

• CHOLINERGIC ANTAGONISTS

A. Actuality. The autonomic nervous system is involved in regulating physiological processes by controlling basic life functions of various organs and metabolic processes. Cholinergic antagonists (cholinoblockers, parasympatholytics) drugs are widely used in ophthalmology, neurology, anesthesiology, gastroenterology, urology, surgery, etc. They exhibit various pharmacodynamic actions on the vegetative nervous system and have a broad pharmacotherapeutic use.

B. The purpose of the training is to familiarize the student with the main medicines of these groups, the principles of their selection according to the main indications, as well as the possible adverse reactions and measures to prevent them.

C. Learning objectives:

1) The student must **know:** cholinoblockers, characteristics, classification, mechanism of action, dosage forms and routes of administration, doses, indications, contraindications, adverse reactions, clinical picture of intoxications and their treatment.

2) The student must **be able to:** make out prescriptions of mandatory drugs in various forms and indicate them in various diseases and pathological conditions.

D. Initial level of knowledge required for interdisciplinary integration:

Biochemistry. The neurotransmitter of the cholinergic synapse (acetylcholine). Structure, regulation of neurotransmitter biosynthesis, and its inactivation, action of acetylcholine on lipid, carbohydrate and protein metabolism.

Histology. Parasympathetic vegetative nervous system, morpho-functional features. Structure of cholinergic synapse.

Human physiology. Functions of sympathetic and parasympathetic vegetative systems. Their action on the functions of the innervated organs.

Pathophysiology. Deregulation of the excitability and conductivity of neurons. Synaptic conduction disorders. Pathology of the vegetative nervous system.

E. Self-training questions:

1. Classification of cholinoblocking drugs.
2. Classification and sources of M-cholinoblockers (antimuscarinics).
3. The action of M-cholinoblockers on the cardiovascular and the central nervous systems. Effects on eye function caused by M- cholinoblockers.
4. The action of M-cholinoblockers on the tone of smooth muscles of the bronchi, gastrointestinal tract, bile ducts and urinary system. Action on the secretion of sweat, gastric, intestinal and salivary glands.
5. Indications, contraindications and adverse reactions of M-cholinoblocking drugs.
6. Clinical picture of poisoning with atropine and plants, containing this alkaloid. First aid measures in these intoxications. Antidotes and their mechanism.
7. N-cholinoblockers (antinicotines). Classification. Mechanism of action.
8. Ganglion blocking drugs (ganglioblockers). Classification by chemical structure, duration of action, location and mechanism of action. The action of

ganglioblockers on the cardiovascular system, the digestive tract, and on the uterus.

9. Indications, contraindications and adverse reactions of ganglioblockers.
10. Miorelaxants with peripheral action (neuromuscular blocking agents). Classification of miorelaxants by duration of action and by the mechanism of action.
11. Mechanism of action of depolarising, nondepolarizing and mixed miorelaxants. Indications, contraindications and side effects of miorelaxants.
12. Miorelaxants' antagonists and principles of decurarization.
13. Centrally acting M,N-cholinoblockers. Mechanism of action. Indications, contraindications and adverse reactions.
14. Peripherally acting M,N-cholinoblockers. Mechanism of action. Indications, contraindications and adverse reactions.

F. Independent work (is done in written form while preparing for the lesson)

1.) Brief characteristics of compulsory drugs: (Medicinal form. Method of administration. Doses (maximum for one intake, for 24 hours, therapeutic). Mechanism of action. Indications. Contraindications. Adverse reactions.)

1. Atropine sulphate. 2. Scopolamine hydrobromide. 3. Tropicamide. 4. Platifylline hydrotartrate. 5. Hexamethonium. 6. Treprium iodide. 7. Suxamethonium. 8. Melictin. 9. Pirenzepine. 10. Tubocurarine chloride. 11. Ipratropium bromide. 12. Trihexyphenidyl hydrochloride. 13. Adifenin.

2.) Questions on medical prescriptions.

To prescribe the following drugs in all the possible medicinal forms: 1. Atropine sulphate. 2. Scopolamine hydrobromide. 3. Tropicamide. 4. Platifylline hydrotartrate. 5. Hexamethonium. 6. Treprium iodide. 7. Suxamethonium. 8. Melictin. 9. Pirenzepine. 10. Tubocurarine chloride. 11. Ipratropium bromide. 12. Trihexyphenidyl hydrochloride. 13. Adifenin.

