Poltava State Medical University

Department of Pharmacology, Clinical Pharmacology and Pharmacy

Lecture

CHOLINERGIC DRUGS. ADRENERGIC DRUGS

AUTONOMIC NERVOUS SYSTEM

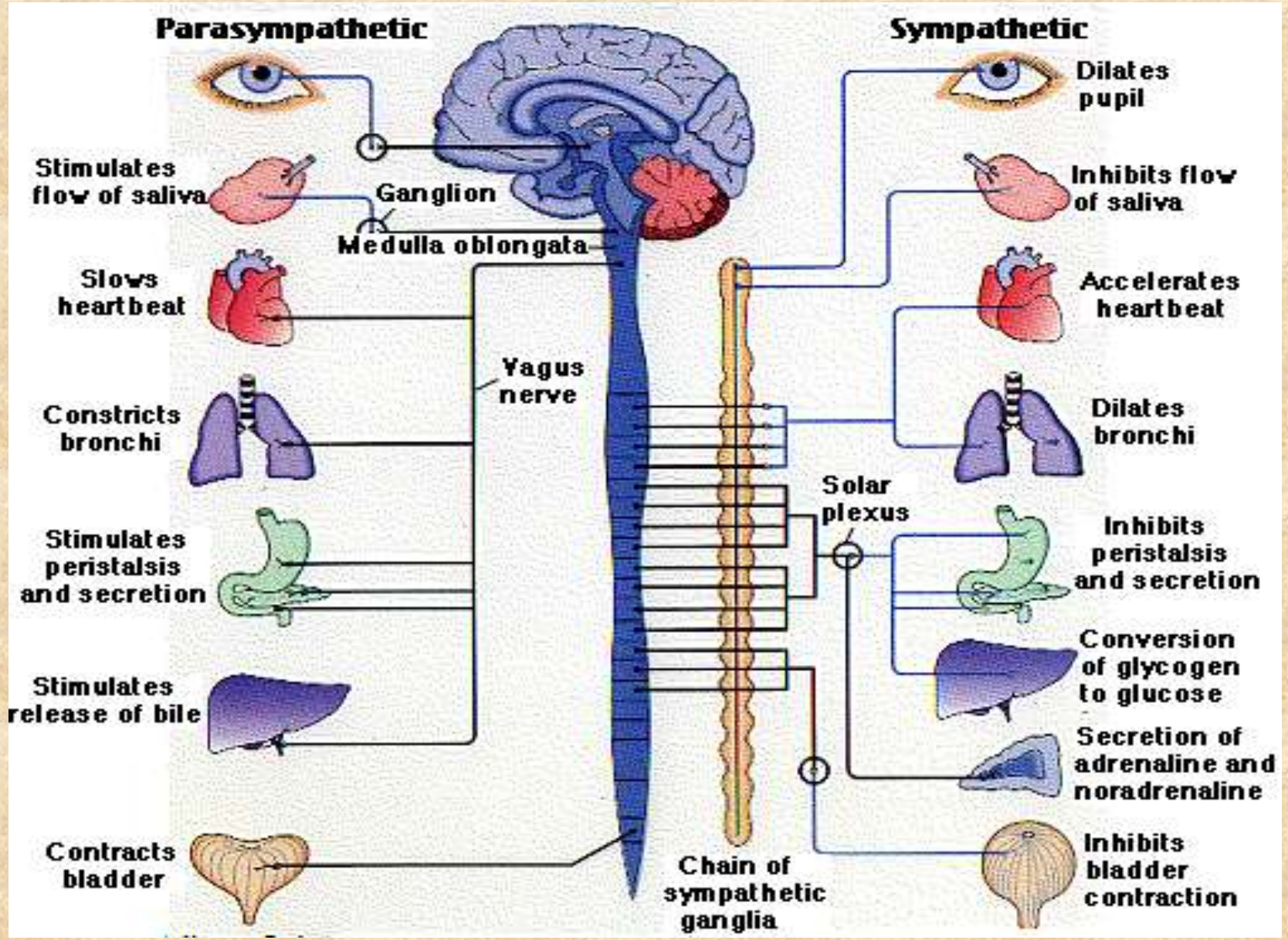
Autonomic nervous **system regulates the function of internal organs.**

It is divided into two sections:

- ***sympathetic system***
- ***parasympathetic system***

They exert opposite actions.

ANS: ANATOMY AND FUNCTION

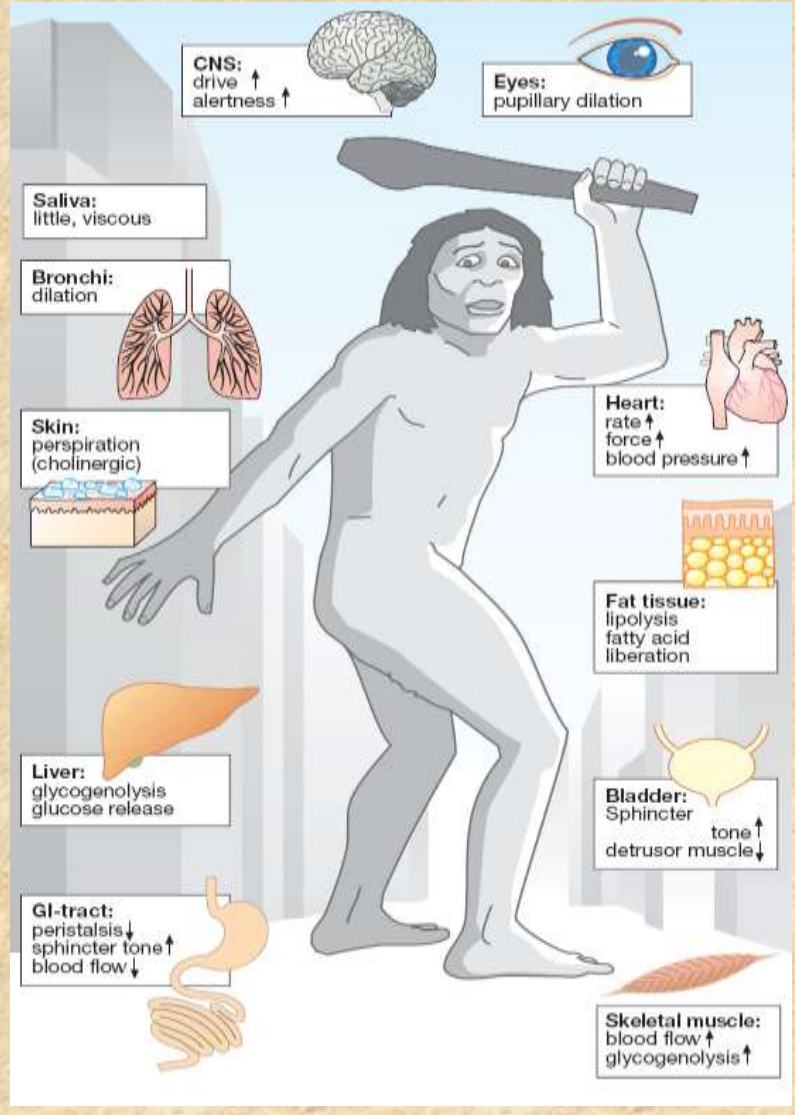


SYMPATHETIC SYSTEM (SANS)

Centers (the 1st neuron): thoraco-lumbal region of the spinal cord.

Ganglia (the 2nd neuron): near the spinal cord (Thruncus sympaticus)

RESPONSES TO SYMPATHETIC ACTIVATION

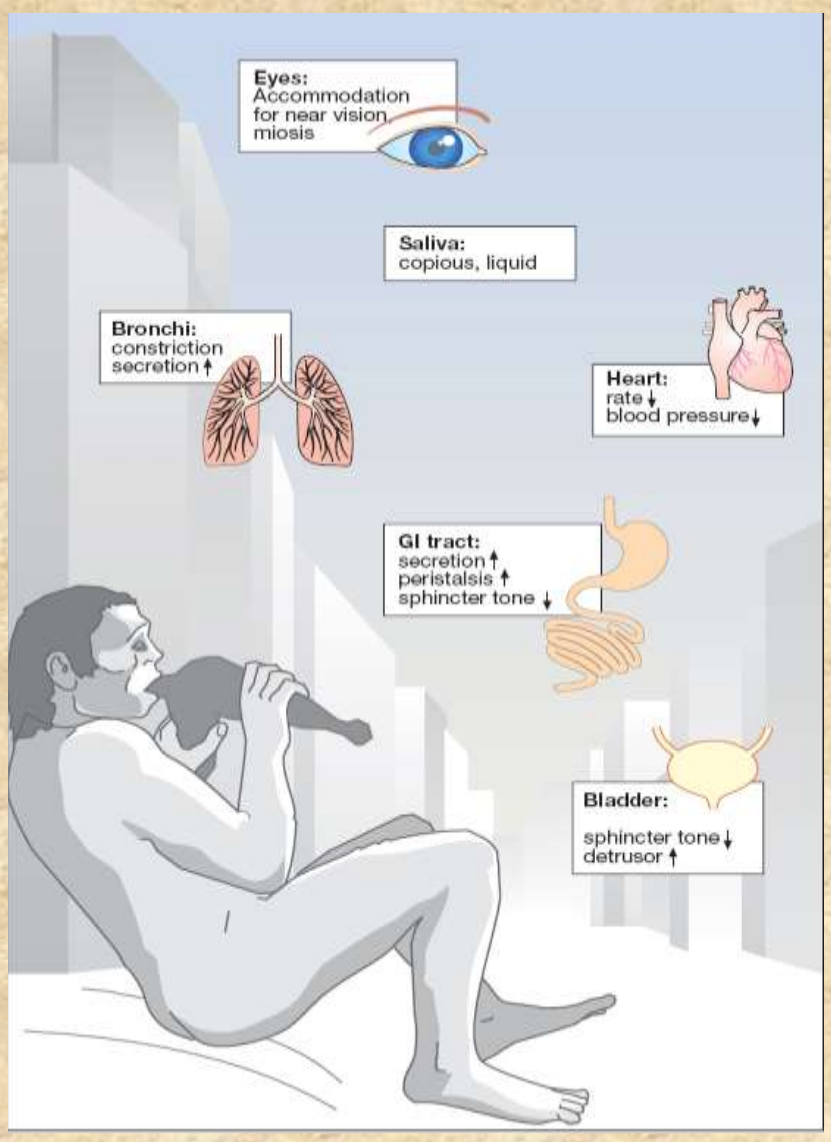


PARASYMPATHETIC SYSTEM (PANS)

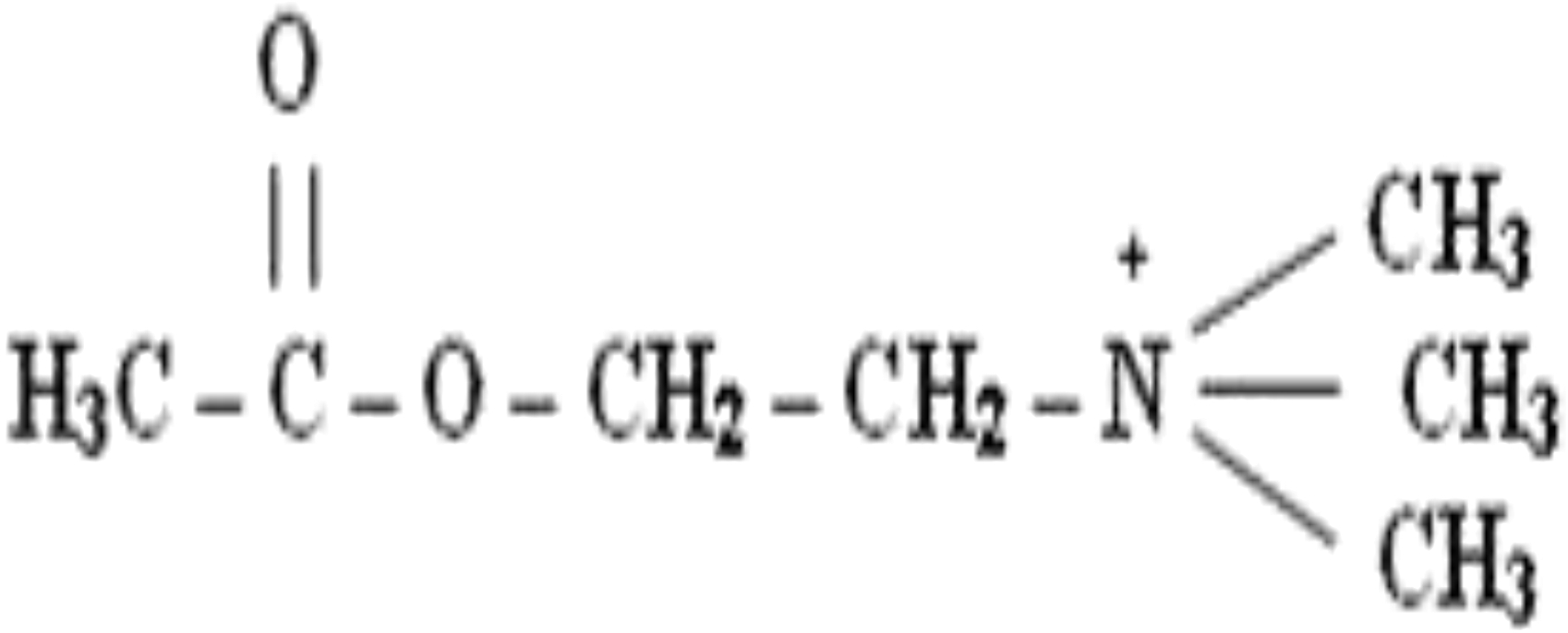
Centers (the 1st neuron): medulla of brain, sacral region of the spinal cord.

Ganglia (the 2nd neuron): in the tissues of effector organs or near them.

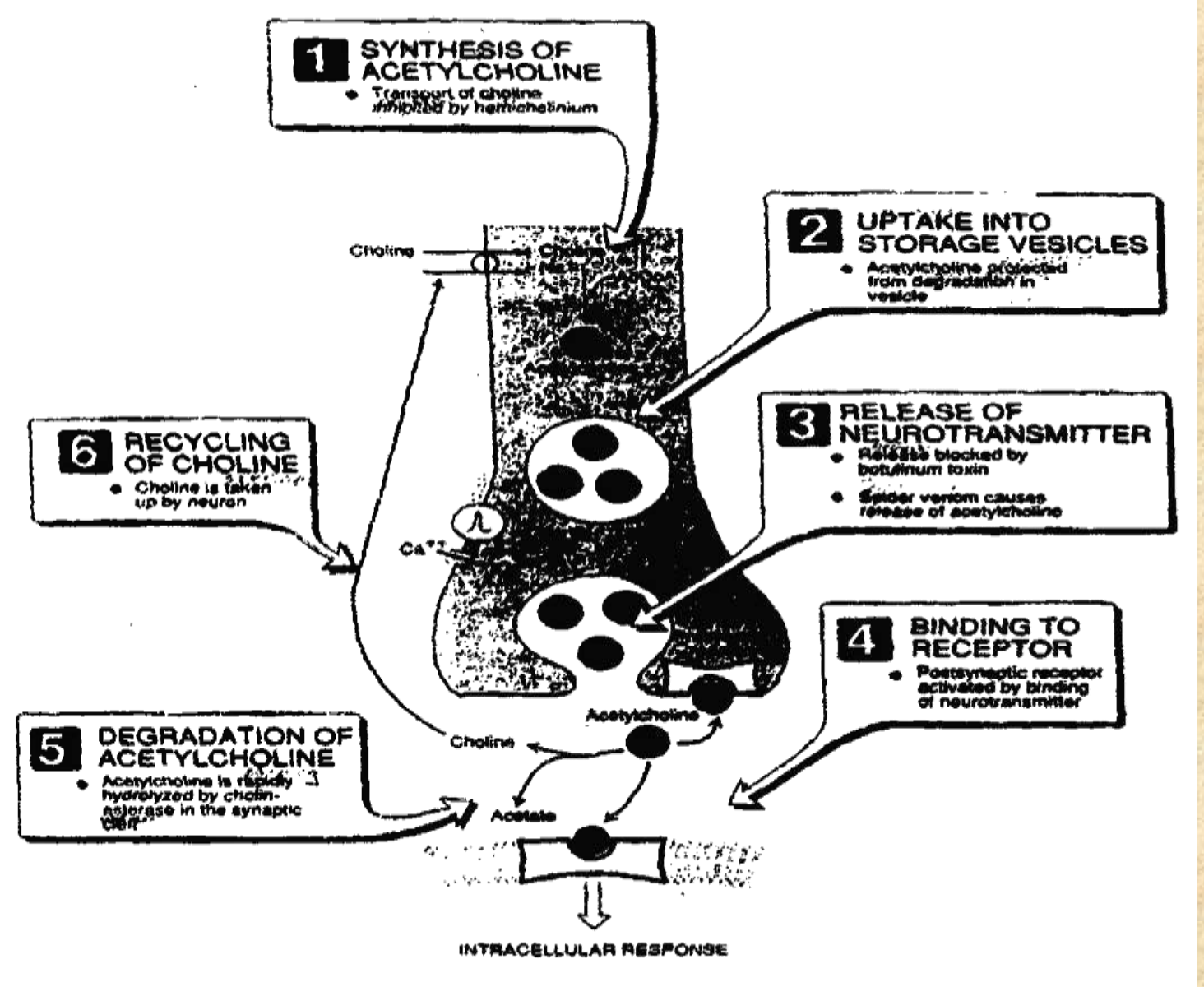
RESPONSES TO PARA-SYMPATHETIC ACTIVATION



ACETYLCHOLINE AS NEUROTRANSMITTER IN PANS



CHOLINERGIC SYNAPSE



CHOLINERGIC RECEPTORS

M-cholinoreceptor:

- **Agonists are acetylcholine and muscarine.**
- **Antagonist is atropine.**

N-cholinoreceptor:

- **Agonists are acetylcholine and nicotine (low dose).**
- **Antagonist is nicotine (bigger dose).**

