Pharmacology of Autonomic Nervous System (2)

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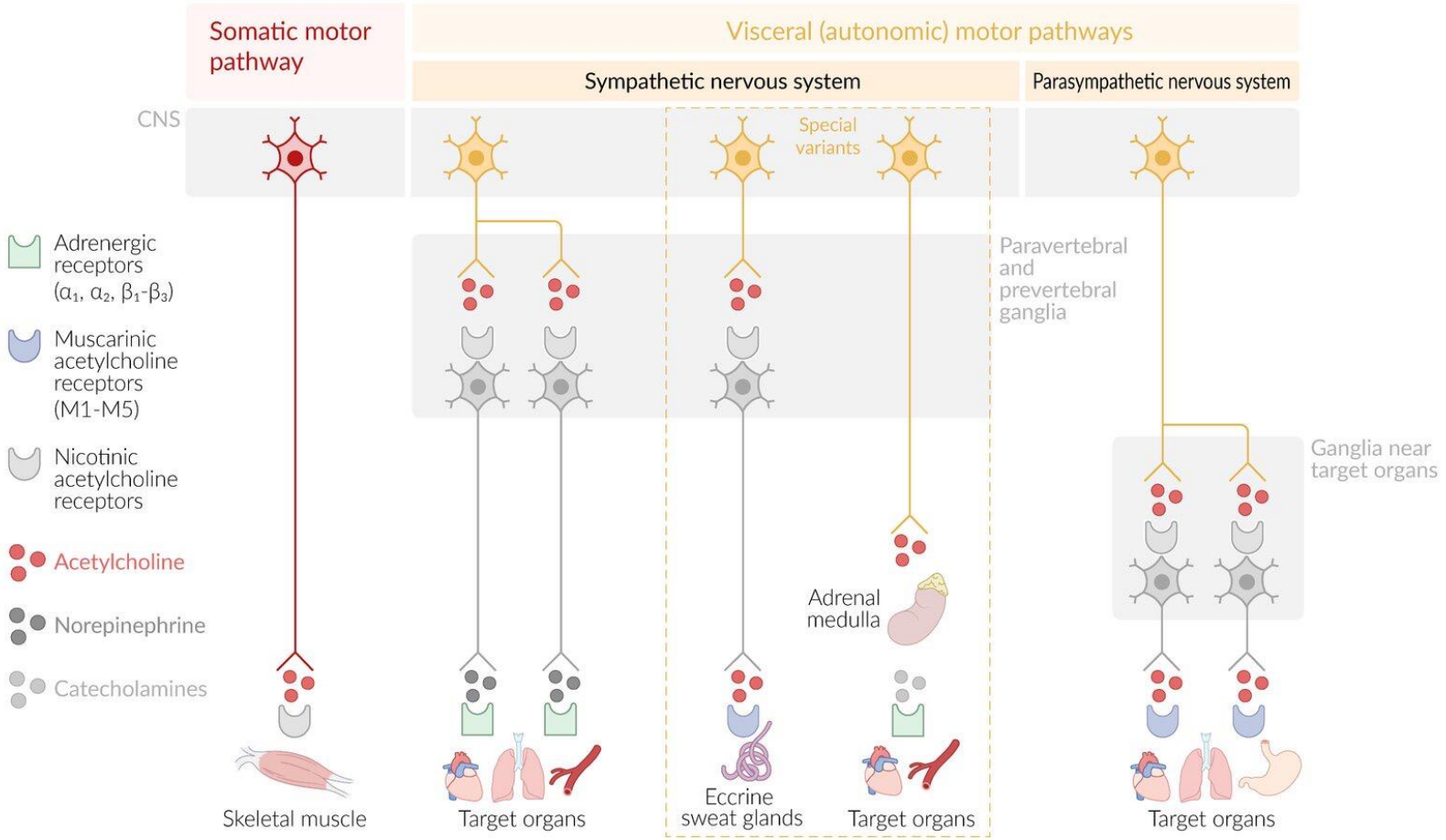
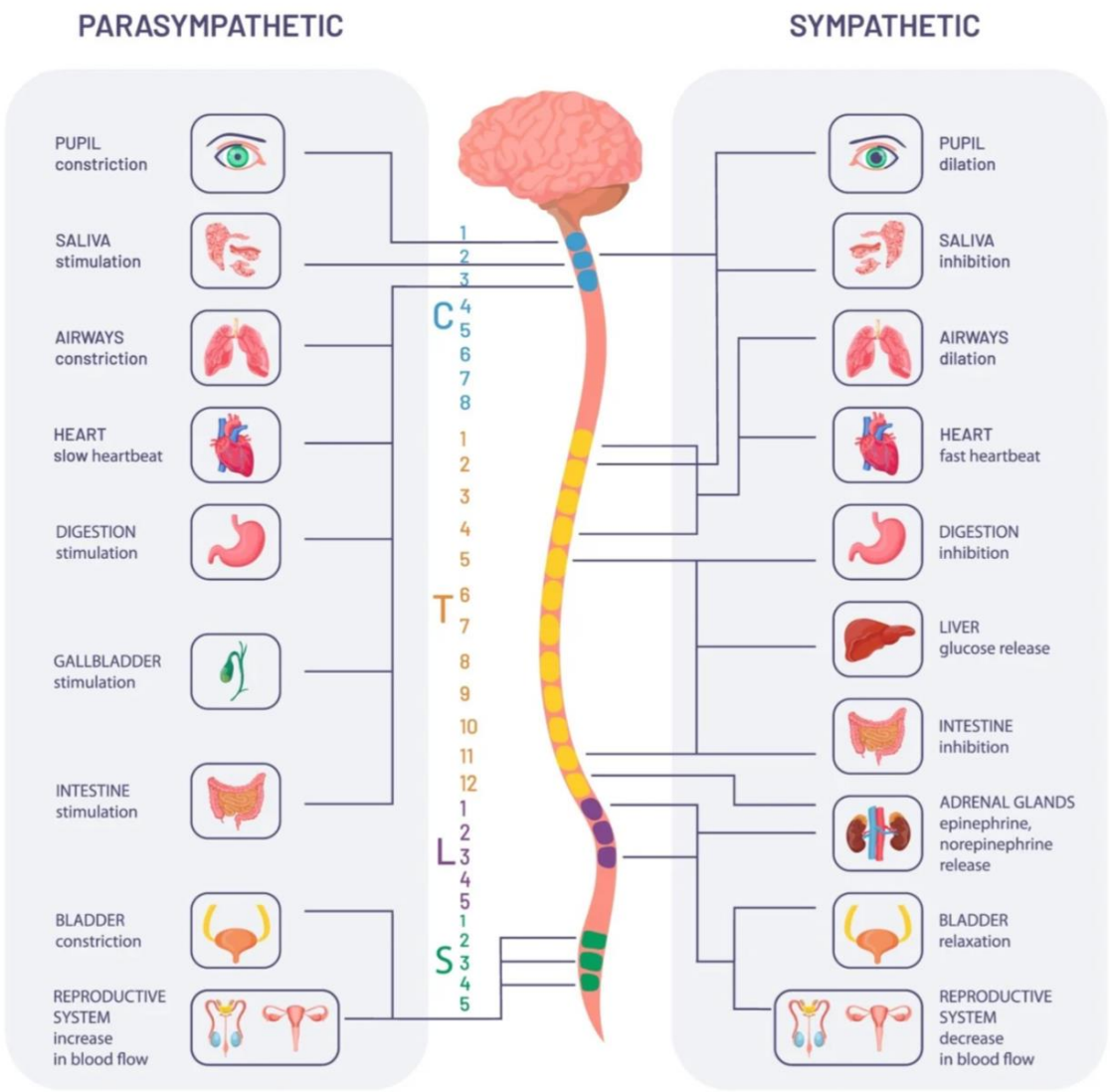
Adrenergic drugs



Definitions

- Neurotramsmitters:
- Neurotransmitters are the chemical mediators released by the neurons to transmit the signals through the synapse.
- Sympathomimetic: a drug that activates sympathetic nervous system.
- Parasympathomimetic: a drug that activates parasympathetic nervous system.
- Sympatholytic: a drug that decreases or blocks sympathetic response.
- Parasympatholytic: a drug that decreases or blocks parasympathetic response.
- Adrenaline (ADR) = epinephrine.
- Noradrenaline (NA)= norepinephrine.

