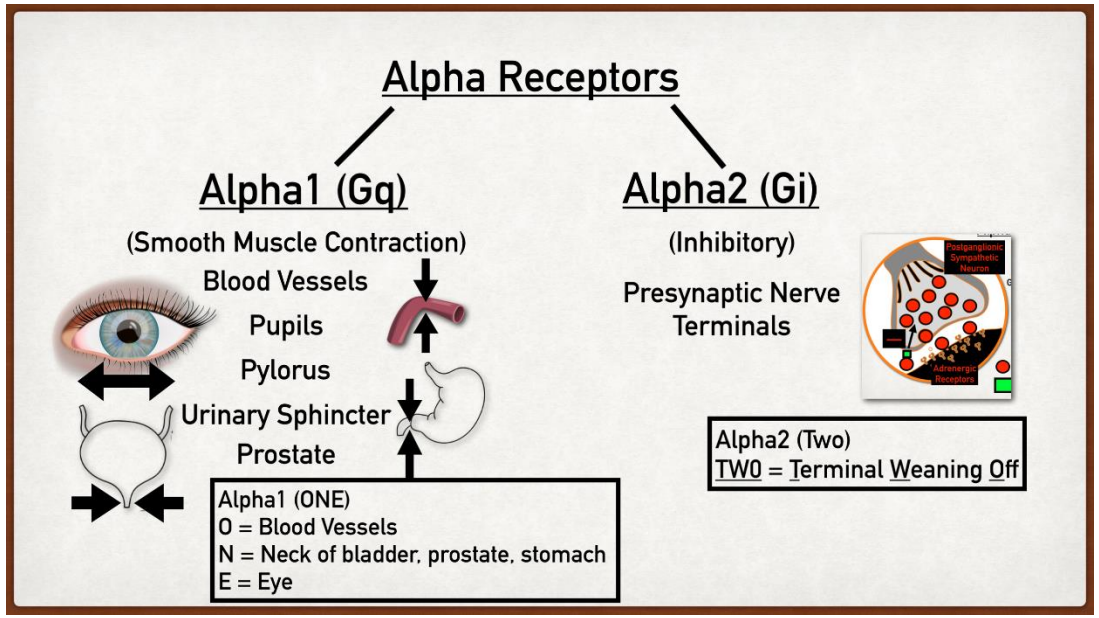
alpha = NO E = NOrEpinephrine
bEta = has an E = Epinephrine

Alpha = think of alpha in animal kingdom = dominant/strong = smooth muscle contraction
Beta = think of beta fish = chill and relaxed = smooth muscle relaxation

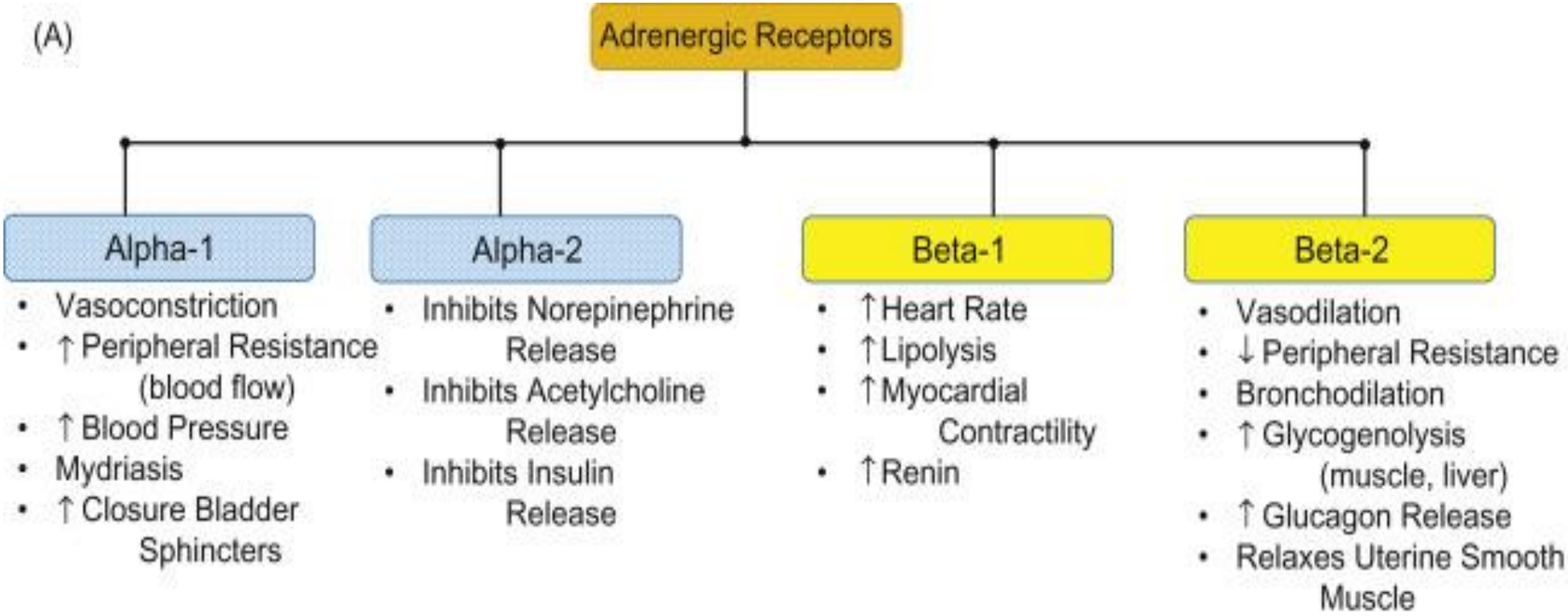
norepinephrine or epinephrine stimulates