Fly agarics is for muscarine

Tobacco is for nicotine

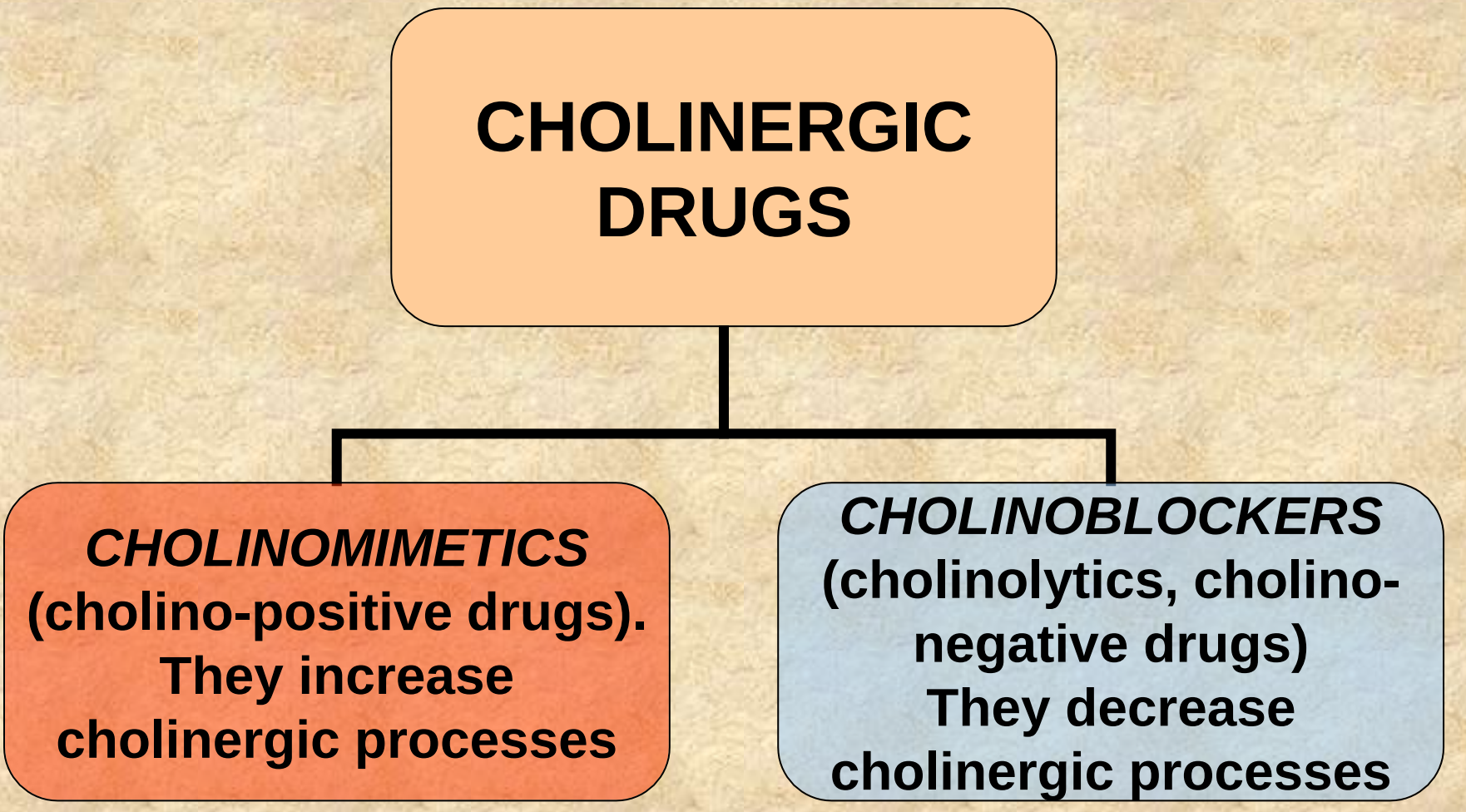
LOCATION OF N-CHOLINORECEPTORS

- CNS
- Adrenal medulla
- Carotid glomerulus
- Sympathetic and parasympathetic ganglia
- Skeletal muscles

LOCATION OF M-CHOLINORECEPTORS

- CNS
- Eye
- Heart
- Blood vessels
- Bronchi (smooth muscles, glands)
- Gut (smooth muscles, glands)
- Urinary bladder
- Uterus
- Sweat glands

CHOLINERGIC DRUGS



CHOLINOMIMETICS: Classification

A. M-,N-cholinomimetics

1. Direct-acting

– Acetylcholine

– Carbachol

2. Indirect-acting (anticholinesterases)

– Neostigmine (Proserinum)

– Physostigmine

– Pyridostigmine

– Galanthamine

– Isoflurophate (Phosphacolum)

B. M-cholinomimetics

– Pilocarpine

– Acecliodine

C. N-cholinomimetics

– Cytisine (Cytitonum)

– Lobeline

DRUGS WITH M-CHOLINOMIMETIC EFFECTS
(DIRECT-ACTING M-,N- AND M-CHOLINOMIMETICS)

M-cholinomimetic effects	Indications
Miosis **(constriction of pupils).** ***Spasm of accomodation*** **(regulation of eye lens on near vision).** ***Decrease in intra-eye pressure*****.**	**Glaucoma**
Stimulation of glands secretion. ***Increase in salivation.***	**Xerostomia**
Increase in smooth muscles tone.	**Atonia of intestine and urinary bladder after surgeries**
Bradycardia. ***Blood vessels dilatation.***	**Some kinds of tachyarrhythmia**

DIRECT-ACTING M-,N- AND M-CHOLINOMIMETICS:

PECULIARITIES OF PREPARATIONS

- ***Carbachol*** (Carbacholinum) has chemical structure similar to acetylcholine, but is non destroyed by cholinesterases; is direct acting M-, N-cholinomimetic with prevalence of M-cholinergic activity; now is applied topically for treatment of glaucoma (eye drops).
- ***Pilocarpine*** is an alkaloid from Pilocarpus pinnatifolius, is M-cholinomimetic; has strong systemic M-cholinomimetic activity, but is toxic; is now used only for treatment of glaucoma (eye drops, eye ointment, or eye membranes), seldom is used in xerostomia.
- ***Aceclidine*** is a synthetic preparation; is administered SC, IM, or topically (eye drops); is not toxic; does not penetrate CNS; is M-cholinomimetic; is used for treatment of atonia of intestine and urinary bladder as well as for glaucoma.

PILOCARPUS PINNATIFOLIUS CONTAINING PILOCARPINE

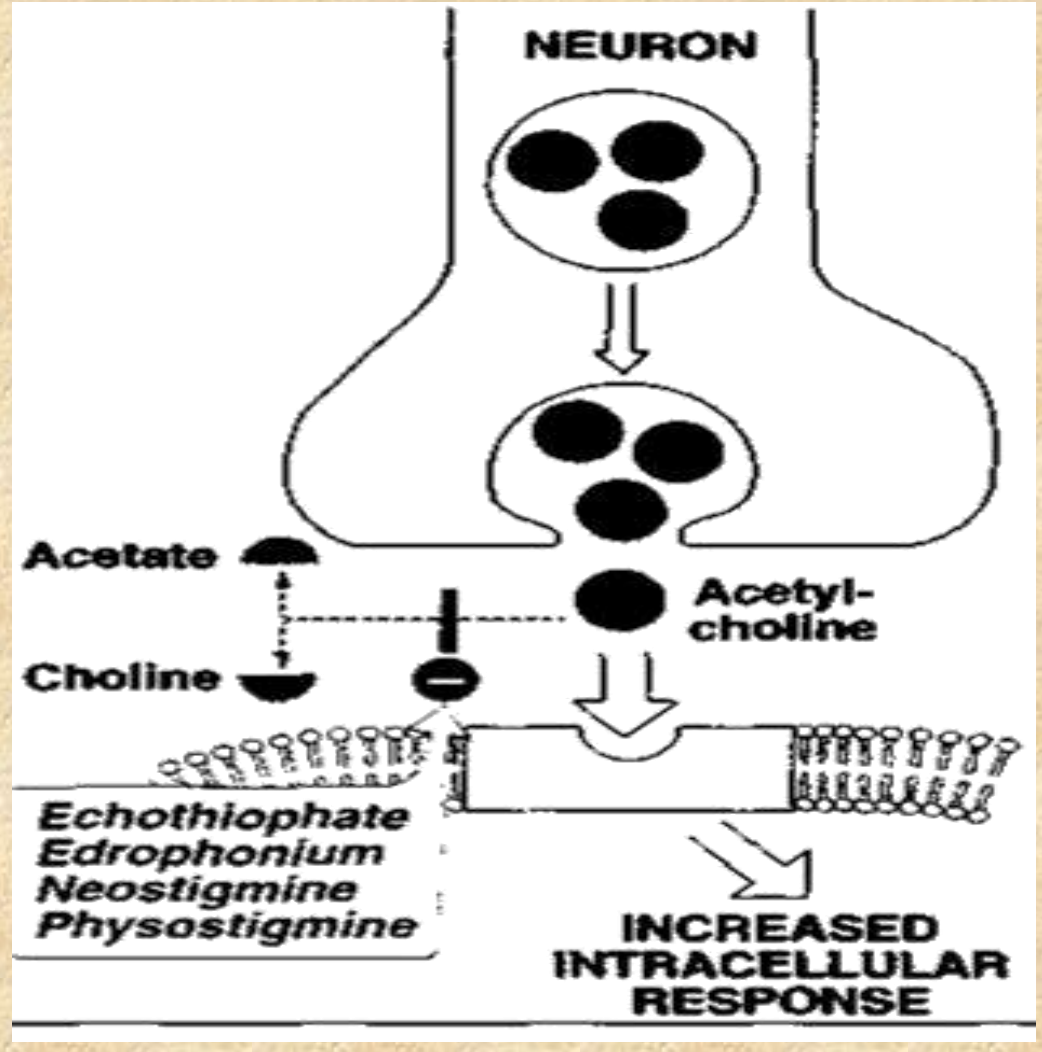
DIRECT-ACTING M-, N- AND M-CHOLINOMIMETICS: SIDE-EFFECTS

- Hypersalivation
- Pain in the abdomen
- Diarrhea
- Spasm of bronchi
- Bradycardia
- Frequent urination
- Sweatiness

ANTICHOLINESTERASES

ANTICHOLINESTERASES **are indirect-acting M-,N-cholinomimetics with reversible or irreversible type of action.**

ANTICHOLINESTERASES:
MECHANISM OF ACTION



ANTICHOLINESTERASES:
PHARMACODYNAMICS

- all typical M-cholinomimetic effects in the internal organs
- increase in neuromuscular transmission resulting from accumulation of acetylcholine at the neuromuscular junctions

ANTICHOLINESTERASES:
INDICATIONS

- Neurological diseases (paralysis, neuritis)
- Myasthenia gravis
- Atonia of the intestine and urinary bladder after surgeries
- Some kinds of arrhythmia
- Acute poisonings with atropine and anti depolarizing myorelaxants
- Glaucoma
- Xerostomia

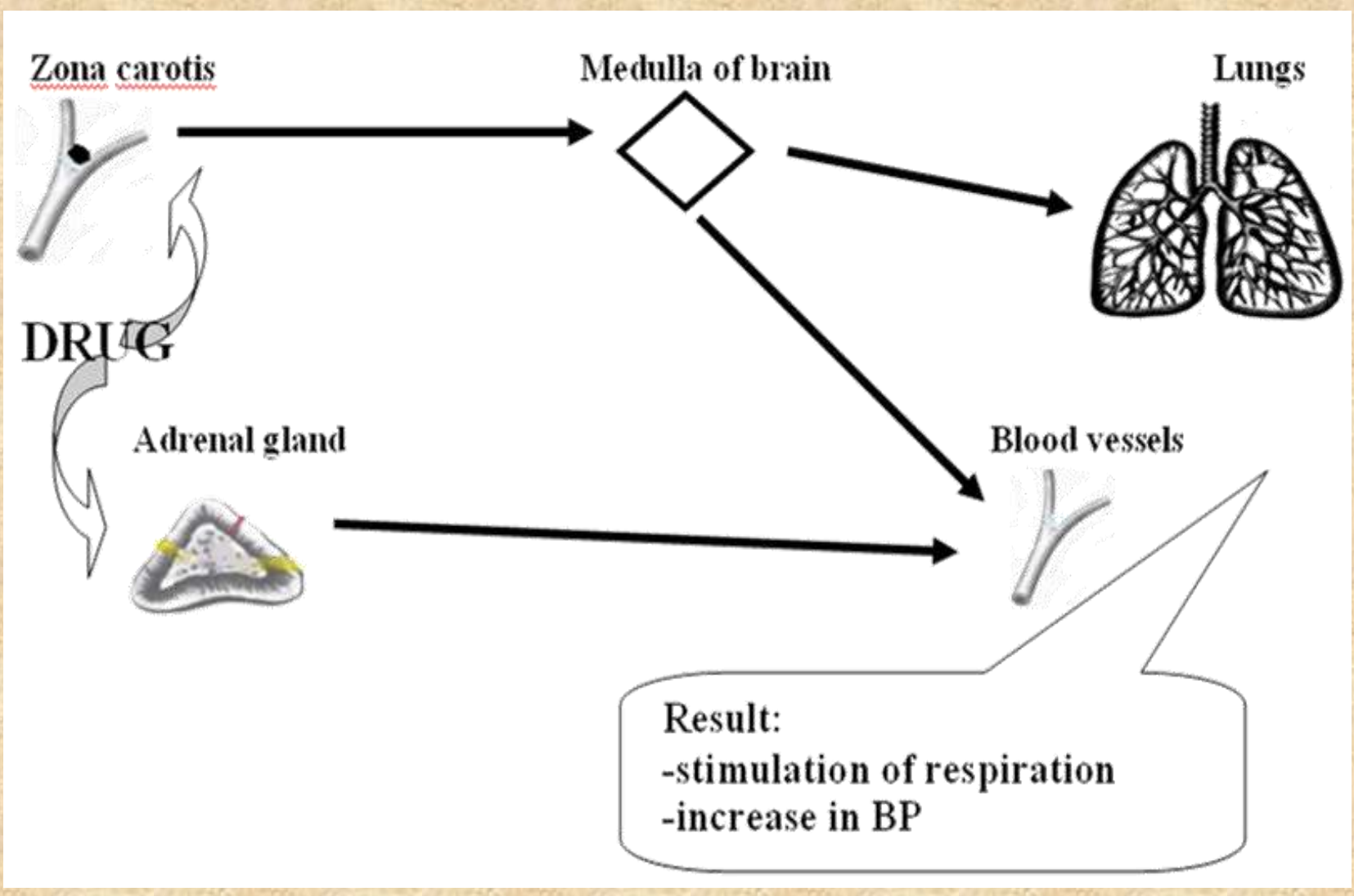
ANTICHOLINESTERASES:
PECULIARITIES OF PREPARATIONS

- ***Physostigmine*** **is an alkaloid from Phyzostigma venenosum; is well absorbed; penetrates CNS; has reversible action; is used for treatment of glaucoma, intoxication by atropine, cholinoblockers and tricyclic antidepressants, early stages of Alzheimer's disease; is toxic.**
- ***Galantamine*** **is an alkaloid from Galanthus Woronowi; is administered SC, IM; penetrates CNS; has reversible action; is used for treatment of paralysis, neuritis and other neurological diseases; is not used in glaucoma due to its irritation action.**
- ***Neostigmine*** **is a synthetic preparation; is administered orally, SC, IV, topically (eye drops); does not penetrate CNS; has reversible action (4-6 hrs); is used for paralysis, neuritis, myasthenia gravis, atonia of intestine and urinary bladder, some kinds of arrhythmia, glaucoma, poisoning with atropine, overdose of tubocurarine; may be used for stimulation of labour activity; in dentistry is applied for xerostomia.** ***Pyridostigmine*** **acts longer, but is less active than neostigmine; is used orally for treatment of neurological diseases and myasthenia gravis.**
- ***Phosphacolum*** **is irreversibly acting anticholinesterase with long-lasting action; is toxic and use only for glaucoma.**

MEDICINAL PLANTS CONTAINING ANTICHOLINESTERASES:

PHYZOSTIGMA VENENOSUM (left); GALANTHUS WORONOWI (right)

N-CHOLINOMIMETICS:
MECHANISM OF ACTION



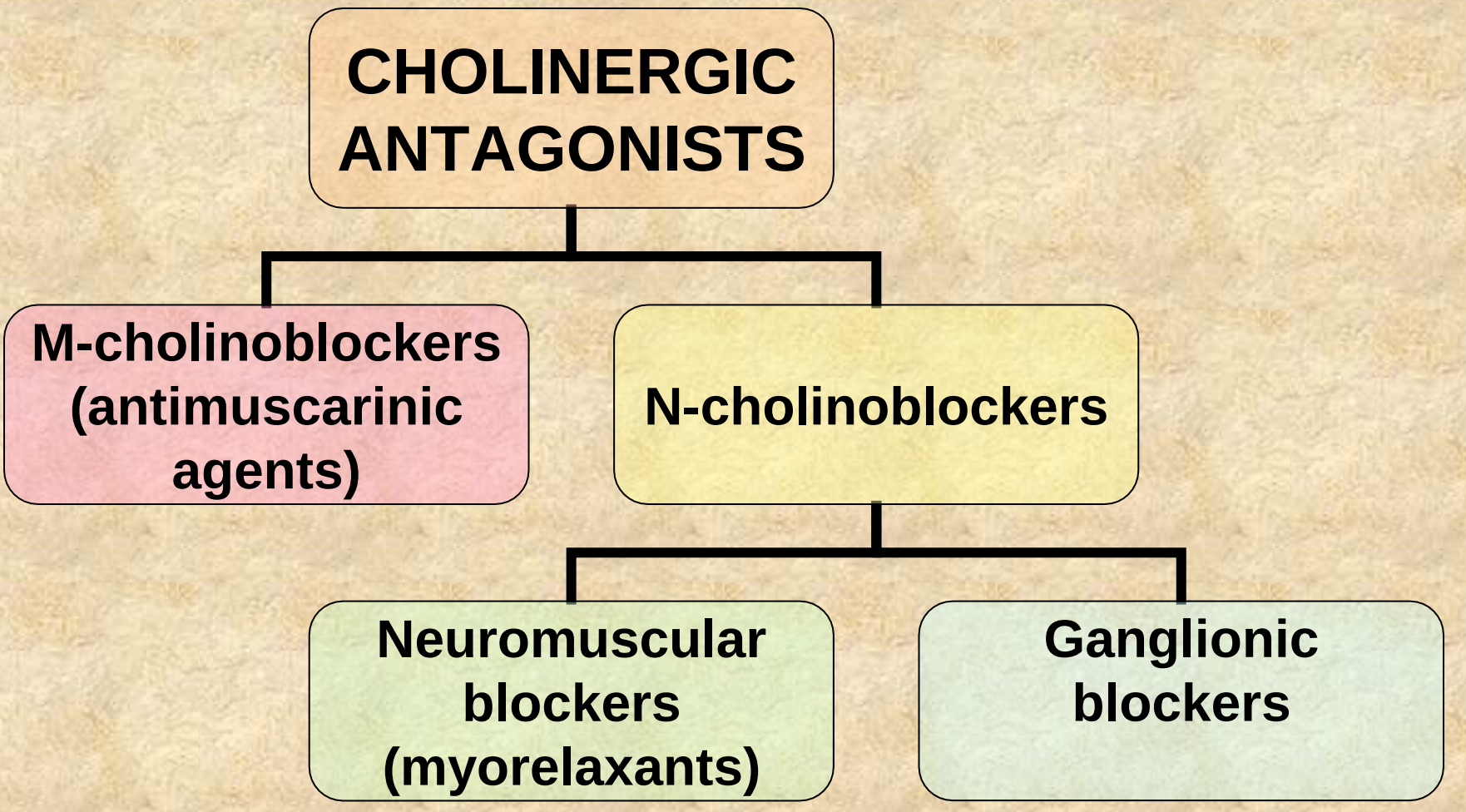
N-CHOLINOMIMETICS:
INDICATIONS

- **Respiratory arrest (IV)**
- **Asphyxia (IV)**
- **Treatment of tobacco abuse (orally, combined tablets)**