Sympathetic VS. Parasympathetic NS



Synthesis and metabolism of catecholamines

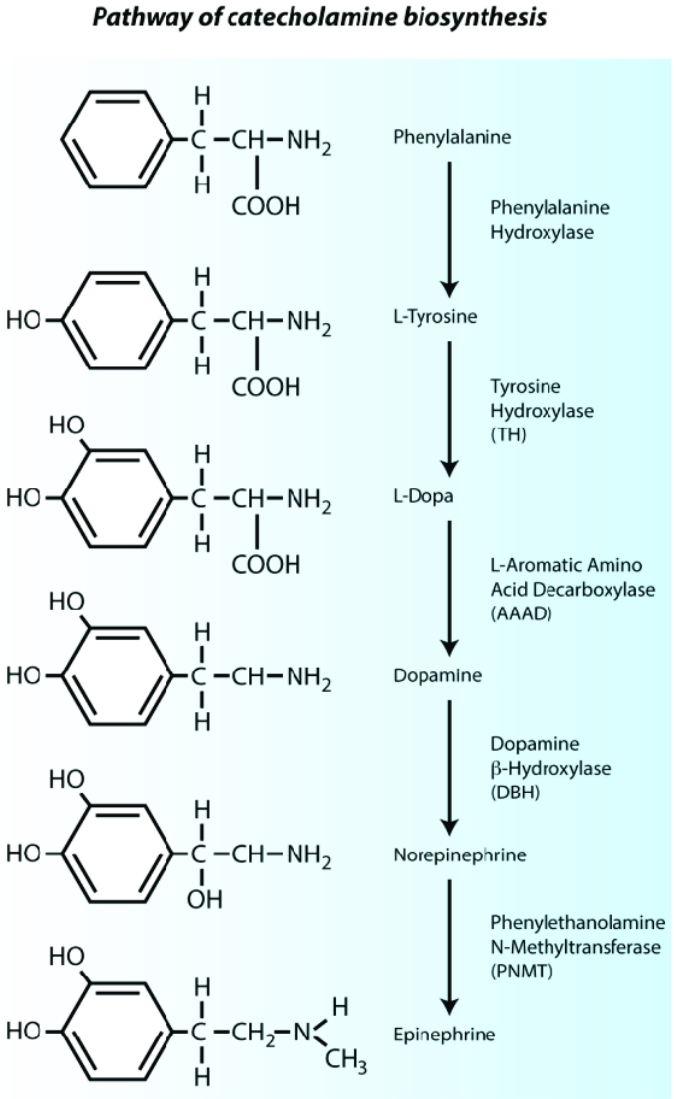
Catecholamines (CAs) are synthesized from the amino acid phenylalanine.

Synthesis of NA occurs in all adrenergic neurons.

Synthesis of ADR occurs only in the adrenal medullary cells.

Part of NA leaking out from vesicles into the cytoplasm and axonal transport is first attacked by MAO.

Diffused into circulation is first acted upon by catechol-o-methyl transferase (COMT) in the liver and other tissues.