- the alpha, beta-1 and beta-2 receptors and thus it is an alpha agonist, a beta-1 agonist and a beta-2 agonist.
- When we administer epinephrine or adrenaline to a patient, we expect alpha, beta-1 and beta-2 agonist effects; we expect an:
- Increase in blood pressure
- Increased heart rate
- Increased cardiac contractility
- Dilation of the bronchioles in the lungs
- Dilation of the vessels in the skeletal muscles


Effects of the sympathetic nervous system on the cardiovascular system
β1 β2
Both increase heart rate, contractility and speed conduction
β2
Stimulation leads to vasodilation
α1
Stimulation causes vasoconstriction
Sympathetic neurotransmitters are noradrenaline and adrenaline


Alpha Receptors
Alpha1 (Gq)
(Smooth Muscle Contraction)
Blood Vessels
Pupils
Pylorus
Urinary Sphincter
Prostate
Alpha1 (ONE)
O = Blood Vessels
N = Neck of bladder, prostate, stomach
E = Eye
Alpha2 (Gi)
(Inhibitory)
Presynaptic Nerve Terminals
Alpha2 (Two)
TWO = Terminal Weaning Off

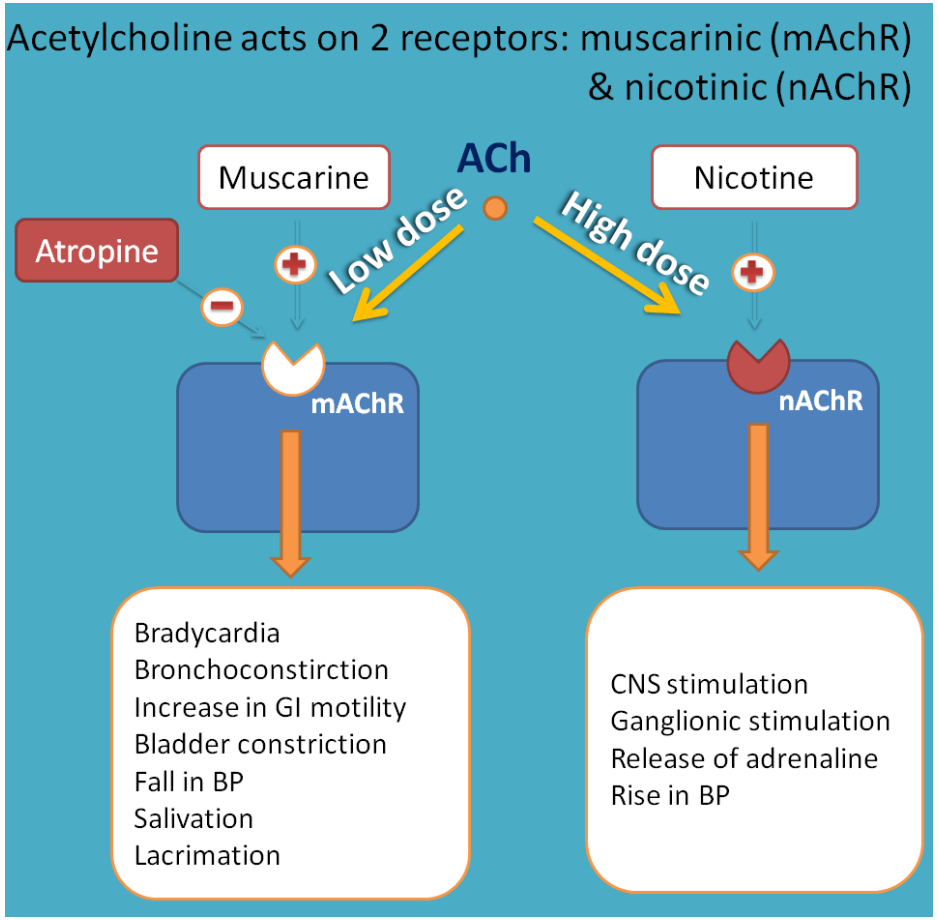
(A)



(B)

Alpha-1	Alpha-2	Beta-1	Beta-2
NE > E	E > NE	E = NE	E >> NE
NE = Norepinephrine; E = Epinephrine			

- **Nicotinic Receptors:** The N1 receptors occur in the neuromuscular junctions.
- The N2 receptors occur in the brain, autonomic and parasympathetic nervous system.