N-CHOLINOMIMETICS:
PECULIARITIES OF PREPARATIONS

- ***Cytitonum*** **is a name of cytisine solution; is administered IV, acts 3-5 min; stimulates N-cholinoreceptors; reflexly stimulates respiration and increase BP; is used for emergence help in respiratory arrest and collapse.**
- ***Lobeline*** **is an alkaloid; is administered IV and acts during 3-5 min; mechanism of action is similar to Cytitonum; is used for emergence help in respiratory arrest, asphyxia, asphyxia of newborns, rarely in pneumonia; is not used for collapse due its ability to cause transitory decrease in BP resulting from stimulation of n. vagus center.**

CHOLINERGIC ANTAGONISTS



M-CHOLINOBLOCKERS:
CLASSIFICATION

A. Non-selective preparations

1. Natural agents

- **Atropine sulfate**
- **Hyoscine (Scopolamine hydrobromide)**
- **Platyphylline hydrotartrate**
- **Belldoonna dry extract**

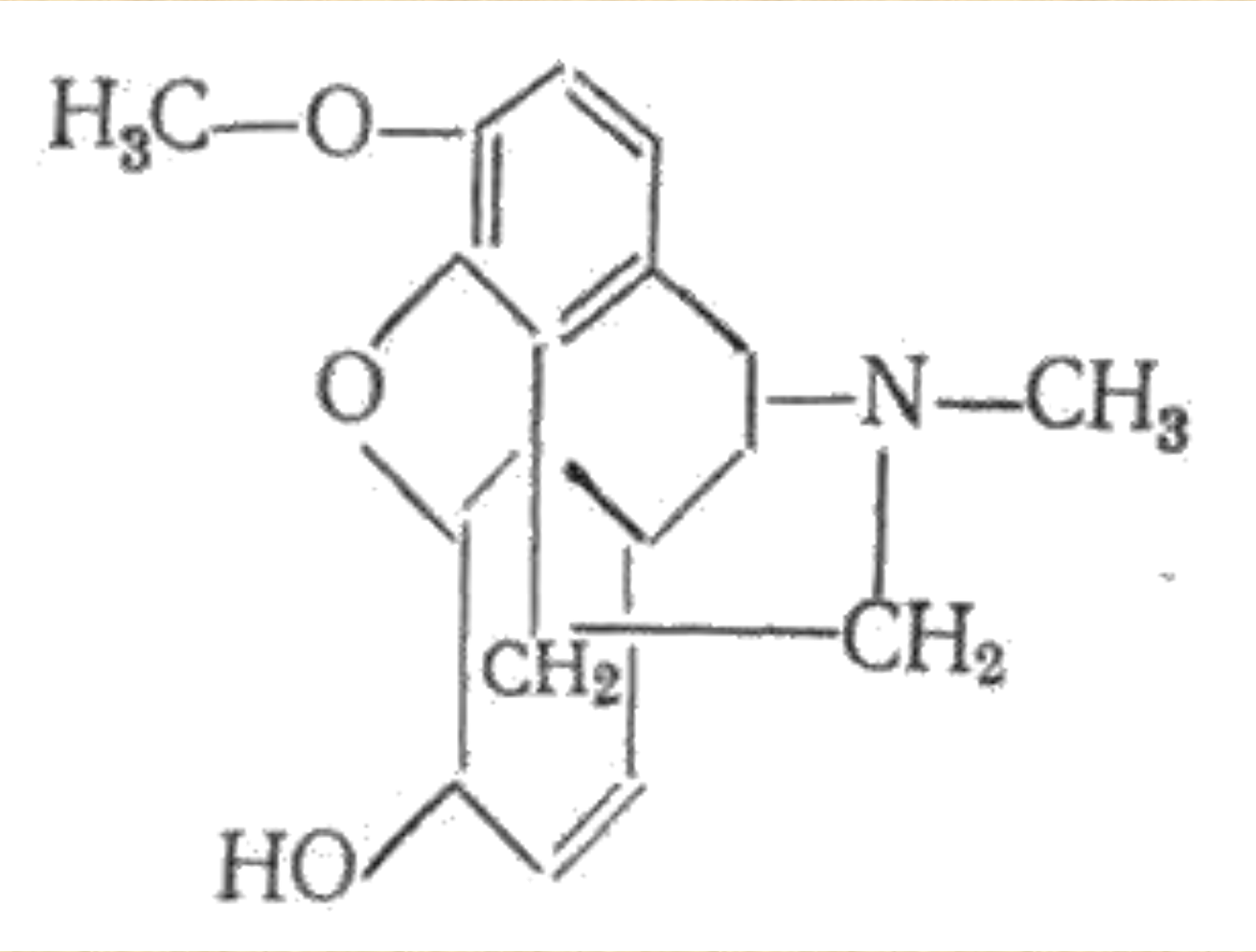
2. Synthetic agents

- **Methacine**
- **Ipratropium bromide (atrovent)**
- **Butylscopolamine (buscopan)**
- **Prifinium bromide (riabal)**
- **Ipratropium bromide (Atrovent)**
- **Tropicamide**

B. Selective preparations

- **Pirenzepine (Gastrocepine)**

ATROPINE:
CHEMICAL STRUCTURE



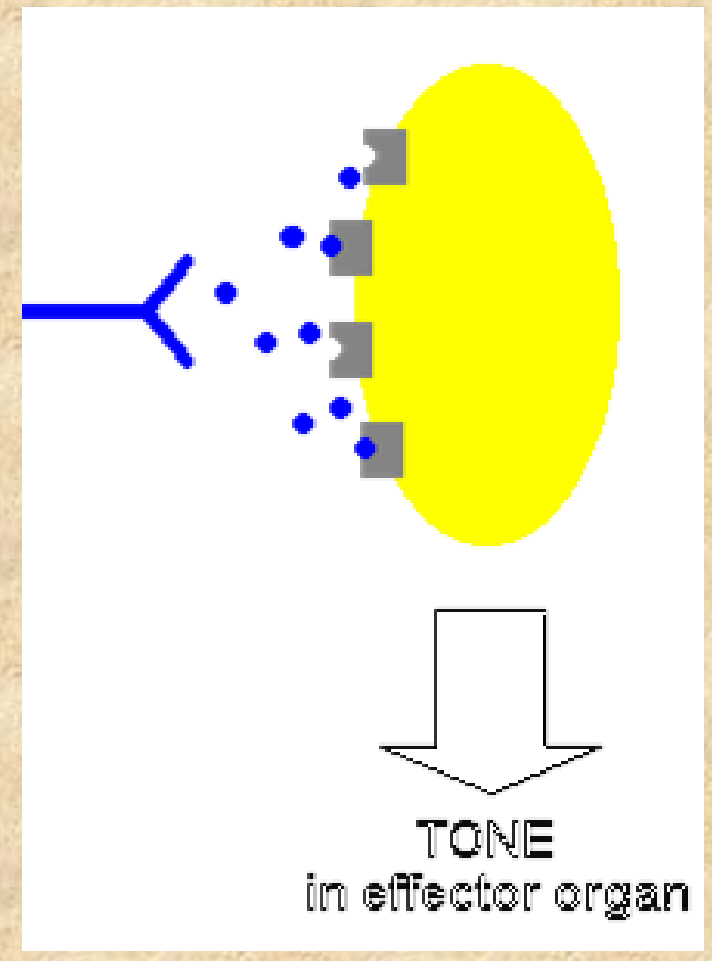
ATROPINE:
ATROPA BELLADONNA CONTAINING ATROPINE

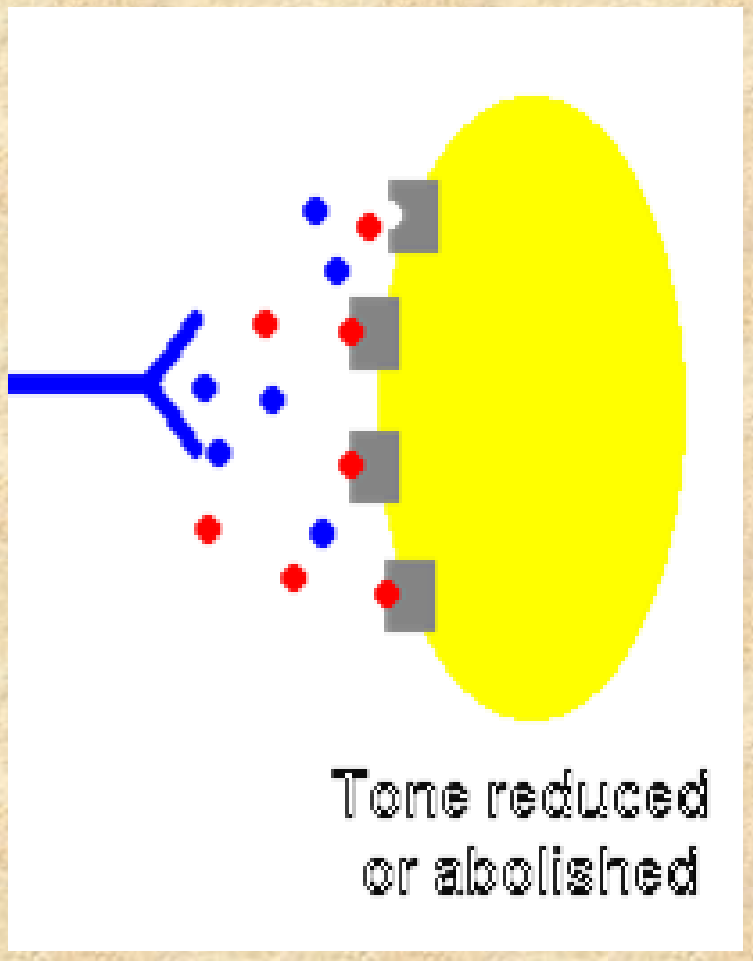
ATROPINE:
PHARMACOKINETICS

- is administered orally, IM, SC; is applied topically (eye drops)
- is absorbed in the gut
- is bound with plasma proteins (18%)
- penetrates CNS and placenta
- is metabolized in the liver by atropinase
- is excreted with urine
- has T ½ = 2 hrs; acts on internal organs during 4 hrs; influences on the eye during 7-10 days.

ATROPINE :

MECHANISM OF ACTION (SYNAPSE WITHOUT (LEFT) AND WITH ATROPINE (RIGHT)





ATROPINE:
PHARMACODYNAMICS

- *in the site of application:* **weak local anesthesia**
- *in the CNS:* **therapeutic doses - sedation and antiparkinsonian effect, big doses - excitation, hallucinations, coma**
- **in the eye: midriasis, cycloplegia (paralysis of accomodation), increase in intraocular pressure**
- *in the cardiovascular system:* **therapeutic doses – tachycardia**
- *in the respiratory system:* **dilation of bronchi, decrease in secretion of bronchial glands**
- *in the gut:* **reduce of secretion of saliva and gastric juice, decrease in the tone and motility; antispasmotic activity**
- *in the urinary system:* **relaxation of smooth muscles of urinary bladder and urinary pathways**
- **inhibition in secretion of sweat**
- *antidote properties* **in acute poisonings with M-cholinomimetics, anticholinesterases and toxic mushrooms containing muscarine; reduce in vagal action of morphine and general anesthetics.**

ATROPINE:
ACTION ON THE EYE

NORMAL CONDITION

INSTILLATION OF ATROPINE

ATROPINE:
INDICATIONS

- Trauma of the eye, inflammation in the eye
- Diagnostic of eye diseases, measurement of refraction for selection of glasses
- Bradycardia, A-V block
- Hypersalivation
- Gastric ulcer, gastritis with acid hypersecretion
- Acute pancreatitis
- Cholecystitis
- Colic
- Enuresis
- Premedication
- Acute poisonings with muscarine-containing mushrooms, M-cholinomimetics, anticholinesterases, and morphine.

ATROPINE:

SIDE EFFECTS AND CONTRAINDICATIONS

SIDE EFFECTS

1. Photophobia
2. Blurred vision
3. An increase in intraocular pressure
4. Tachycardia
5. Dry mouse
6. Constipation
7. Retention of urine
8. Flushed skin
9. Rise in body t^{o}

CONTRAINDICATIONS

1. Glaucoma
2. Tachycardia, tachy-arrhythmia
3. Atonia of GI tract
4. Prostate hyperplasia
5. Hepatic insufficiency
6. Hyperthyroidism
7. High body temperature
8. Toxicosis of pregnancy
9. Cerebral pathology in children
10. Childhood or old age

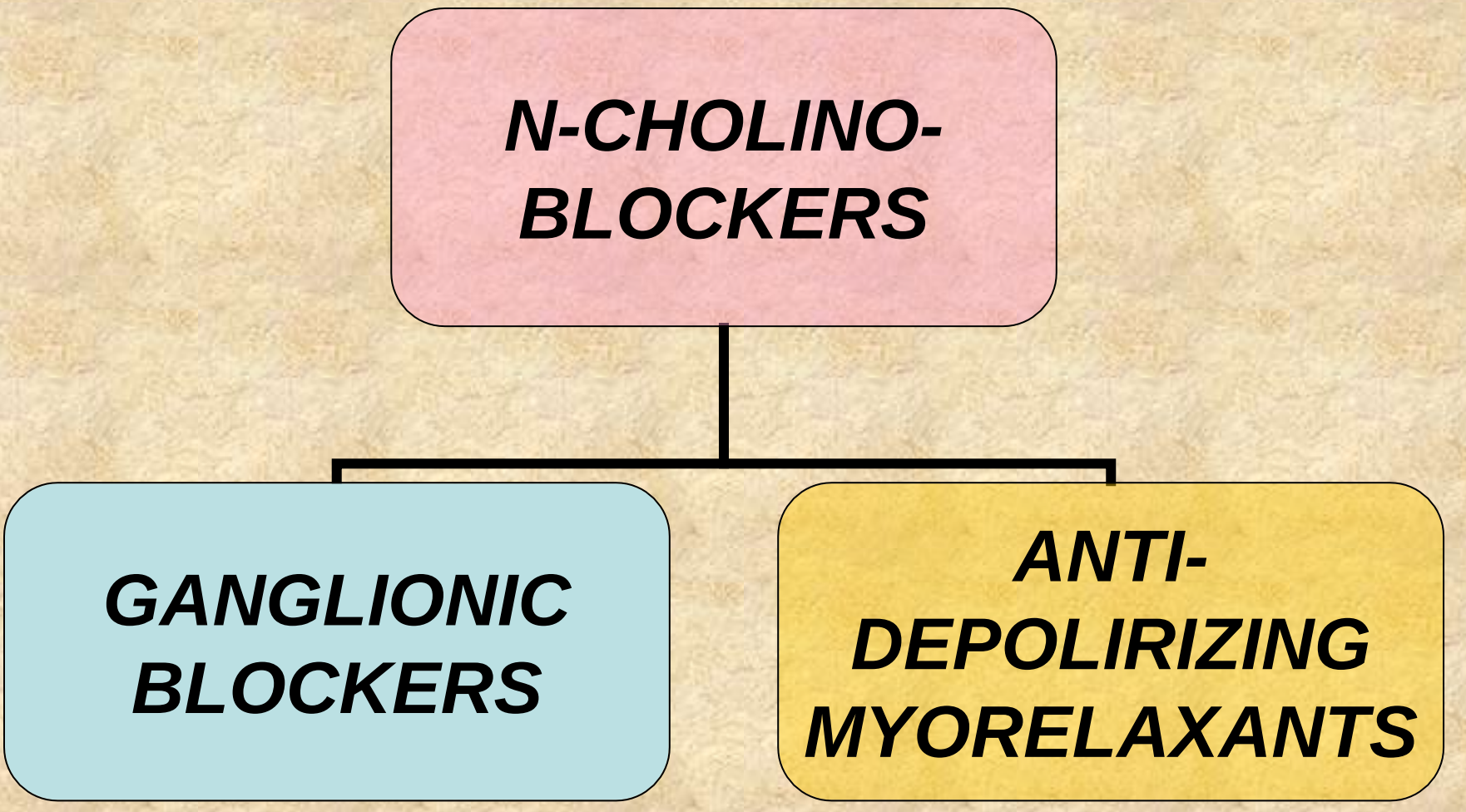
M-CHOLINOBLOCKERS:
PECULIARITIES OF OTHER PREPARATIONS

- ***Scopolamine*** **is an alkaloid containing in Scopolia. central action is greater and longer than the same of atropine; it inhibits VIII pair of cranial nerves, produces sedation and short-memory blocking, has antiparkinsonian effect; is used for prevention and treatment of motion sickness, Parkinson's disease, and for premedication.**
- ***Platyphylline*** **is an alkaloid from Senecio platyphylus; central action is less than the same of atropine; dilates blood vessels and lowers BP; may be used to treat spasms of blood vessels and hypertension.**
- ***Methacine*** **is a synthetic preparation; is more potent than atropine in dilation of bronchi, inhibition of gasrtric secretion, and decrease of uterus tone; does not penetrate CNS, does not act on the eye, has poor influence on the heart rate; is used in bronchial asthma, ulcer of stomach, colic, premedication, and danger of pregnancy interruption.**
- ***Pirenzepine*** **is a selective M1-cholinoblocker inhibiting gastric secretion; does not penetrate CNS and placenta; is used for treatment of ulcer of stomach and duodenum, prevention of peptic ulcers caused by stress; side-effects are minimal in comparison with atropine.**
- ***Ipratropium bromide*** **is M-cholinoblocker in the form of aerosol; is not absorbed in lungs and acts on M-cholinoreceptors only in bronchi; dilates bronchi; is used for prevention of bronchial asthma attack; may cause unpleasant taste.**