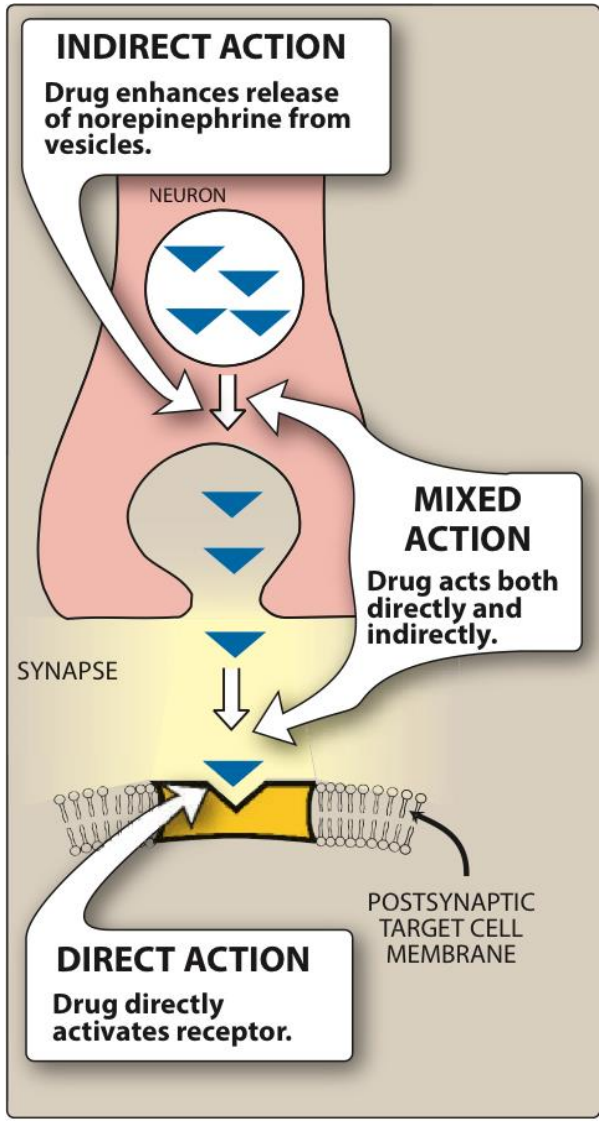
Adrenergic drugs (Sympathomimetics)

These are drugs with actions like that of ADR or of sympathetic stimulation.

Direct sympathomimetics: They act directly as agonists on α and/or β adrenoceptors like ADR, NA, isoprenaline (Iso), phenylephrine, methoxamine, oxylometazoline,salbutamol.

Indirect sympathomimetics: They act on adrenergic neuron to release NA which then acts on the adrenoceptors tyramine, amphetamine.

Mixed action sympathomimetics: They act directly as well as indirectly like ephedrine, dopamine, mephentermine.



Differences between α and β adrenergic receptors		
	α	β
1. Rank order of potency of agonists	Adr ≥ NA > Iso	Iso > Adr > NA
2. Antagonist	Phenoxybenzamine	Propranolol
3. Effector pathway	K^+ channel ↑	Ca^{2+} channel ↑

Alpha VS. Beta receptors

Mechanism of action

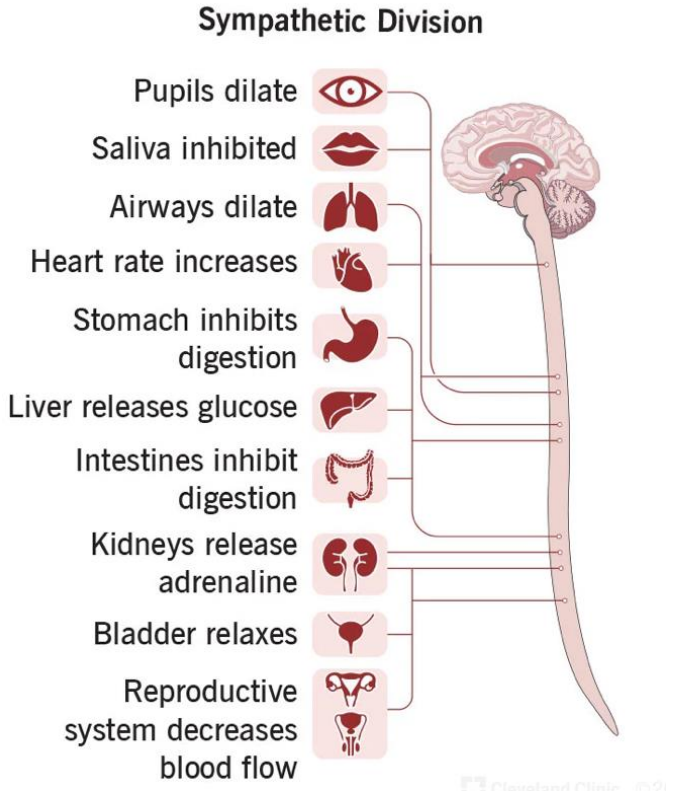
The peripheral actions of CAs are mediated by α, β receptors depending on the predominant receptor type present in a given tissue.