Acetylcholine acts on 2 receptors: muscarinic (mAchR) & nicotinic (nAChR)
Muscarine
ACh
Nicotine
Atropine
Low dose
High dose
mAChR
nAChR
Bradycardia
Bronchoconstirction
Increase in GI motility
Bladder constriction
Fall in BP
Salivation
Lacrimation
CNS stimulation
Ganglionic stimulation
Release of adrenaline
Rise in BP

Nicotinic receptors (nAhRs) are a group of cholinergic receptors (excitatory receptors.)

- that also interact with nicotine in tobacco.
- They form pores through the cell membrane of the post-ganglionic nerves.
- serve as ligand-gated ion channels, they mediate the fast transmission of nerve impulses at synapses.
- are permeable to cations such as sodium, potassium, and calcium.
- The formation of the ion channel upon the binding of the agonist results in the depolarization of the cell membrane of the neuron.
- This allows the fast transmission of the signal. The two types of nicotinic receptors are N1 and N2. The **N1 receptors** are muscle-type receptors found in the neuromuscular junctions. They are responsible for muscular contractions and relaxations. The **N2 receptors** are neuronal-type receptors found in the synapses between neurons. They are involved in cognitive function, memory, learning, arousal, reward, motor control, and analgesia.

Difference Between Nicotinic and Muscarinic Receptors

- two main types of cholinergic receptors.
- They are integral membrane proteins activated by the binding of acetylcholine, a neurotransmitter. Though the same neurotransmitter binds to both types of receptors, the mechanism of action is different in each receptor. The **main difference** between nicotinic and muscarinic receptors is that **nicotinic receptors become ion channels for sodium upon binding of the acetylcholine to the receptor whereas muscarinic receptors phosphorylate various second messengers**. Nicotinic receptors are also called **ionotropic acetylcholine receptors** while muscarinic receptors are also called **metabotropic acetylcholine receptors** depending on their action.

Muscarinic receptors (mAChRs) are a group of cholinergic receptors

- that interact with muscarine.
- Muscarine is a water-soluble toxin derived from a mushroom (*Amanita muscaria).*
- The muscarinic receptors primarily occur in the central nervous system.
- They are a type of G-protein coupled receptors.
- Thus, upon activation of the muscarine receptor by the binding of the agonist, the intracellular G-proteins are activated, converting GTP to GDP.

Muscarinic receptors

- refer to a group of G-protein coupled cholinergic receptors that phosphorylate second messengers.
- occur in the brain, heart, and smooth muscles.

A large number of physiological functions such as heart rate and force, the release of neurotransmitters, and contraction of smooth muscles are mediated by muscarinic receptors.

- if muscarinic receptors are blocked?
- That would cause the heart rate and contractility to increase, dilation of the bronchioles and less production of secretions in the body

The five types of muscarinic receptors

- M1, M2, M3, M4, and M5. They are categorized based on the physiological function.
- The M1 receptors commonly occur in secretory glands.
- The M2 is found in cardiac tissue,
- the M3 is found in both secretory glands and smooth muscles.
- The M1, M3, and M5 activate phospholipase C, increasing the intracellular calcium levels.
- The M2 and M4 inhibit adenylate cyclase, decreasing the cAMP levels.
- The M1, M2, and M5 are excitatory receptors while M3 and M4 are inhibitory receptors.

Similarities Between Nicotinic and Muscarinic Receptors

- cholinergic receptors.
- respond to the neurotransmitter, acetylcholine.
- found on the post-ganglionic neurons of both sympathetic and parasympathetic nervous systems.

G protein coupled receptors

- form a large group of proteins that are cell surface receptors that detect molecules outside the cell and activate cellular responses.
- Coupling with G proteins, they are called seven-transmembrane receptors because they pass through the cell membrane seven times.
- G protein-coupled receptors are found only in eukaryotes, yeast, flagellates, and animals.
- The ligands that bind and activate these receptors include light-sensitive compounds, odors, hormones, and neurotransmitters, and vary in size from small molecules to peptides to large proteins.
- G protein-coupled receptors are involved in many diseases.
- There are two principal signal transduction pathways involving the G protein-coupled receptors:
- the cAMP signal pathway and
- the phosphatidylinositol signal pathway.
- Muscarinic ACh receptors (mAChRs) that, depending on their coupling to **G-protein α-subunits**, can inhibit or excite post synaptic neuron.