M-CHOLINOBLOCKERS:
PECULIARITIES OF OTHER PREPARATIONS

- ***Preparations of Bbelladonna (extracts, tinctures)*** **are used as antispasmodic and analgesic agents for stomach ulcer, cholelithiasis and spasms of smooth muscles of the abdominal cavity organs, bradycardia due to overexcitation of n. vagus. They are the ingredients of some combined preparations.**
- ***Butylscopolamine*** **is a semisynthetic derivative of scopolamine which does not penetrate blood-brain barrier and has not central action. It is used to treat abdominal pain, esophageal spasms, renal colic, and bladder spasms. The drug is effective in reducing the duration of the first stage of labor. Side effects may include sleepiness, vision changes, triggering of glaucoma, and allergy.**
- ***Prifinium bromide (riabal)*** **is slowly absorbed into the gut and quickly excreted; blocks peripheral M-cholinoreceptors in the GI tract normalizes the peristalsis of the stomach, corrects increased motor activity of the GI tract. The drug is used in nausea and vomiting caused by functional spasms in infants, abdominal pain syndrome with functional disorders of the colon; spasms of smooth muscles of the GII tract. Side effects are dry mouth, mydriasis, disturbances of accommodation, drowsiness.**
- ***Tropicamide*** **blocks M-cholinoreceptors of the sphincter in the iris and ciliary muscle, causing short-term mydriasis and accommodation paralysisis; is used in ophthalmology for examination of the ocular fundus, investigation of refraction, as well as in inflammatory processes of the eye. It is applied as eye drops**

N-CHOLINOBLOCKERS



GANGLIONIC BLOCKERS

GANGLIONIC BLOCKERS **are medicinal drugs which block N-cholinorecepors in the symphathetic and parasympathetic ganglia.**

GANGLIONIC BLOCKERS:
CLASSIFICATION

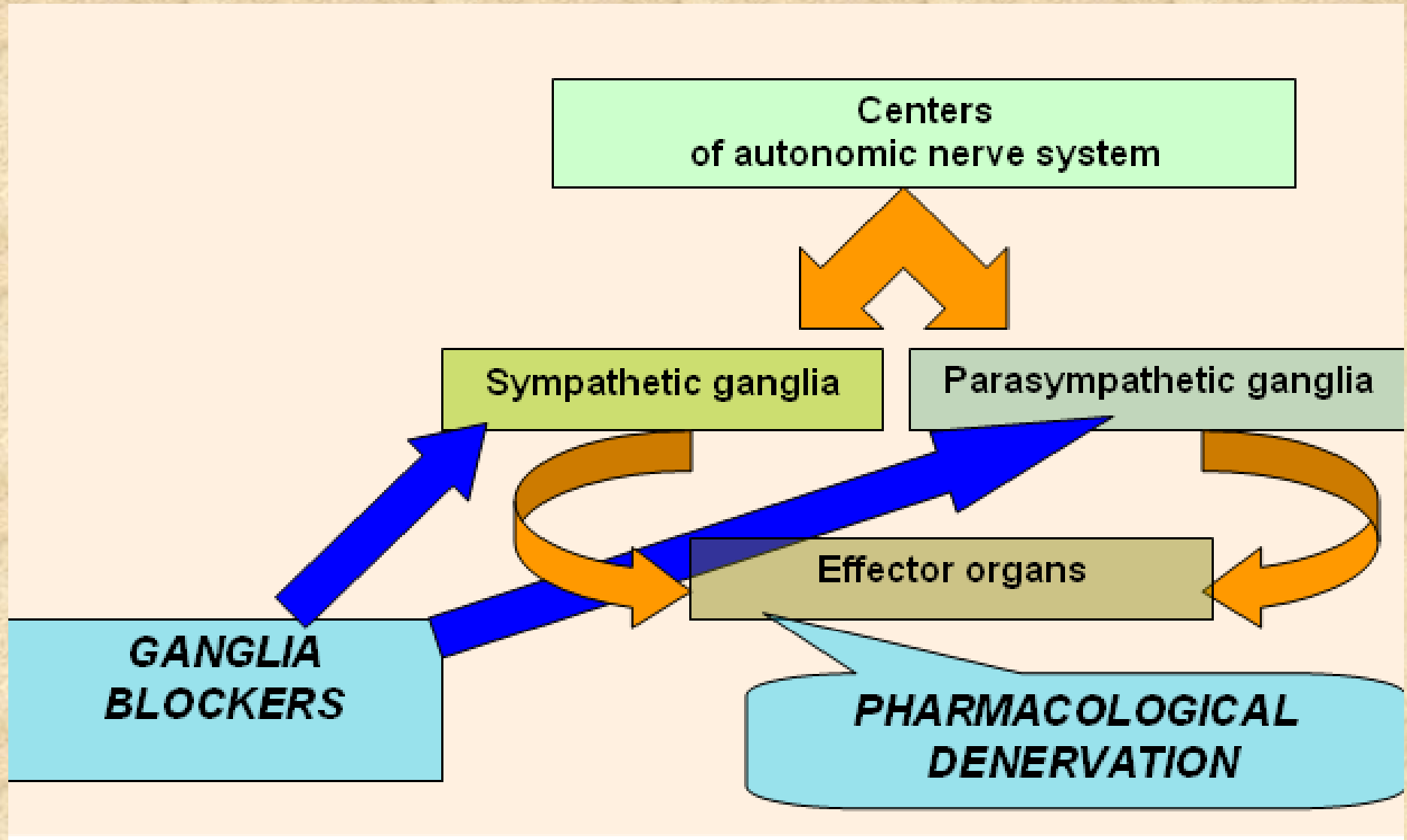
1. Quaternary amines

- Hexamethonium (Benzohexonium)
- Hygronium
- Pentamine

2. Tertiary amines

- Pachycarpine
- Pirilene

GANGLIONIC BLOCKERS:
MECHANISM OF ACTION



GANGLIONIC BLOCKERS:
PHARMACODYNAMICS

- dilation of blood vessels, redistribution of blood in the body, lowering of BP
- dilation of bronchi
- a decrease in secretion and motility of the gut, a reduce in spasm of the smooth muscles
- a decrease in the tone of urinary bladder and urinary pathways
- an increase in sensitivity of myometrium to oxytocin and stimulation of uterus contractions in the labor
- a decrease in sweat secretion
- changes in intraocular pressure.

GANGLIONIC BLOCKERS:
INDICATIONS

- Hypertensive emergence
- Hypertension (rarely)
- Controlled hypotension in surgeries
- Edema of lungs
- Edema of the brain
- Bronchial asthma attack
- Colic
- Ulcer of the stomach (rarely).

GANGLIONIC BLOCKERS:
SIDE EFFECTS AND CONTRAINDICATIONS

SIDE EFFECTS

1. *Hypotension*
2. *Orthostatic collapse (postural hypotension)*
3. *Dry mouth*
4. *Constipation*
5. *Retention of urination*
6. *Increase of intraocular pressure in patients with closed-angle glaucoma.*

CONTRAINDICATIONS

1. *Hypotension, collapse*
2. *Severe atherosclerosis*
3. *Closed-angle glaucoma*
4. *Atony of the gut*
5. *Adenoma of prostate*
6. *Severe diseases of heart, liver, and kidney.*

GANGLIONIC BLOCKERS:
PECULIARITIES OF PREPARATIONS

- ***Hexamethonium (Benzohexonium)*** **is administered orally, IM, IV; does not penetrates CNS; acts during 3-4 hrs; has all typical properties.**
- ***Hygronium*** **is a short-acting potent ganglia blocker; is administered by IV infusion; is used for controlled hypotension in surgeries, edema of lungs, edema of brain, severe hypertensive crisis.**
- ***Pentamine*** **is less potent than hexamethonium, acts during 1,5 hrs, is administered IV, IM for emergence help in acute hypertension, bronchial asthma attack, colic, for controlled hypotension in surgeries.**
- ***Pirilene*** **is a synthetic preparation, tertiary amine, is taken by mouth, is well absorbed in the gut, penetrates CNS, acts during 6-8 hrs; is used to treat gangliolitis, spasms of peripheral blood vessels, bronchial asthma, gastric ulcer (rarely).**

MYORELAXANTS

Myorelaxants (neoromuscular blockers) **are cholinergic drugs interfere with transmission of nervous impulses in the synapses of skeletal muscles causing their relaxation.**

MYORELAXANTS:
CLASSIFICATION

1. Non-depolarizing agents

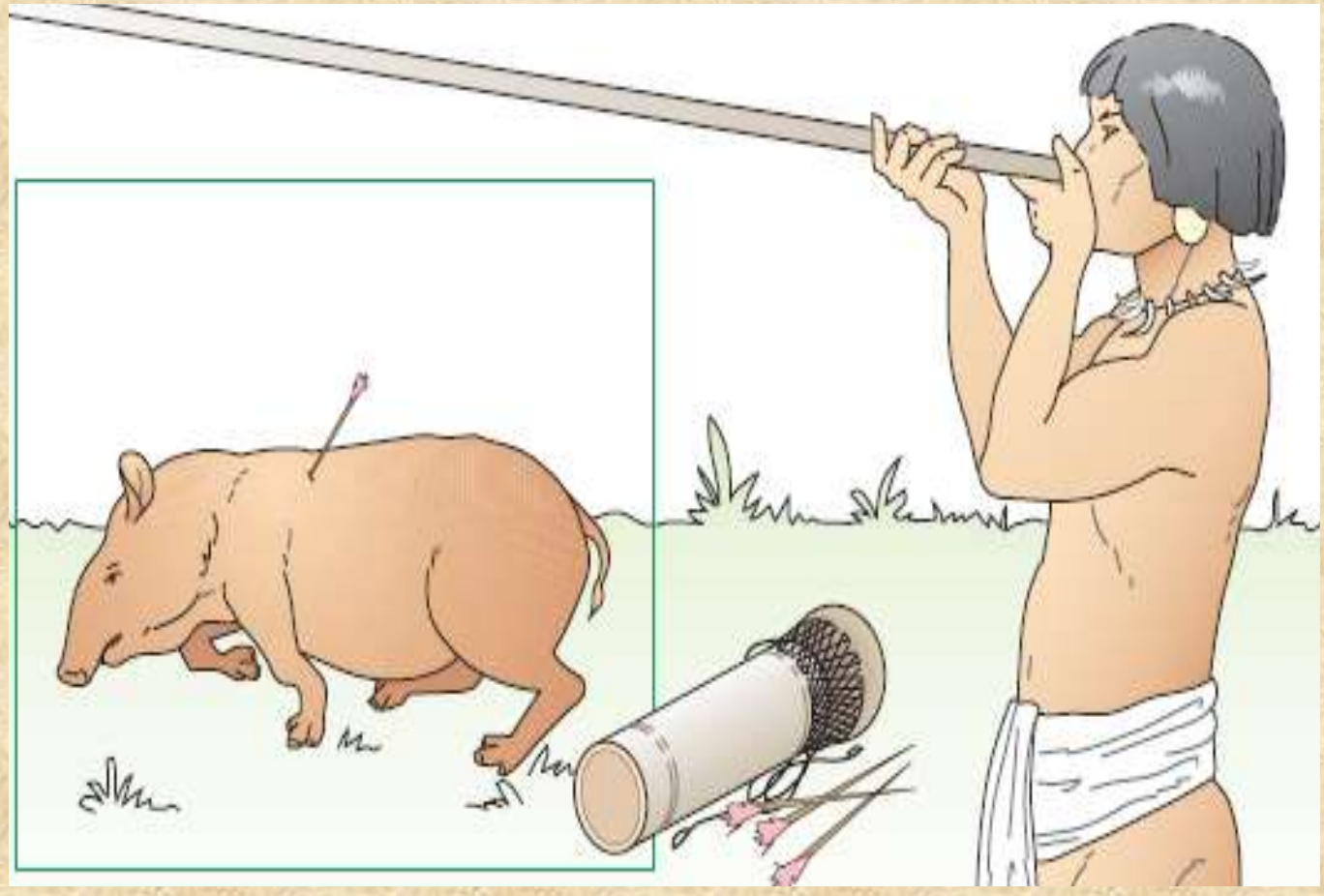
- **d-Tubocurarine chloride**
- **Pancuronium bromide**
- **Pipecuronium bromide**
- **Rocuronium bromide**

2. Depolarizing agents

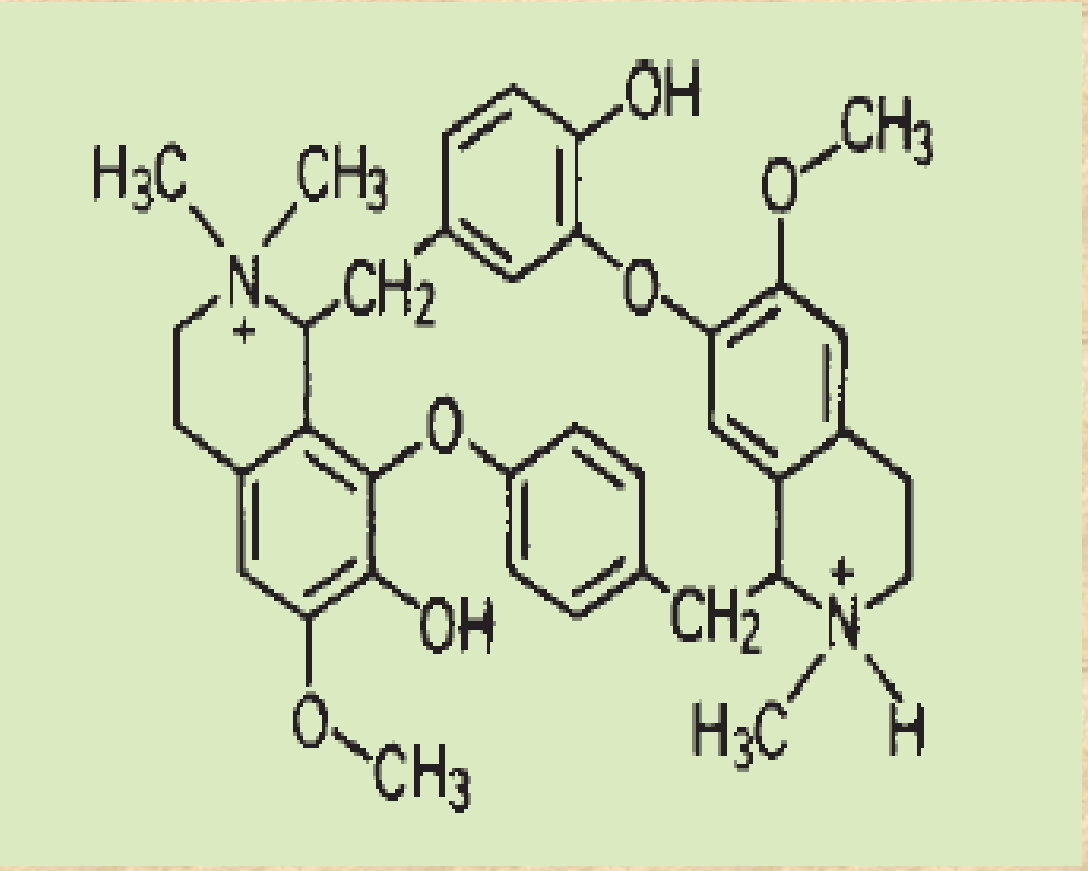
Succinylcholine (Dithylinum)

TUBOCURARINE:

AN ALKALOID FROM PLANT-DERIVED ARROW POISON OF SOUTH AMERICAN NATIVES



TUBOCURARINE:
CHEMICAL STRUCTURE

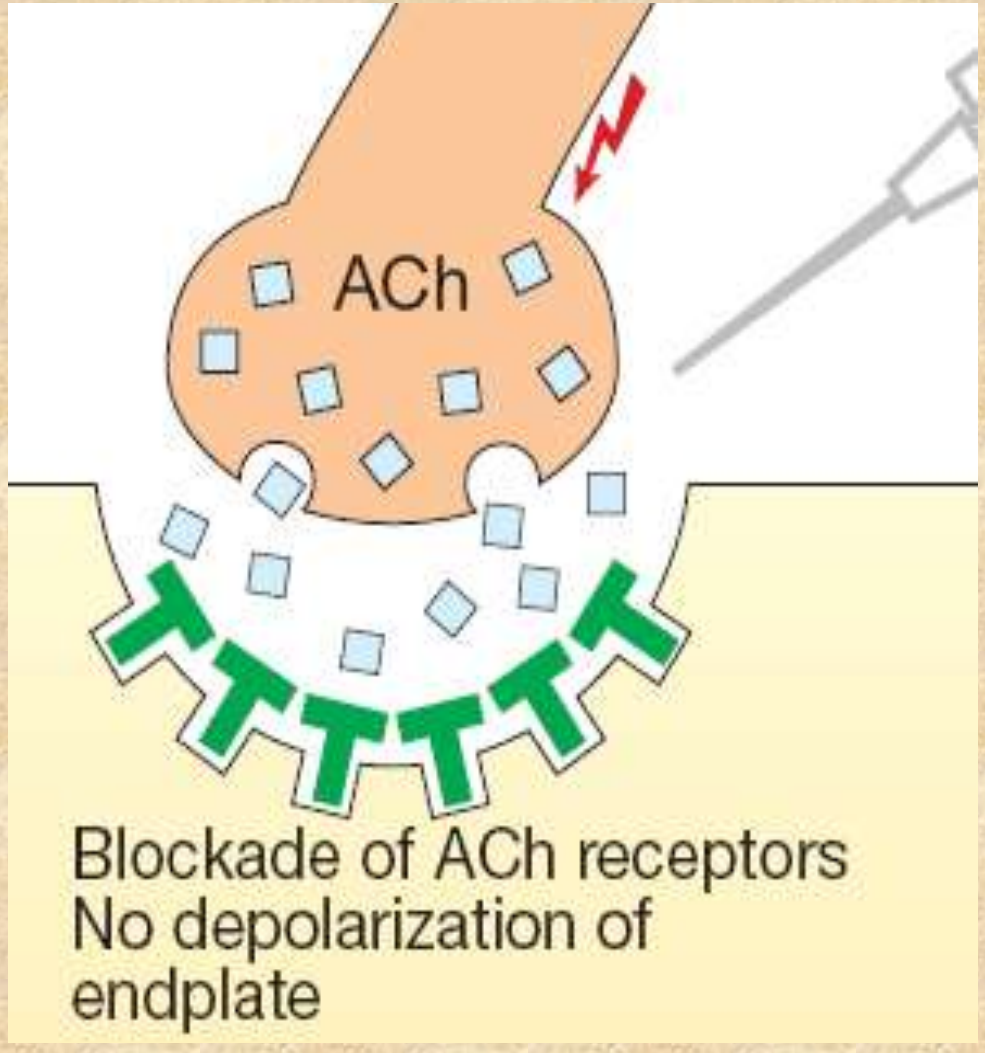


TUBOCURARINE:
PHARMACOKINETICS

- **is administered IV**
- **is not absorbed in the gut due to presence of quaternary nitrogen atoms**
- **does not penetrate CNS**
- **total myorelaxation is developed in 20-30 min and lasts about 20-40 min, restoration of muscle tone lasts**

  20-30 min

TUBOCURARINE:
MECHANISM OF ACTION



TUBOCURARINE:
PHARMACODYNAMICS AND INDICATIONS

PHARMACODYNICS

muscular paralysis in the muscles of fingers, neck, face, extremities, trunk, then in the intercostal muscles, and diaphragm (with inability to breath).