Drugs that affect Autonomic Nervous System will affect: Heart, Blood Vessels, Pancreas, Ureters, Bladder, Eyes, Pupils, Lacrimal Gland, Lung Airways, Brain.

Adr: $\alpha_1 + \alpha_2 + \beta_1 + \beta_2$

NA: $\alpha_1 + \alpha_2 + \beta_1$ but no β_2 action

Iso: $\beta_1 + \beta_2$ but no α action



Therapeutic classification of adrenergic drugs

Pressor agents:

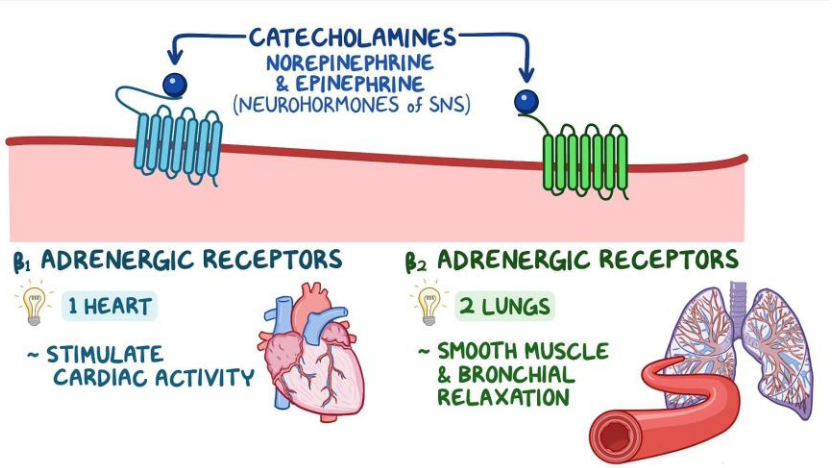
NA, Phenylephrine, Ephedrine, Methoxamine, and DA.

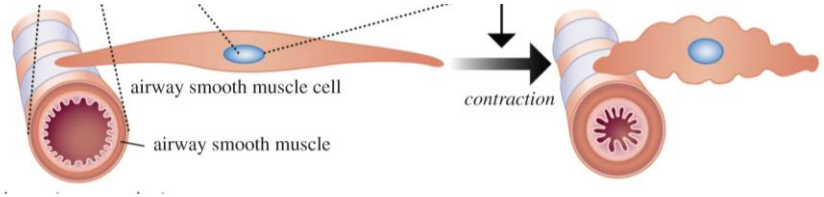
Cardiac stimulants:

ADR, Dobutamine and Iso.

Bronchodilators:

Iso, Terbutaline, Salbutamol, Bambuterol (Albuterol), Salmeterol, and Formoterol.





Therapeutic classification of adrenergic drugs

Nasal decongestants:

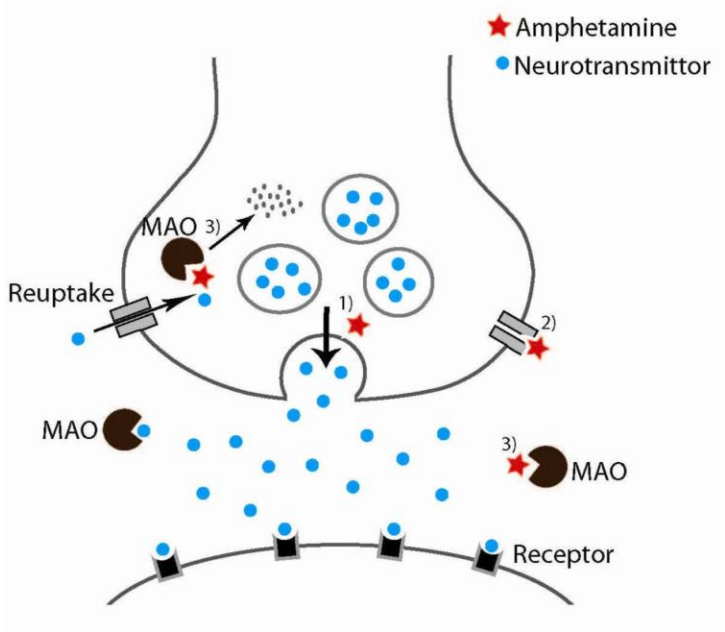
Phenylephrine, Naphazoline, Pseudoephedrine, and Oxymetazoline

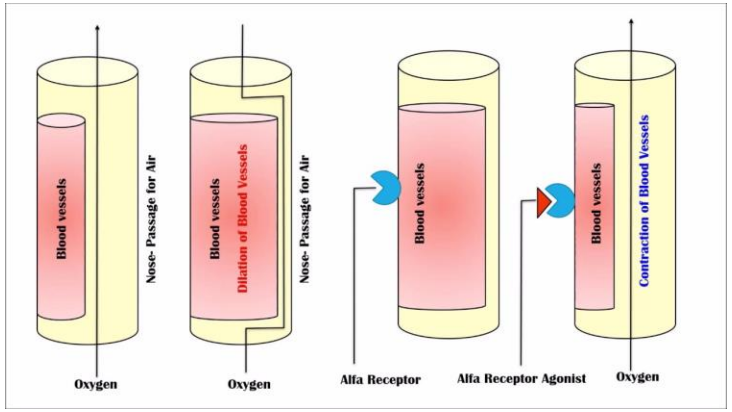
CNS stimulants:

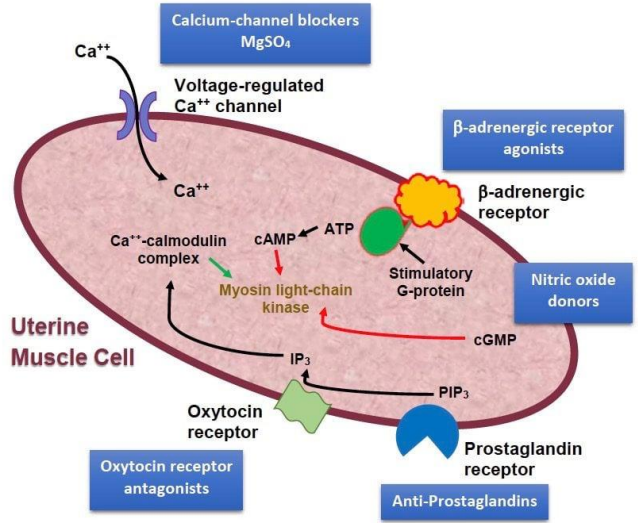
Amphetamine, Methamphetamine, and Dexamphetamine.

Uterine relaxants and vasodilators:

Ritodrine and terbutaline.







Effect of sympathetic stimulation on cardiovascular system

All cardiac actions are predominantly β1 receptor-mediated. When BP rises markedly, reflex bradycardia occurs due to stimulation of the vagal tone.