<i>Nr.</i>	<i>Denumirea medicamentului</i>	<i>Forma de livrare, doza</i>
1.	Atropine sulphate	Ampoules sol.0.05%-1ml and 0.1%-1ml Vials (for internal use) sol.0.1%-10ml Tablets 0.0005 Vials (ophthalmic drops) sol.0.1%-10ml Ointment (ophthalmic) 1%-5.0 Ophthalmic films 0.0016
2.	Scopolamine hydrobromide	Ampoules sol.0.25%-1ml Vials (ophthalmic drops) sol.0.25%-5ml Ointment (ophthalmic) 0.25%-5.0
3.	Tropicamide	Vials (ophthalmic drops) sol.0.5%-15ml and 1%-15ml
4.	Platifylline hydrotartrate	Tablets 0.005 Ampoules sol.0.2%-1ml Sup. rectal 0.01 Vials (ophthalmic drops) sol.1%-5ml and 2%-5ml
5.	Hexamethonium	Tablets 0.1 and 0.25

		Ampoules sol.2.5%-1ml
6.	Trepyrium iodide	Vials (liof.powder) 0.1
7.	Suxamethonium	Soil vials. 2%-5ml and 10ml Vials (liof.powder) 0.1 and 0.2
8.	Melictin	Tablets 0,02
9.	Pirenzepine	Tablets 0.025 and 0.05 Ampoules sol.0.5%-2ml
10.	Tubocurarine chloride	Ampoules sol.1%-1.5 ml
11.	Ipratropium bromide	Vials (for inhalations) sol.0.025%-20ml Aerosol 15ml
12.	Trihexyphenidyl hydrochloride	Tablets 0.001; 0.002 and 0.005
13.	Adifenin	Ampoules sol.0.25%-1ml

List the groups and drugs used in (for): intoxication with atropine containing plants, intestinal spasms, gastric ulcer disease with hypersecretion, fundoscopic eye examination, premedication, hypersalivation, prophylaxis of kinetosis, skeletal muscle relaxation, tracheal intubation, bone fragments reposition, hypertensive crisis, controlled hypotension, bronchial asthma.

3.) Tests (Guidelines for Laboratory Work in Pharmacology).

4.) Tables

Table 1

Pharmacological effects, indications and side effects of M-cholinoblockers

Systems and organs	Parameters	The effect	Indications	Adverse effects
Eye	Diameter of the pupil			
	Accommodation			
	Intraocular pressure			
Exocrine glands	Tear			
	Salivary			
	Sweat			
Bronchi	Tone			
	Secretion			
Heart	Heart rate			
	A-V conduction			
Blood vessels	Tone			
GIT	Sphincter tone			
	Peristalsis			
	Secretion			
Urinary bladder	The tone of the detrusor			
	Urine elimination			
Myometrium	Tone			

Table 2

Comparative characteristic of M-cholinoblockers used in ophthalmology

Drug's name	Duration of midriasis (hours, days)	Duration of accommodation paralysis (cycloplegia) (hours, days)
Atropine sulphate		
Homatropine hydrobromide		
Tropicamide		

Table 3

Indications of M-cholinoblockers

Indications	Atropine	Scopolamine	Homatropine	Tropicamide	Methocinium iodid	Ipratropium	Pirenzepine
Iritis, iridocyclitis							
Fundoscopy eye exam							
Eye refraction exam							
Spasms of smooth muscles of internal organs							
Bronchial asthma							
Hypersalivation							
Ulcer disease							
Bradycardia and AV block							
Premedication							
Kinetosis							
Overdose of cholinomimetics							

Note! The presence of the indication is marked with the "+"

Table 4

Pharmacological effects, indications and side effects of ganglioblockers

Systems and organs	Parameters	The effect	Indications	Adverse effects
Eye	Diameter of the pupil			
	Accommodation			
	Intraocular pressure			
Exocrine glands	Tear			
	Salivary			

	Sweat			
Bronchi	Tone			
	Secretion			
Heart	Heart rate			
	A-V conduction			
Blood vessels	Tone			
GIT	Sphincter tone			
	Peristalsis			
	Secretion			
Urinary bladder	The tone of the detrusor			
	Urine elimination			

Table 5

The comparative characteristic of antidepolarizing and depolarizing miorelaxants

Parameters	Peripheral non-depolarizing miorelaxant (ex. tubocurarine)	Peripheral depolarizing miorelaxant (ex. suxamethonium)
Influence on cell membrane (stabilization or depolarization)		
Duration of action (min)		
Fasciculations of muscles (+/-)		
Interaction with anticholinesterase drugs (synergism, antagonism, clinical importance)		

G. Interactive activity

- 1.) **Clinical case** (Guidelines for Laboratory Work in Pharmacology).
- 2.) **Virtual situations** (Guidelines for Laboratory Work in Pharmacology).
- 3.) **Virtual didactic movie.**
- 4.) **The problem of situation**

A patient with a gastric ulcer was given a medicine. But immediately after disappearance of heartburn and abdominal pain, xerostomia, cardiac palpitations, and decreased visual acuity occurred.

What drug was given to the patient? What was the cause of the complications that occurred? Which medicine can be used instead without causing these undesirable effects?