INDICATIONS

1. **Myorelaxation under the conditions of general anesthesia**
2. **Seizures caused by seizure poisons and some infections.**

TUBOCURARINE:
SIDE EFFECTS

- ✓ **Spasm of bronchi and urticaria (due to histamine release from mast cells)**
- ✓ **Lowering of BP (due to weak ganglia blocking activity).**

✱The duration of action of d-tubocurarine can be shortened by the administration of neostigmine or other anticholinesterase.

NON-DEPOLARIZING MYORELAXANTS: other preparations

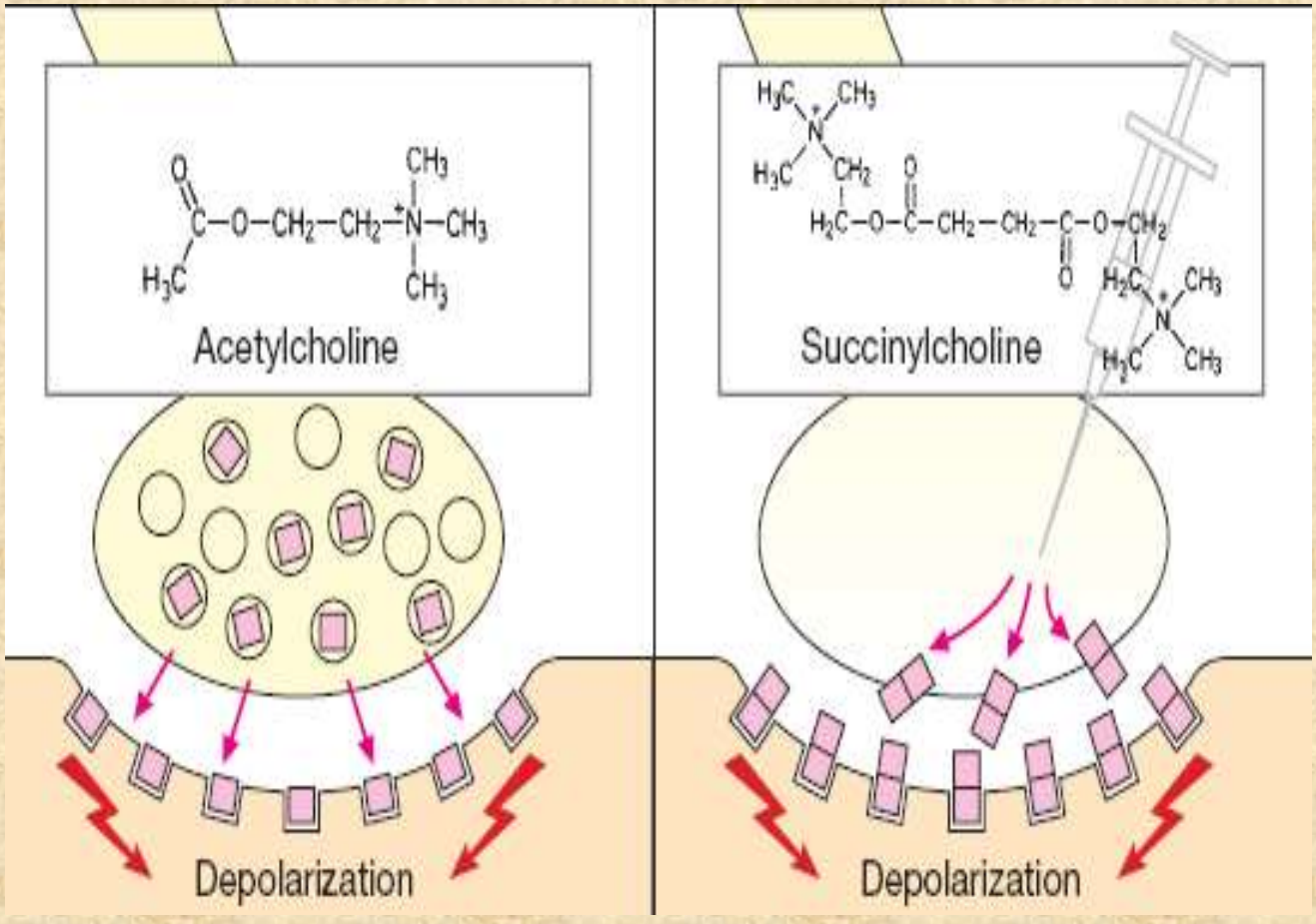
Pancuronium **is a synthetic compound, is more potent than tubocurarine, has longer duration of action, does not cause release of histamine or ganglionic blockade, may cause increased heart rate and BP (due to blockade of M2 cardiac receptors).**

Pipecuronium **is similar to pancuronium, does not cause tachycardia and an increase of BP.**

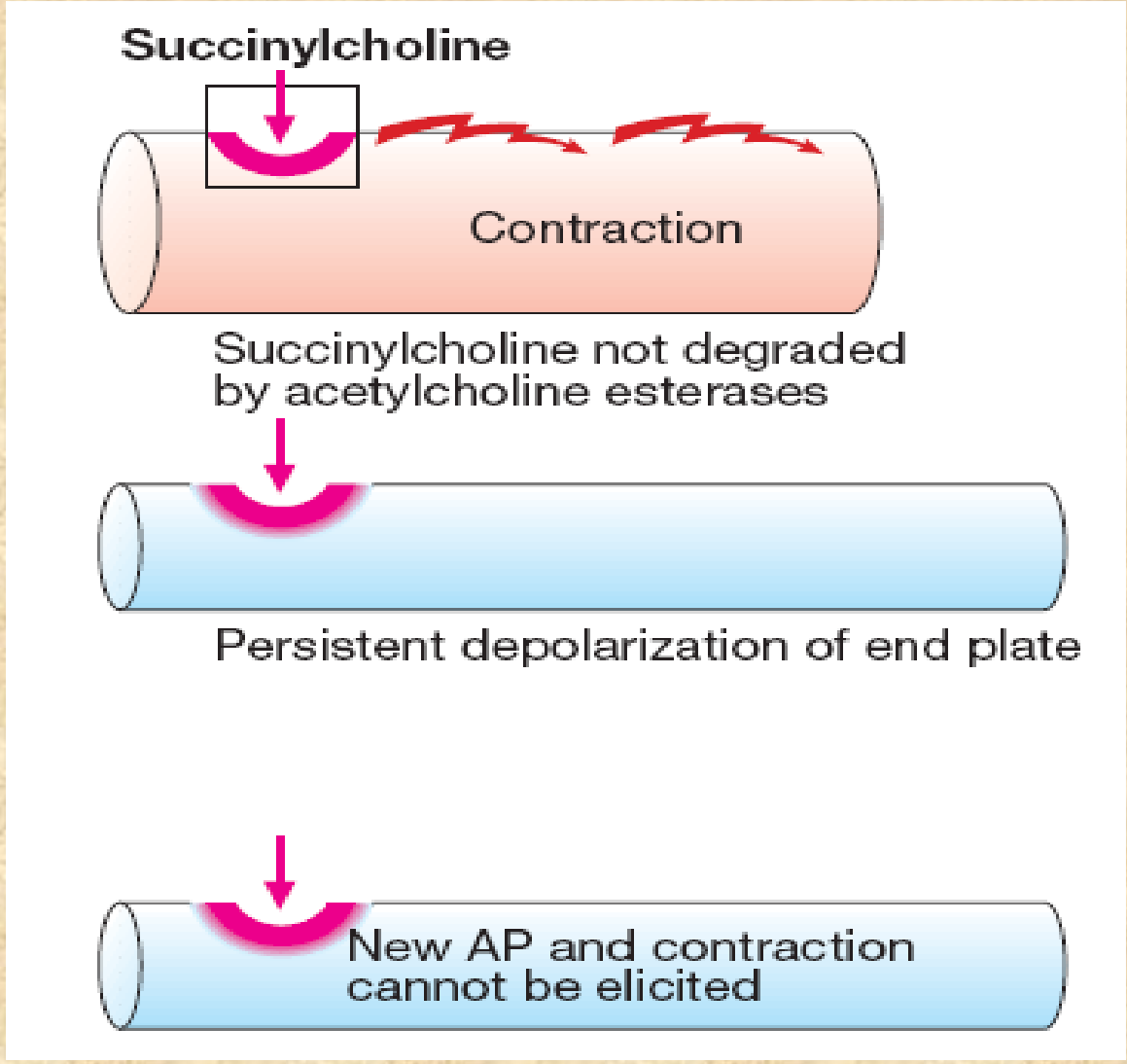
Rokuronium **also is an antagonist of N-cholinergic receptors of skeletal muscules; inhibits neuromuscular transmission and causes myorelaxation, has weak vagolytic effect, does not affect the release of histamine. The duration of action is 22 minutes in adults.**

SUCCINYLCHOLINE

It is double acetylcholine molecule, agonist of N-cholinoreceptors, *depolirizing agent*.



SUCCINYLCHOLINE:
MECHANISM OF ACTION

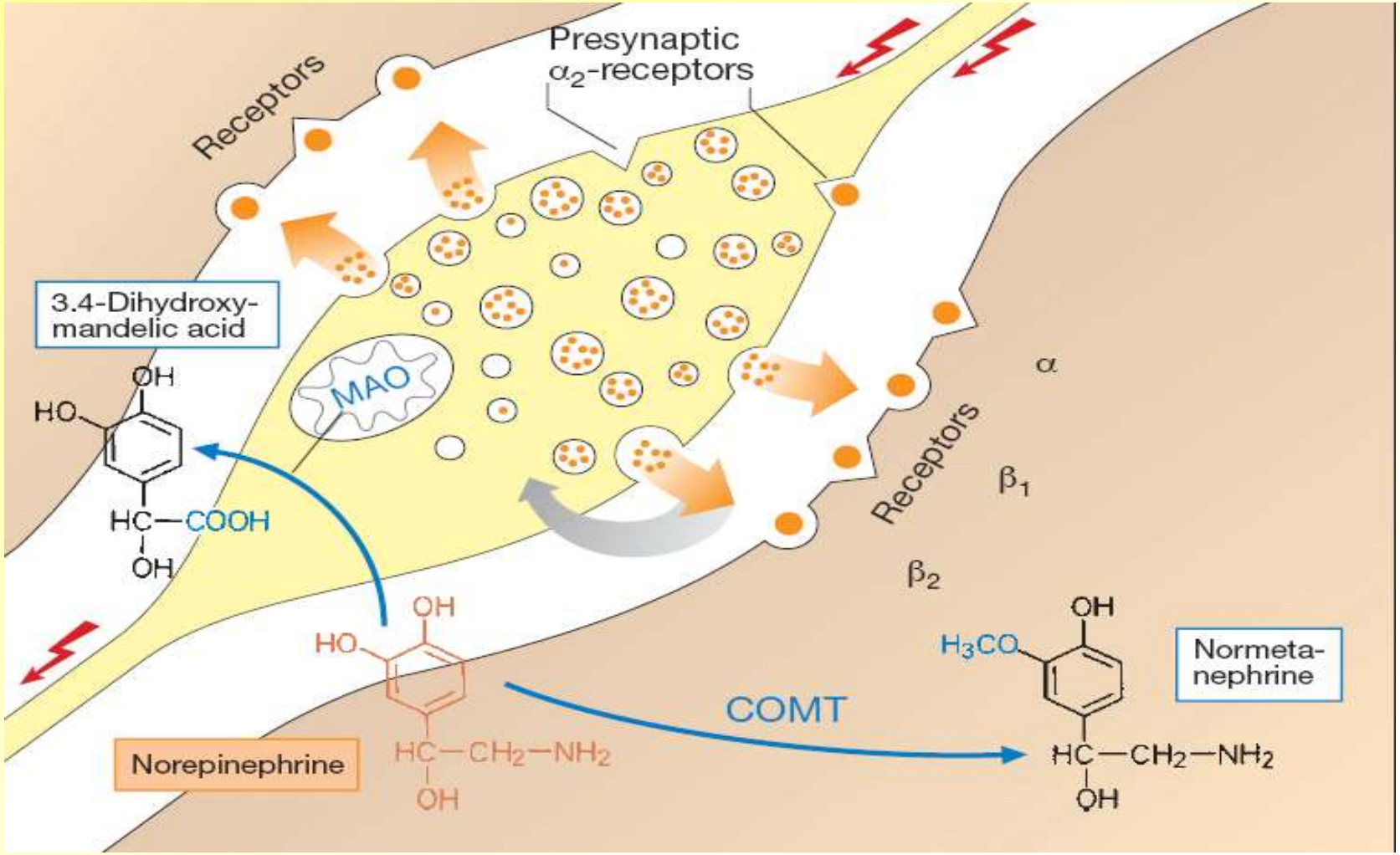


SUCCINYLCHOLINE

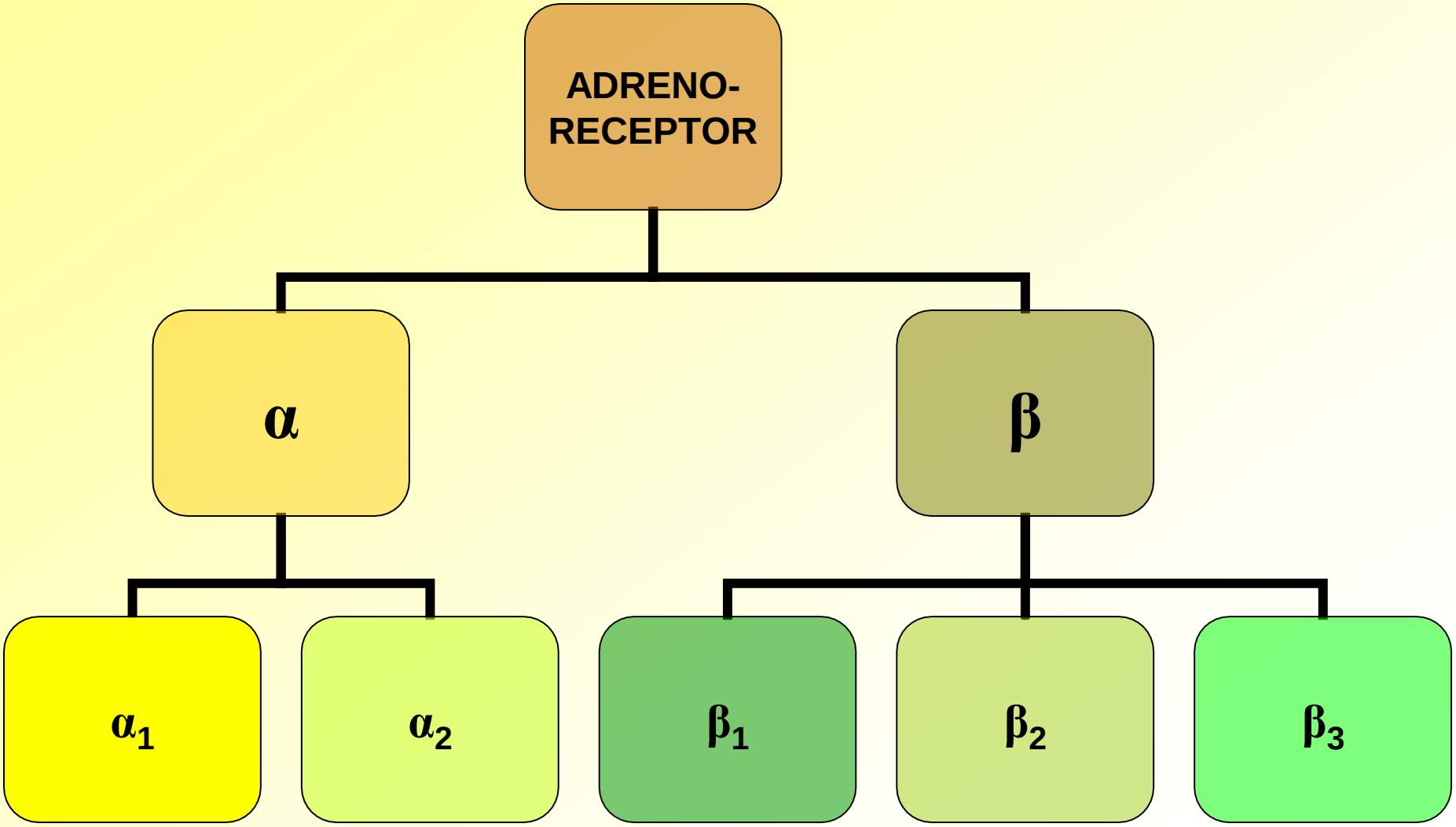
- ***PHARMACODYNAMICS*: is administered IV; has short duration of action; total myorelaxation and stop of breathing lasts 3-5 min; is destroyed by butiryl cholinesterase in blood**
- ***PHARMACODINAMICS*: myorelaxation**
- ***INDICATIONS*: short surgeries, intubation of thrachea, endoscopy, reposition of bone fractures**
- ***SIDE EFFECTS*: fibrillation of skeletal muscles at the start of action, hyperkalemia, cardiac arrhythmia, increase of intraocular pressure, pain in skeletal muscles after the surgery**
- ***IDIOSYNCRASY*: long-lasting apnea in patients deficient on butiryl cholinesterase.**

✱Emergence help is hemotransfusion and artificial lungs ventilation.