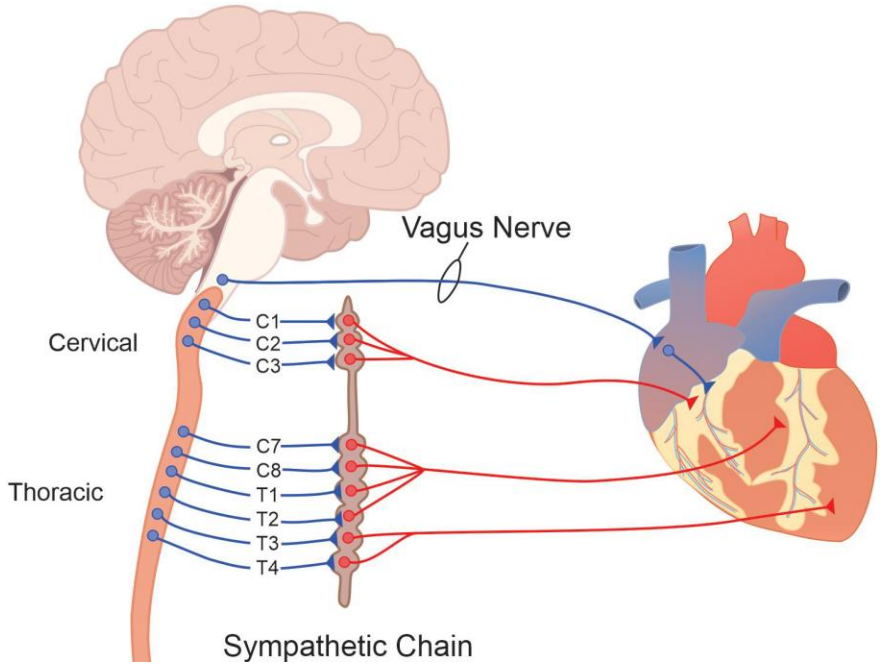
ADR increases heart rate by increasing the automaticity of SA node.It also activates latent pacemakers in AV node. Force of cardiac contraction is increased.

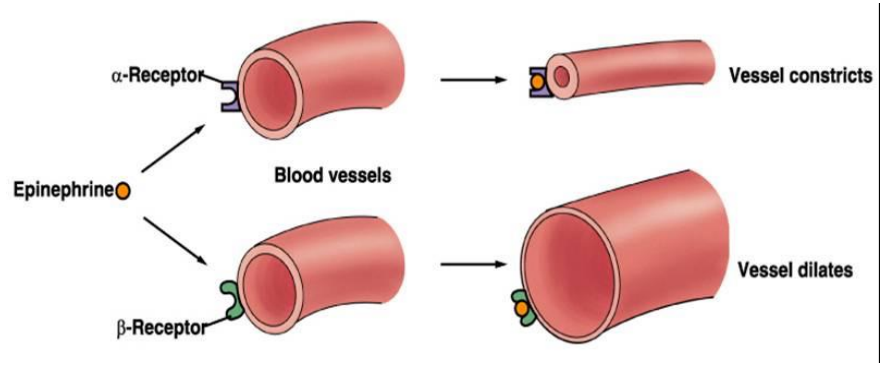
Cardiac output and oxygen consumption of the heart are markedly enhanced Blood vessels.

Both vasoconstriction (α) and vasodilatation (β2) can occur depending on the drug, its dose, and vascular bed.

Constriction predominates in cutaneous, mucous membranes, and renal beds. Vasoconstriction occurs through both α1 and α2 receptors.

Dilatation predominates in skeletal muscles, the liver, and coronaries. The direct effect on cerebral vessels is not prominent





Effect of sympathetic stimulation on respiratory system

ADR and Iso but not NA are potent bronchodilators (β2) when the bronchi are constricted. ADR can directly stimulate the respiratory center (RC), but this action is seldom manifest at clinically used doses.

Bronchial asthma: Adrenergic drugs, especially β2 stimulants, are the primary drugs for the relief of reversible airway obstruction

Selective β 2 agonists: Salbutamol, terbutaline, and its long-acting prodrug bambuterol, salmeterol, formoterol, and ritodrine.

They cause bronchodilation, vasodilation, and uterine relaxation without producing significant cardiac stimulation.

Salbutamol has a β2:β1 action ratio of about 10.

They are primarily used in bronchial asthma. Occasionally ritodrine is employed to depress uterine contractions and delay premature labor.

The most important side effect is muscle tremor.