ADRENERGIC SYNAPSE



TYPES OF ADRENOCEPTORS



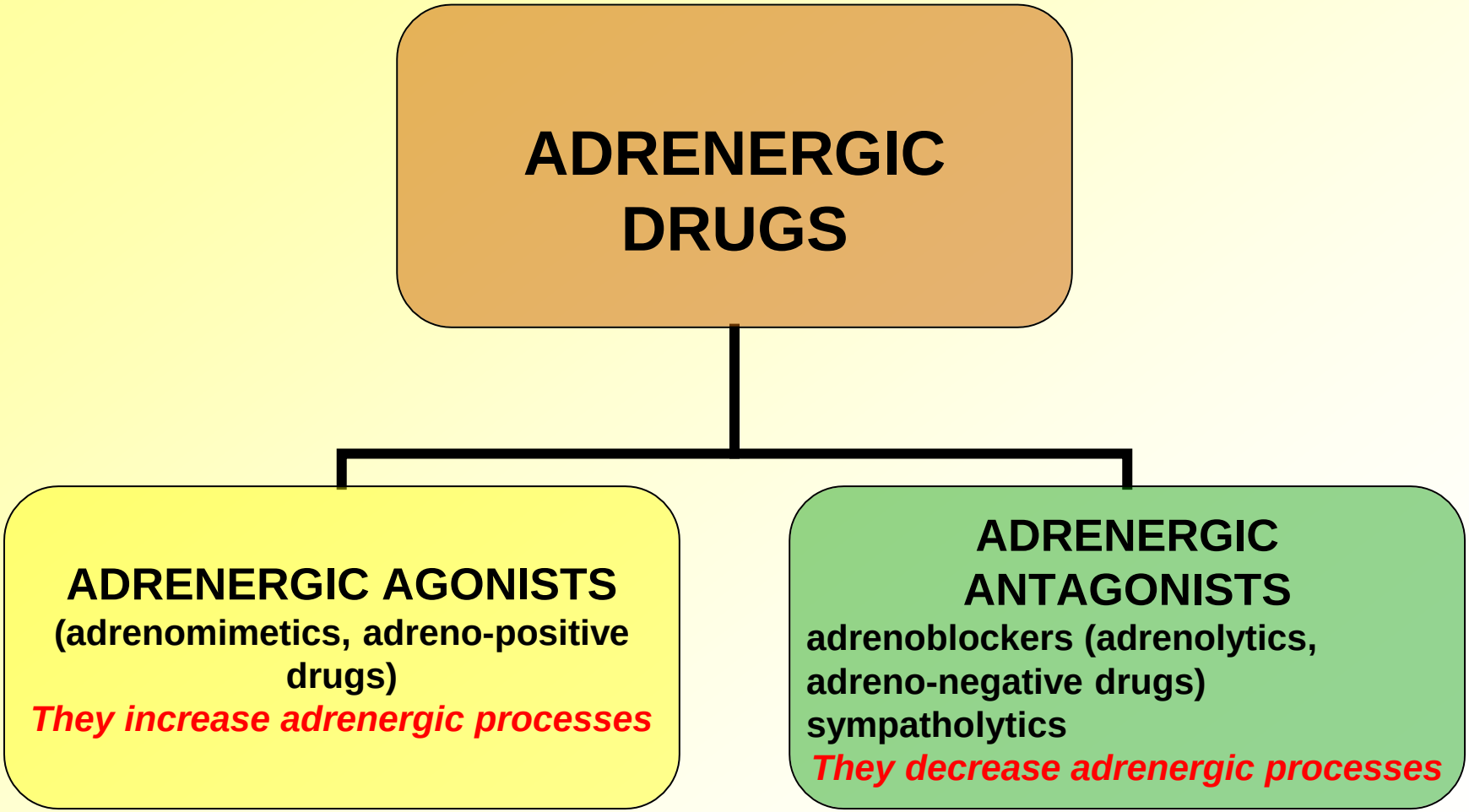
LOCATION AND EFFECTS OF α-ADRENOCEPTORS

Receptor	Location	Effect
α1	Blood vessels Spleen Eye Urinary bladder	Constriction, ↑of BP Constriction Mydriasis ↑ of sphincter closure
α2	Blood vessels Pancreas All adrenergic synapses	Constriction ↓ of insulin release ↓ of norepinephrine release

LOCATION AND EFFECTS OF β-ADRENOCEPTORS

Receptor	Location	Effect
β1	Heart Fat tissue	↑ of rate and contractility ↑ of lipolysis
β2	Blood vessels Bronchi Uterus Pancreas Liver Skeletal muscles	Vasodilation Dilation Relaxation ↑ of glucagon's release ↑ of glycogenolysis ↑ of glycogenolysis
β3	Pancreas Fat tissue Mast cells	↑ of insulin secretion ↑ of lipolysis ↓ of degranulation, ↓ of release of allergy mediators

DRUGS INFLUENCING ADRENERGIC SYNAPSES



ADRENERGIC AGONISTS

(ADRENOMIMETICS)

ADRENOMIMETICS
CLASSIFICATION

A. α-, β-adrenomimetics

1. Direct-acting

– Adrenaline hydrochloride (Epinephrine)

2. Indirect-acting (sympathomimetics)

– Ephedrine hydrochloride

B. α-adrenomimetics

1. Non-selective

– Noradrenaline hydrotartrate (α1, α2 > β)

2. Selective

– Phenylephrine (Mesatonum) (α1)

– Naphazoline (Naphthyzinum) (α2)

– Halazolin (Xylometazoline) (α2)

C. β- adrenomimetics

1. Non-selective

– Isoprenaline (Isadrinum) (β1, β2)

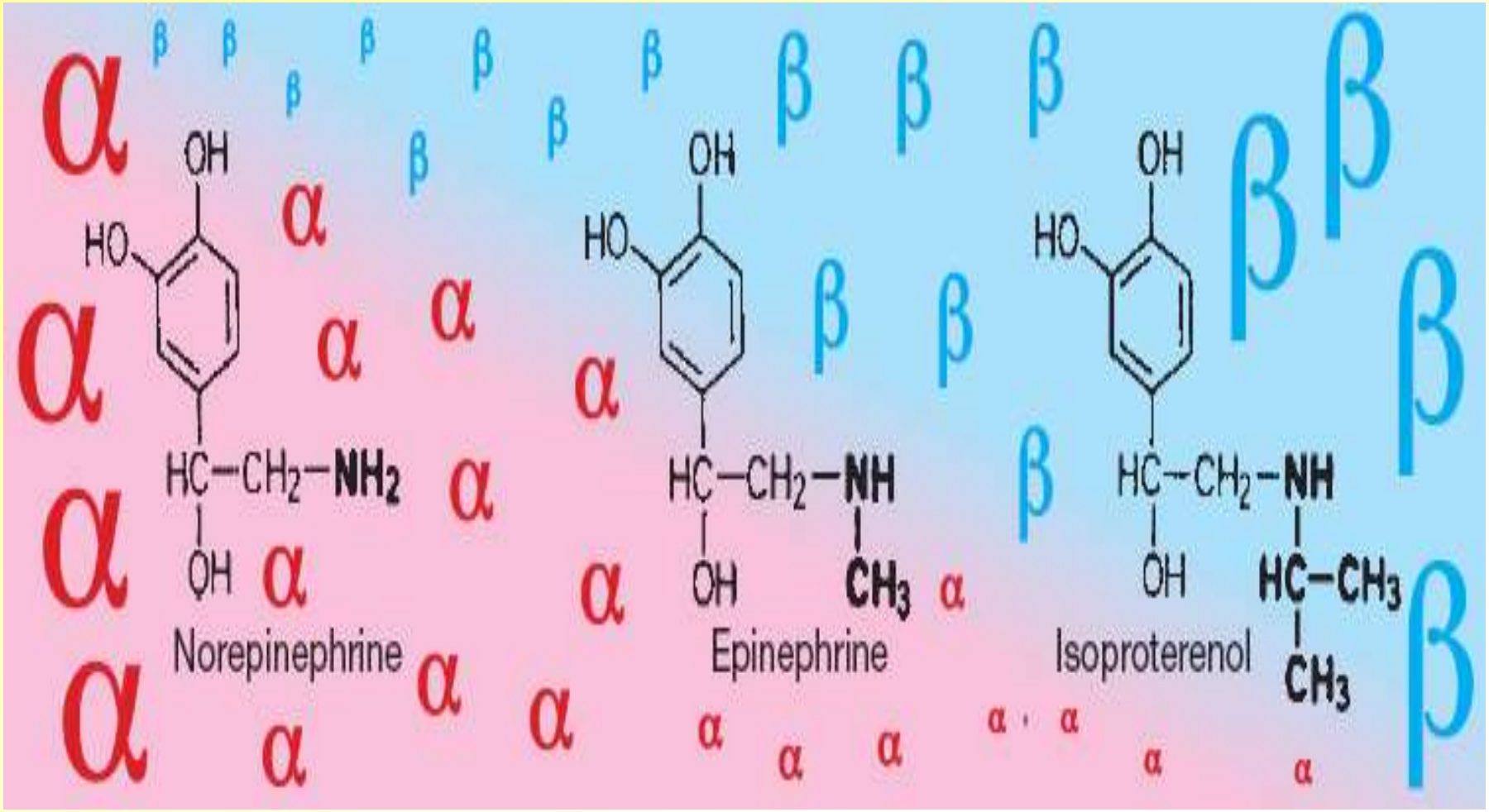
2. Selective

– Dobutamine (β1)

– Salbutamol (Albuterol) (β2)

– Fenoterol (β2)

COMPARISON OF ADRENOMIMETICS-CATECHOLAMINS



ADRENALINE
PHARMACOKINETICS

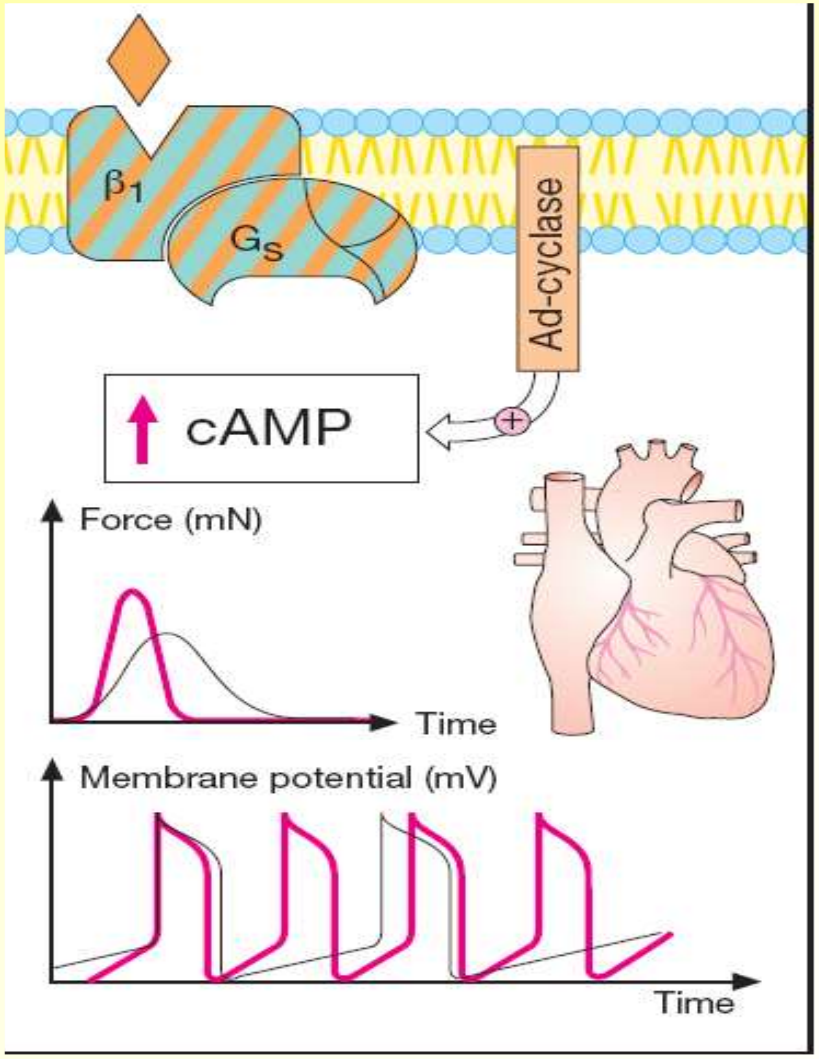
- is administered SC or topically
- is destroyed in the GI tract
- is not administered orally
- does not penetrate CNS
- is biotransformed by enzymes in blood
- acts during 15 min on the intern organs and during 30 min on metabolic processes

ADRENALINE

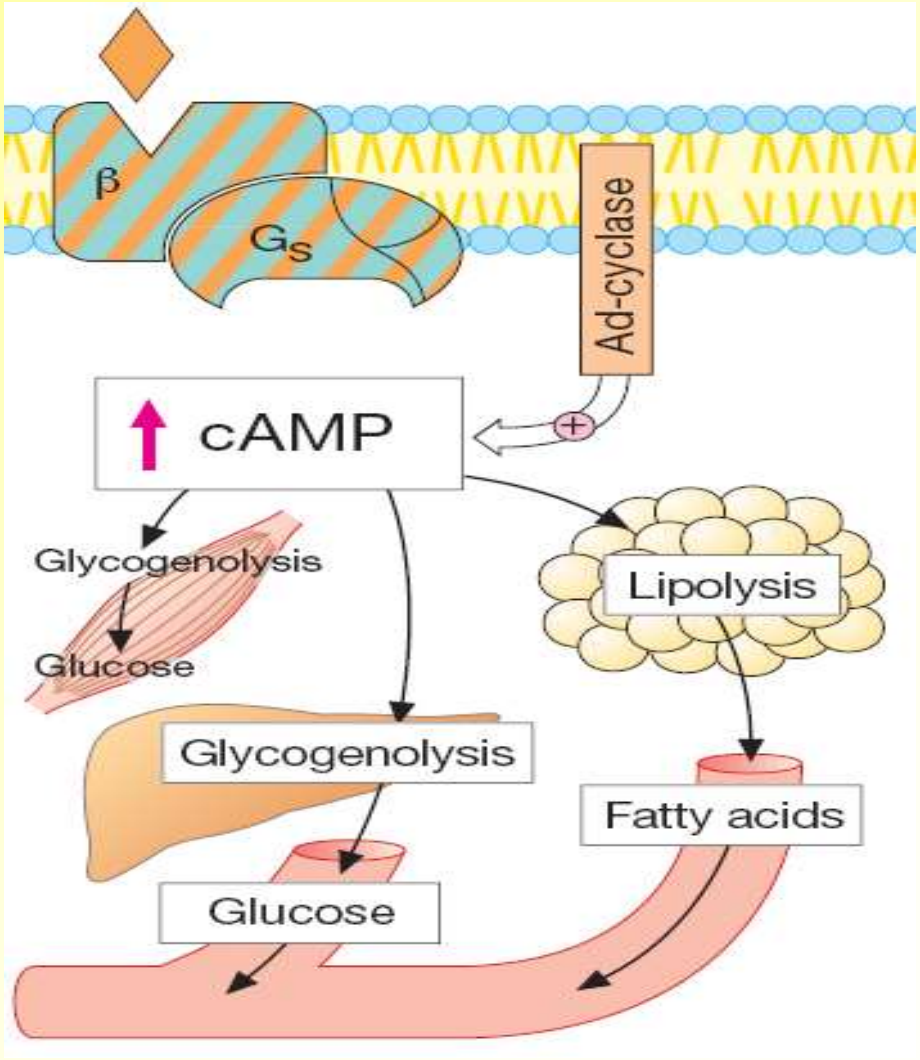
PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	Indications
An increase in automaticity, conductivity, and contractility of the heart Constriction of blood vessels Elevation of BP Bronchodilation An increase in glucose concentration in the blood Inhibition of allergy Mydriasis A decrease in intra-eye pressure	Heart arrest Shock, collapse Bronchial asthma attack Hypoglycemic coma Anaphylactic shock Prolongation of local anethesia Capillary bleeding Acute inflammation of mucosa of the nose or eye Pupil dilation Open-angle glaucoma

ADRENALINE
CARDIAC EFFECTS



ADRENALINE
METABOLIC EFFECTS



ADRENALINE

SIDE-EFFECTS AND CONTRAINDICATIONS

Side-effects

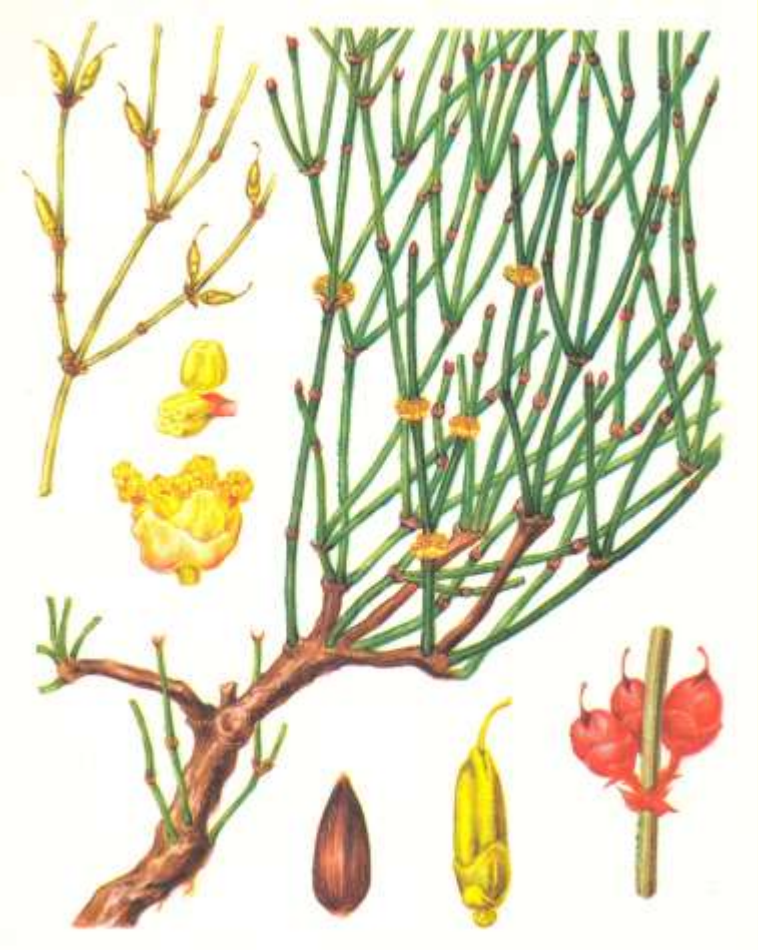
- Excitement, tremor
- Hypertension
- Arrhythmia
- Hyperglycemia

Contraindications

Hypertension, severe atherosclerosis, heart arrhythmia, diabetes mellitus, hyperthyroidism

EPHEDRINE

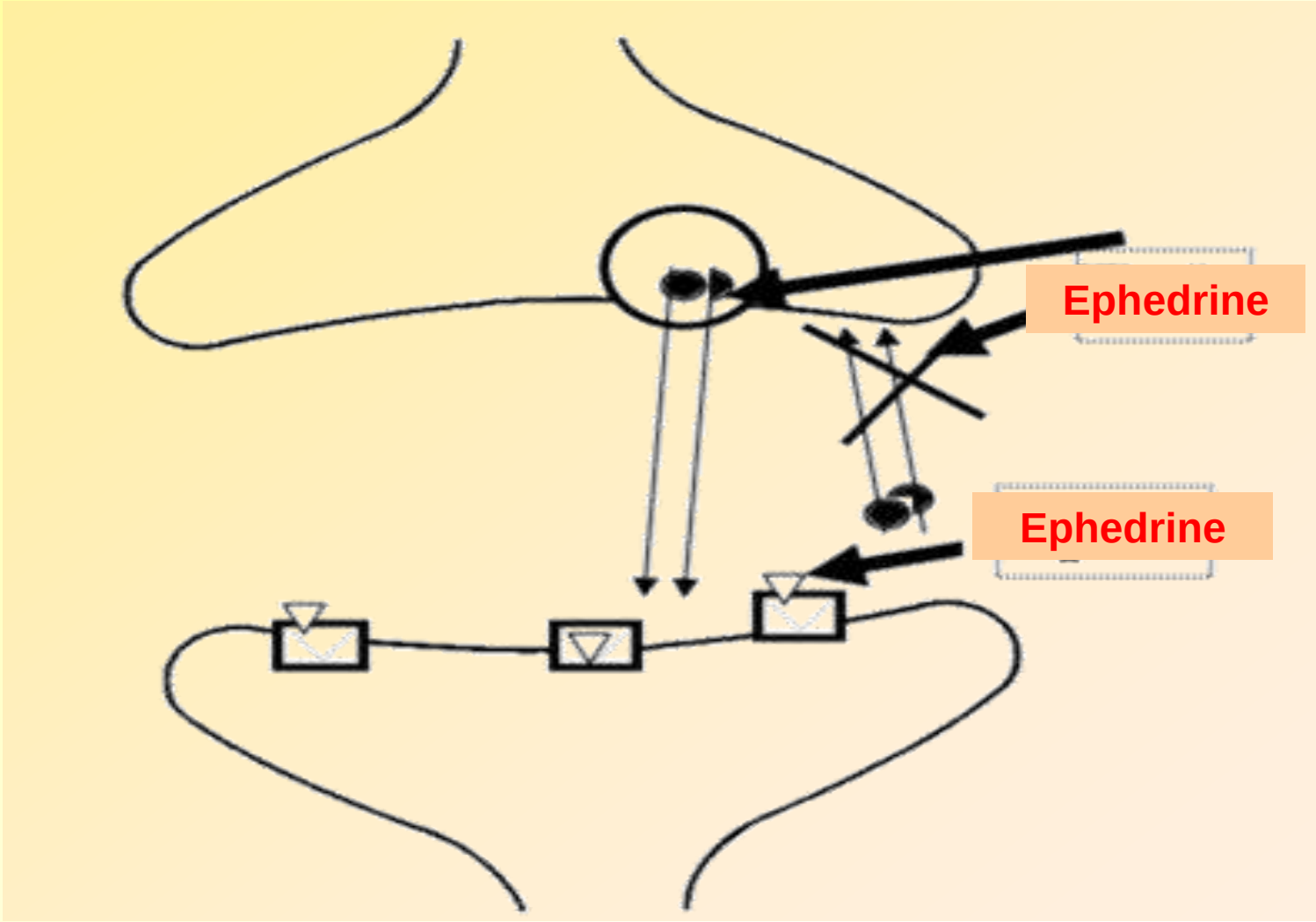
EPHEDRA EQUISETICA CONTAINING EPHEDRINE



EPHEDRINE
PHARMACOKINETICS

- is administered orally, SC, IM, IV, or topically
- is absorbed in the GI tract
- penetrates CNS
- is metabolized in the liver
- is excreted by kidney
- acts during 4-6 hrs

EPHEDRINE
MECHANISM OF ACTION



EPHEDRINE

PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	Indications
Stimulation of CNS, an increase in ability to mental work, euphoria Stimulation of cardiovascular system Vasoconstriction Increase in BP Dilation of bronchi A decrease of GI tract motility Retention of urine Mydriasis	Shock, collapse Anaphylactic shock Bronchial asthma Bronchospasm Bradycardia, A-V block Acute rhinitis Acute conjunctivitis For pupil dilation Narcolepsia Myasthenia Enuresis

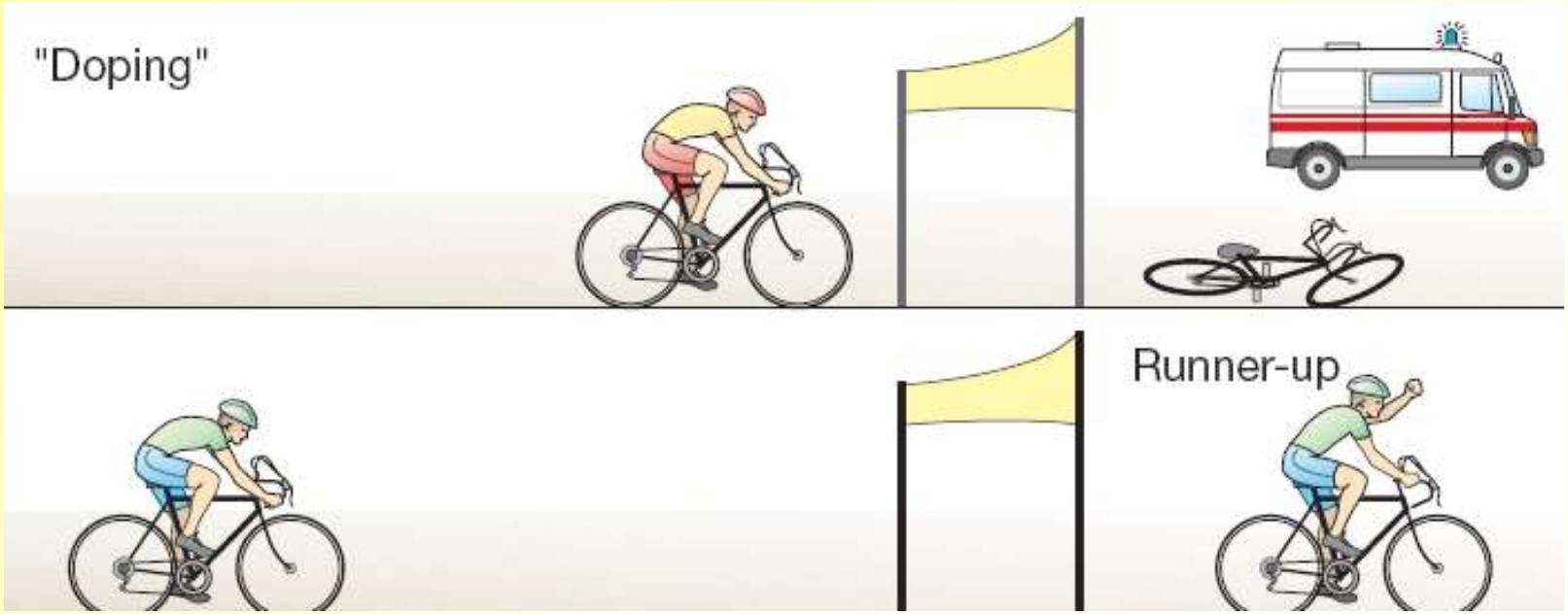
EPHEDRINE
SIDE-EFFECTS

- **Wakefulness**
- **Anxiety, restlessness, insomnia**
- **Tachycardia**
- **Palpitation**
- **Hypertension**
- **Rash on the skin**
- **Tolerance and tachyphylaxis**
- **Drug dependence**

✱ ***It should not be used in sportsmen (as doping)!***

EPHEDRINE

DOPING-EFFECT AND ABUSE POTENTIAL



α – ADRENOMIMETICS

Pharmacodynamics	Indications
Vasoconstriction An increase in BP Mydriasis (without cycloplegia)	Shock, collapse Prolongation of local anesthesia Capillary bleeding Rhinitis, conjunctivitis Glaucoma Diagnostics of eye diseases

α – ADRENOMIMETICS

PECULIARITIES OF PREPARATIONS

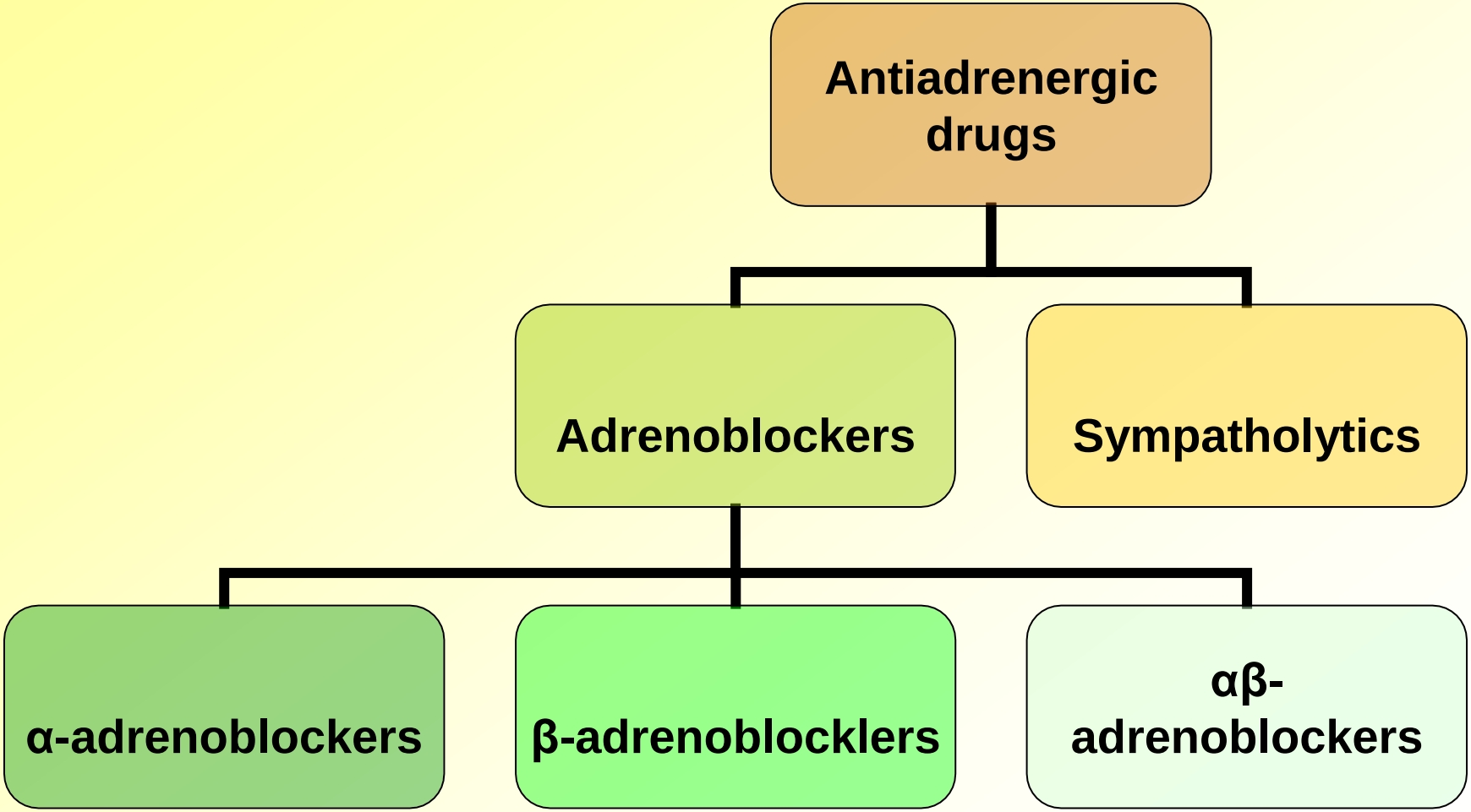
- ***Noradrenaline*** **is catecholamine; has non-selective action on adrenoceptors, especially on α-adrenoceptors; has short-durative action, is administered only by IV infusion for collapse and acute hypotension.**
- ***Phenylephrine (Mesatonum)*** **is non-catecholamine; has selective action on α1-adrenoceptors; may be taken orally, administered SC, IM, IV, or topically, duration of action is 4-6 hrs.**
- ***Naphazoline and halazolin*** **are non-catecholamines; have selective action on α2-adrenoceptors, are used as nasal drops for acute rhinitis, nasal bleeding, and rhinoscopia; cause tolerance and tachyphylaxis.**

β– ADRENOMIMETICS
PECULIARITIES OF PREPARATIONS

- ***Isoprenaline (Isadrinum)*** **is catecholamine; has non-selective action on β1- and β2-adrenoceptpors; is administered subligually, by inhalation, or IV; is used for bronchial asthma attack, heart block, some types of cardiogenous shock.**
- ***Salbutamol*** **is non-catecholamine; has selective action on β2-adrenoceptors, acts longer than isoprenaline; does not act on the heart; is used for bronchial asthma, bronchospasm and before bronchoscopia.**
- ***Fenoterol (Partusisten)*** **is non-catecholamine; has selective action on β2-adrenoceptors, acts during 4-6 hrs; does not act on the heart; is used for bronchial asthma and in danger of pregnancy interruption.**
- ***Dobutamine*** **has selective action on β1-adrenoceptors; increases cardiac output; is administered by IV infusion for emergency treatment of acute heart insufficiency and cardiogenous shock.**

ADREGERGIC ANTAGONISTS

GROUPS OF ADRENERGIC ANTAGONISTS



ADRENERGIC ANTAGONISTS
CLASSIFICATION

A. α-adrenoblockers:

1. Non-selective

– Phentolamine

– Tropaphenum

2. Selective

– Prazosin

– Doxazasin

B. β-adrenoblockers:

1. Non-selective

– Propranolol (Anaprilinum)

2. Selective

– Metoprolol

– Talinolol

– Atenolol

C. α-, β-adrenoblockers:

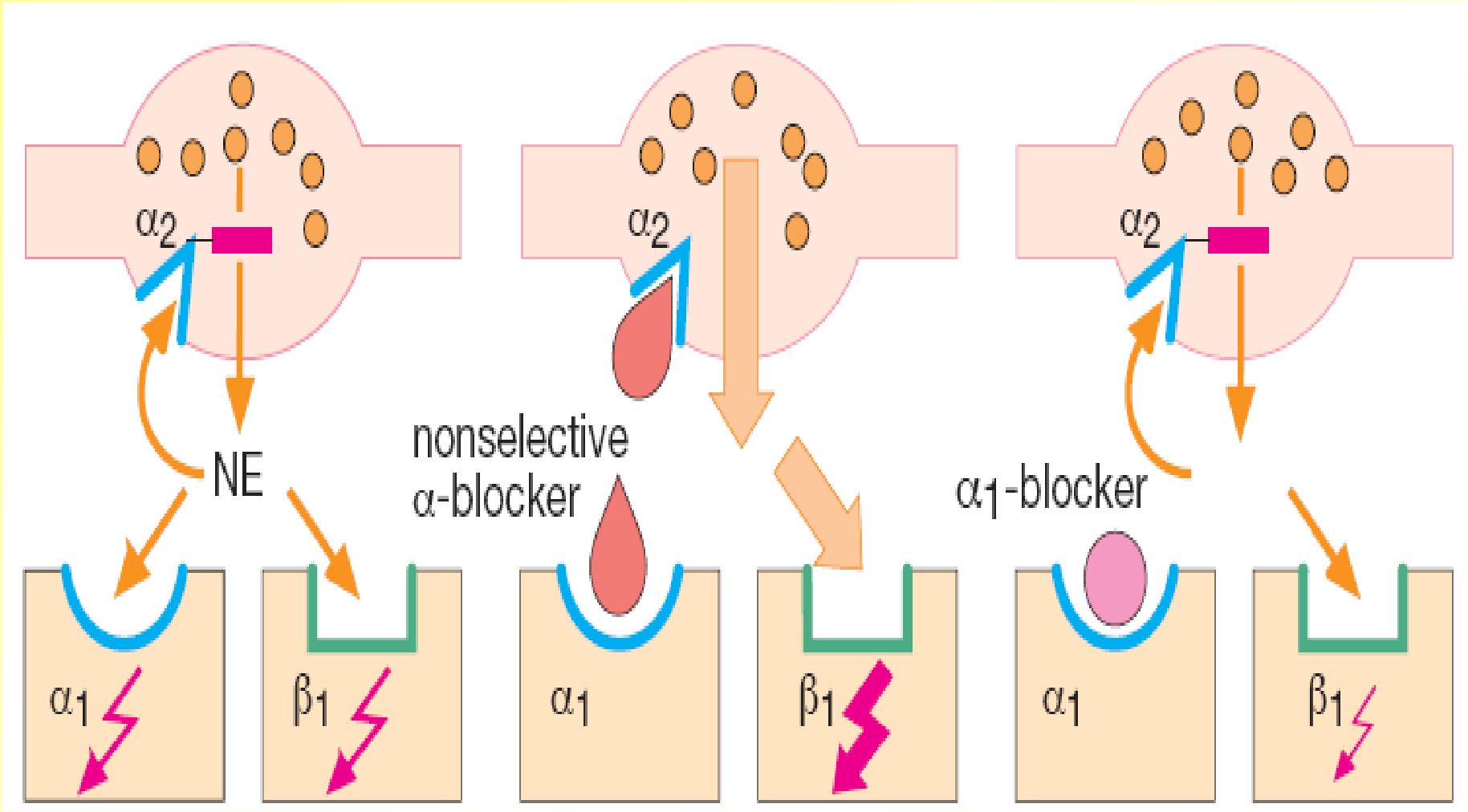
– Labetalol

D. Sympatholytics:

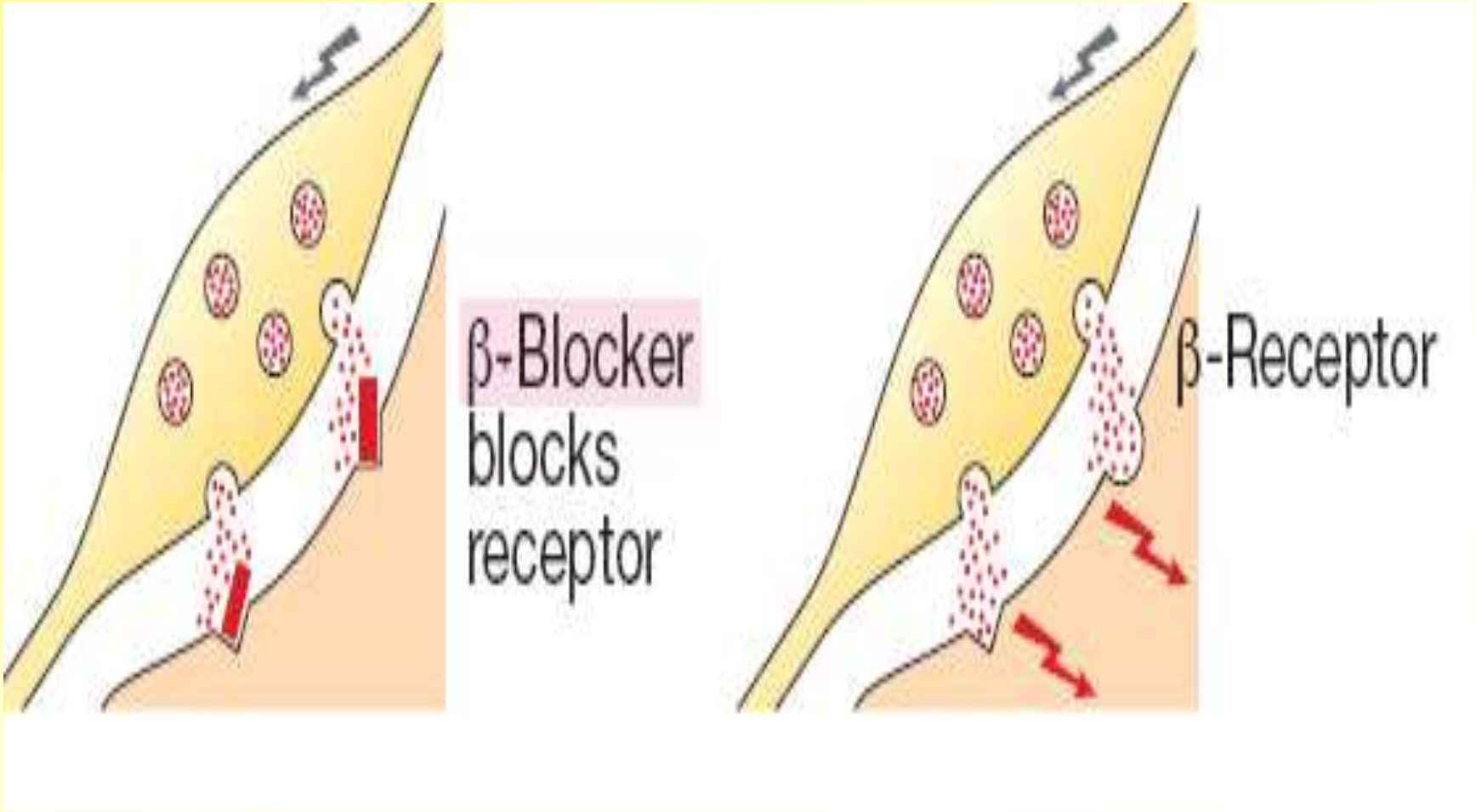
– Guanetidine (Octadinum)

– Reserpine

α-ADRENOBLOCKERS
MECHANISM OF ACTION



PROPRANOLOL
MECHANISM OF ACTION



PROPRANOLOL (ANAPRILINUM)
PHARMACODYNAMICS AND INDICATIONS

Pharmacodynamics	Indications
A decrease in automaticity, excitability, and conductivity of myocardium A decrease of the heart rate (*anti-arrhythmic* effect) A decrease in the heart contractility, striking and minute volume A decrease in consumption of oxygen by myocardium (*antianginal* effect) A decrease in renin secretion in the kidney A decrease in BP (*antihypertensive* effect) A decrease in intraocular pressure Sedative action	Hypertension Ischemic heart disease (angina pectoris, myocardial infarction) Tachyarrhythmia Hyperthyroidism Migraine Glaucoma

PROPRANOLOL (ANAPRILINUM)
SIDE-EFFECTS AND CONTRAINDICATIONS

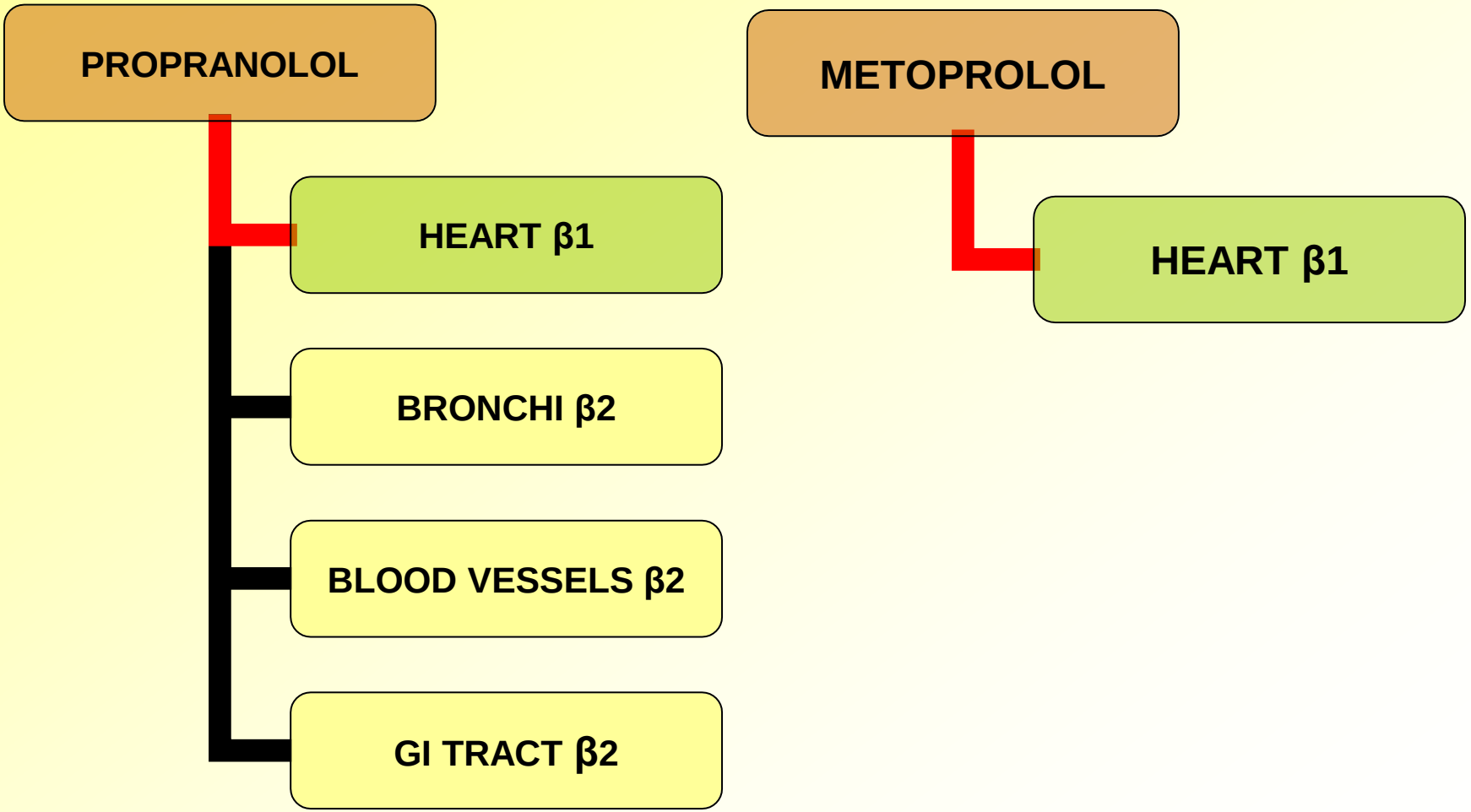
Side-effects

- Bradycardia
- Hypotension
- Increasing of heart incompetence
- Heart block
- Spasm of bronchi
- Hypoglycemia when insulin is given together
- Fatigue, drowsiness, vertigo, depression
- Disturbances of sexual function in men

Contraindications

Bradycardia, hypotension, severe heart failure, heart block, bronchial asthma, ulcerative disease, diabetes mellitus, disturbances of peripheral blood circulation, pregnancy

COMPARISON OF PROPRANOLOL AND CARDIOSELECTIVE β-ADRENOBLOCKERS



β-ADRENOBLOCKERS
PECULIARITIES OF PREPARATIONS

- ***Metoprolol*** **has cardioselective action (on β1-receptors); is taken orally for treatment of hypertension, angina pectoris and arrhythmia; less side-effects: does not cause spasm of bronchi and increase of gastric secretion; may be used in patients with bronchial asthma, ulcerative disease, and diabetes mellitus.**
- ***Talinolol*** **has cardioselective action (on β1-receptors); has *inner sympathomimetic activity* and membrane stabilizing effect (does not decrease heart contractility and conductivity); less side-effects; less contraindications connected with influence on β1-adrenoceptors.**
- ***Atenolol*** **has cardioselective action (on β1-receptors); is similar to metopolol.**

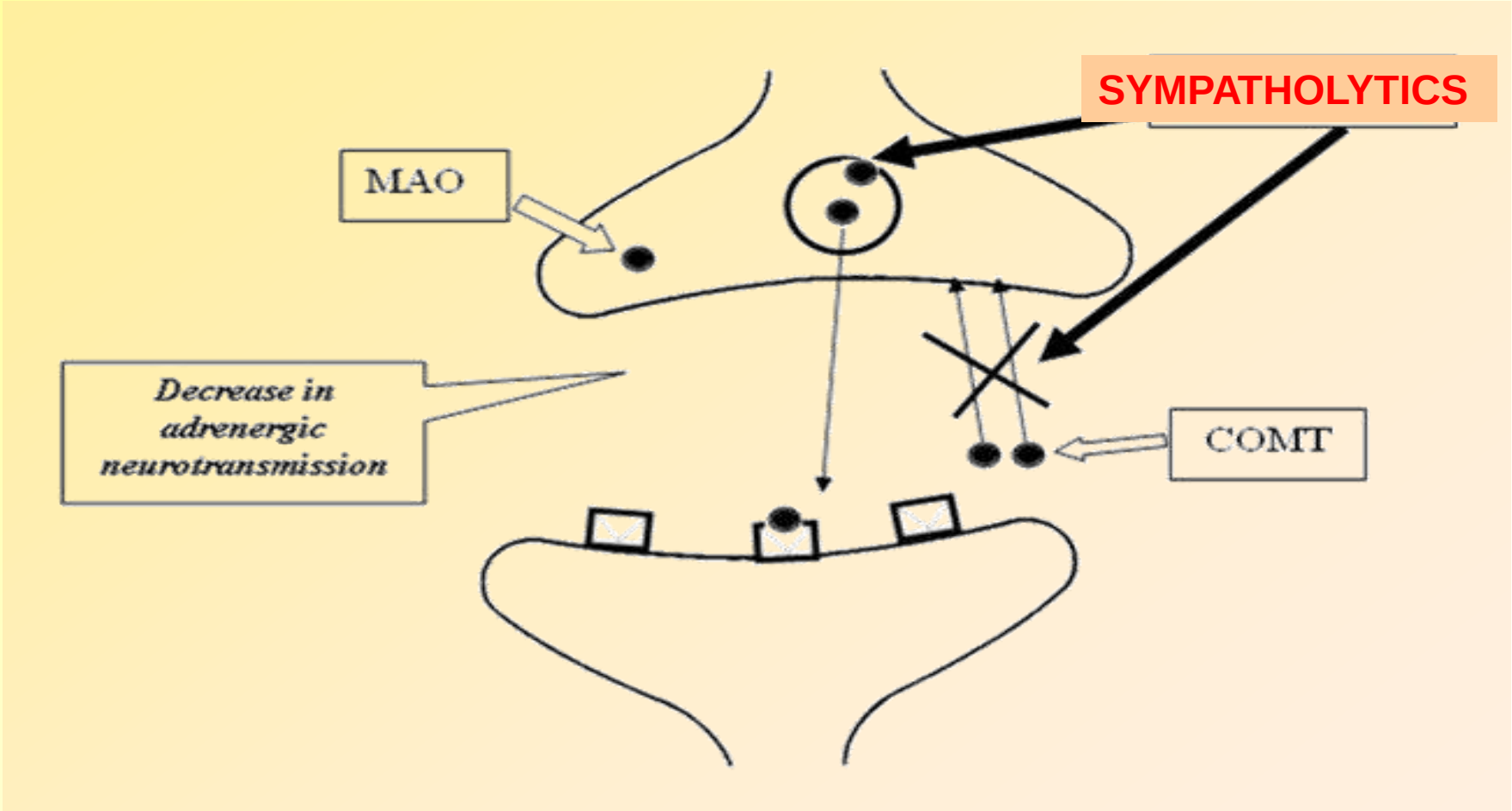
α-, β-ADRENOBLOCKERS LABETALOL

- blocks both α- and β-adrenoceptors
- action on β-receptors is 3 times more intensive than the action on α-receptors
- less active than propranolol
- less active than phentolamine
- is taken orally or IV
- is indicated for control of hypertension
- is contraindicated in heart block, spasm of bronchi, pregnancy

SYMPATHOLYTICS

Sympatholytics **are presynaptically acting anti-adrenergic drugs.**

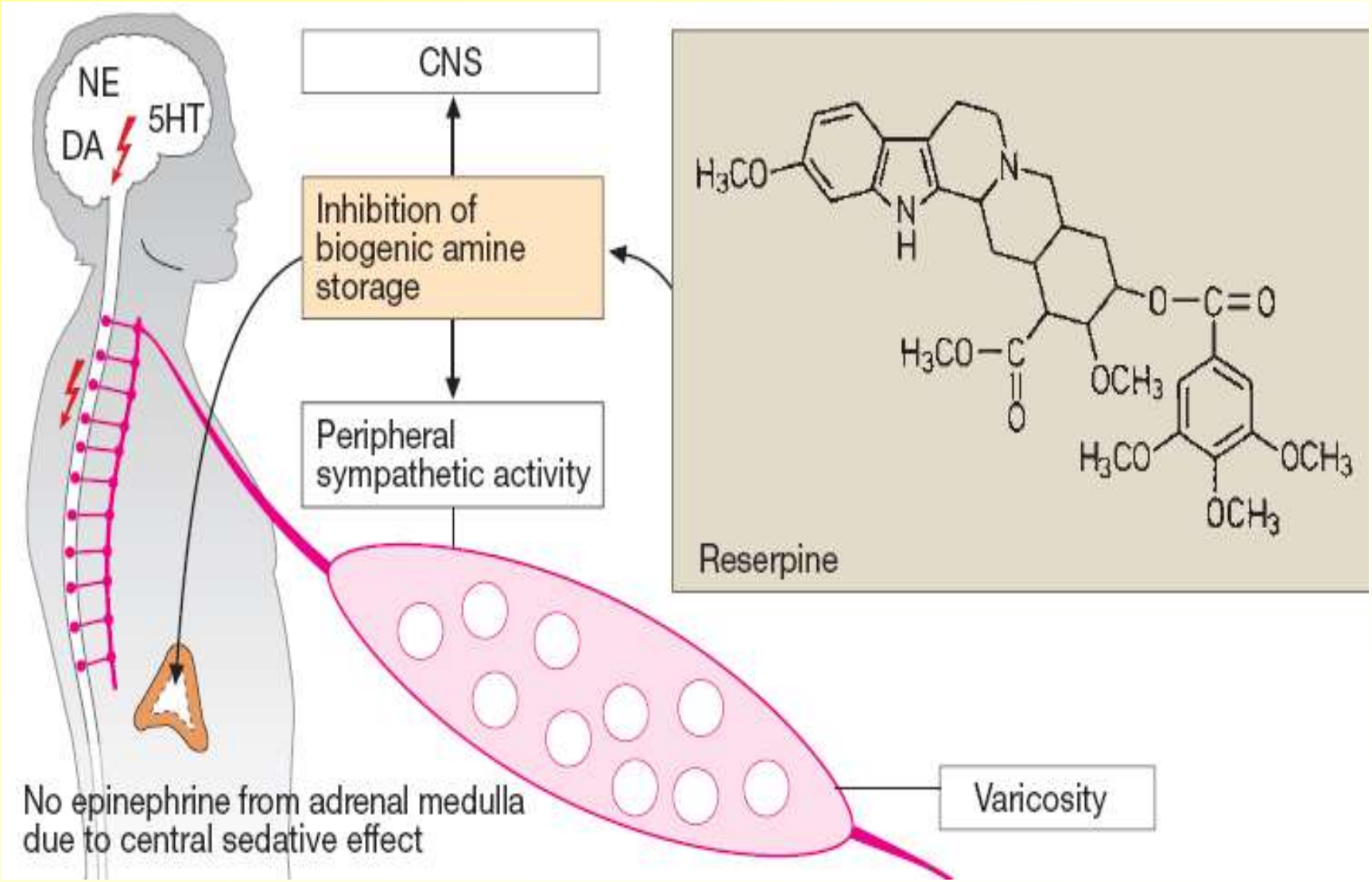
SYMPATHOLYTICS
MECHANISM OF ACTION



RESERPINE

- decreases the storage of norepinephrine
- penetrates CNS, has central and peripheral action
- has antihypertensive, sedative, and antipsychotic action
- is administered orally, IM or IV
- acts 8-12 hrs
- is indicated for hypertension
- may cause disturbances of sleep, depression, bradycardia, spasm of bronchi, stimulation of gastric secretion, diarrhea

RESERPINE
CENTRAL AND PERIPHERAL ACTION



GUANETIDINE (OCTADINUM)

- decreases the storage of norepinephrine, decreases mediator release and re-uptake
- does not penetrate CNS, has only peripheral action
- has antihypertensive action, decreases intraocular pressure
- is taken orally or in the form of eye drops
- action is slow and long (it starts to act in 2-4 days after the beginning of treatment and continues to act during 10-14 days after the ending of treatment)
- is indicated for hypertension, glaucoma, some arrhythmias
- may cause orthostatic hypotension

GUANETIDIN
PERIPHERAL ACTION ONLY