

HORMONES AND THEIR ANTAGONISTS (PART I)

A. Actuality. There are many pathological conditions that appear as a result of insufficiency or hyperfunction of endocrine glands. It is obvious that in the first case hormones are administered as substitution therapy, but in the second case, antihormonal drugs are indicated. Hormonal medications are also used in the treatment of some non-endocrine diseases as pathogenic therapy.

B. The purpose of the training is to study the pharmacology of hormonal drugs and their antagonists, the principles of drug selection in a specific disease and the correct prescription of drugs according to the indications.

C. Learning objectives:

1) The student must **know** the definition and classification of hormonal drugs and their antagonists, pharmacokinetics and pharmacodynamics, medicinal forms and ways of administration, indications, contraindications and side effects.

2) The student must **be able to:** write out hormonal drugs and their antagonists in different medicinal forms, prescribe them according to the pathological state and age of the patient.

D. The initial level of knowledge required for the interdisciplinary integration:

Human anatomy. Endocrine glands.

Human physiology. General characteristics of endocrine glands. Hormones. The participation of humoral factors in the integral reactions within the body. Pituitary gland. The relation between hypophysis and hypothalamus. Neurosecretion. Thyroid gland. Parathyroid gland. Pancreas.

Histology. Endocrine system. The structure of endocrine glands. Endocrine system regulation centers. Hypothalamus. Hypophysis. Epiphysis. Peripheral endocrine glands. Thyroid gland. Parathyroid gland.

Biochemistry: Structure, influence on metabolism and mechanism of action of hypothalamus hormones (liberins, statins), of pituitary, thyroid gland, parathyroid and pancreas.

Pathophysiology. Pathology of endocrine glands. Hyper- and hypofunction of hypophysis, thyroid and parathyroid glands, pancreas.

E. Self-training questions

1. The notion of hormones, hormonal and antihormonal drugs.
2. Classification of hormonal drugs according to the sources, chemical structure and mechanism of action.
3. Mechanism of action of polypeptide and steroid hormones on the cellular level.
4. Hormonal drugs of the hypothalamus: classifications, mechanism of action, indications, contraindications and side effects.
5. Pituitary hormonal preparations. Adenohypophysis hormones: classification, mechanism of action, indications, contraindications and side effects. Neurohypophysis hormones: influence on the tone of myometrium, bowels and blood vessels, influence on diuresis. Indications.
6. Thyroid hormone preparations. Mechanism of action, influence on organs'

functions and metabolism. Indications, contraindications, side effects, pharmacokinetics. Particularities of action and dosage of levothyroxine in children.

7. Antithyroid drugs: classification, mechanism of action, indications, side effects.
8. Parathyroid hormonal preparations: mechanism of action, effects, indications, side effects.
9. Calcitonin: drugs, mechanism of action, indications, side effects.
10. Classification of anti-diabetic drugs according to the mechanism of action.
11. Insulin preparations: classification according to the duration of action, mechanisms of action. Influence of insulin on carbohydrate, protein, lipid, hydrosaline metabolism, on the liver, skeletal muscles and adipose tissue.

Indications, side effects and their pharmacokinetics.

12. Human insulin drugs: peculiarities of action, indications. Drugs used in diabetic coma (hyperglycemia) and hypoglycemia.
13. Glucagon: mechanism of action, indications.
14. Classification of oral antidiabetics. New oral antidiabetic drugs.
15. Sulfonylureas derivatives as antidiabetics: mechanism of action, hypoglycemic effect, others effects, indications, side effects.
16. Biguanides as antidiabetics: mechanism of action, hypoglycemic effect, others effects, indications, side effects.
17. Meglitinides: mechanism of action, hypoglycemic effect, others effects, indications, side effects.
18. Thiazolidinediones: mechanism of action, hypoglycemic effect, others effects, indications, side effects.
19. Tetrazaccharides: mechanism of action, hypoglycemic effect, others effects, indications, side effects.
20. GLP-1 receptor agonists: mechanism of action, hypoglycemic effect, others effects, indications, side effects.
21. DPP-4 inhibitors: mechanism of action, hypoglycemic effect, others effects, indications, side effects.

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

1) Brief characteristics of compulsory drugs:

Down: Drug name. 1. Corticotropin. 2. Oxytocin. 3. Desmopressin 4. Chorionic gonadotropin. 5. Levothyroxine. 6. Thiamazole. 7. Parathyroidin. 8. Calcitonine. 9. Insulin. 10. Glibenclamide. 11. Metformin. 12. Glucagon.

Across: 1. Medicinal form. 2. Ways of administration. 3. Doses. 4. Mechanism of action. 5. Indications. 6. Contraindications. 7. Side effects.

2) Questions on medical prescriptions

To prescribe the following drugs in all the possible medicinal forms: 1. Corticotropin. 2. Oxytocin. 3. Desmopressin 4. Chorionic gonadotropin. 5. Levothyroxine. 6. Thiamazole. 7. Parathyroidin. 8. Calcitonine. 9. Insulin. 10. Glibenclamide. 11. Metformin. 12. Glucagon.

Drugs used in (for): type I diabetes mellitus, type II diabetes mellitus, diabetes insipidus, diabetic coma, myxedema, hyperthyroidism, hypoglycaemic coma, diabetes mellitus and obesity, tetany.

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

4) Clinical case (Guidelines for Laboratory Work in Pharmacology).

5) Virtual situations (Guidelines for Laboratory Work in Pharmacology).

6) Virtual didactic movie “Acute insulin intoxication and first aid measures”

7) Experimental work (Guidelines for laboratory work in Pharmacology).

8) Tables

Table N1

Characteristics of pituitary hormones preparations

Pituitary lobes	Pituitary gland hormones	Drugs	Target organs and tissues	Effects	Indications
Anterior (adenohypophysis)	Somatotropin				
	Adrenocorticotropin				
	Thyrotropin				
	Follicle-stimulating				
	Luteinizing				
	Prolactin				
Intermediate	Melanotropin				
Posterior (neurohypophysis)	Vasopressin				
	Oxytocin				

Table N2

Characteristic of antithyroid drugs

Medications	Thioamides	Iodine drugs	Lithium drugs	B-blockers
Mechanism of action				
Indications				
Side effects				
Pharmacokinetics				

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Table N3

Effects and indications of parathyroid hormone and calcitonin

Hormone	Drugs	Effects				Indications
		Ca ⁺⁺ absorption from GIT	Ca ⁺⁺ level in plasma	Ca ⁺⁺ content in bone tissue	Ca ⁺⁺ reabsorption in the kidneys	
Parathyroid hormone						
Calcitonin						

Note. Presence of the effect show through:

“↑” – increased effect; “↓”- decreased effect.

Table N4

Metabolic effects of insulin

Type of metabolism	Hepatic cells	Addipos tissue	Muscle cells
Carbohydrate	Gluconeogenesis () Glycolysis () Glycogenesis () Glycogenolysis ()	Glucose uptake ()	Glucose uptake () Glycolysis ()
Lipids	Lipogenesis () Lipolysis ()	Triglyceride synthesis ()	-
Protein	Protein catabolism ()		Amino acid uptake () Protein synthesis ()

Note. Presence of the effect show through:

“↑” – increased effect; “↓”- decreased effect.

Table N5

Comparative characteristics of oral antidiabetics

Groups of antidiabetics	Mechanism of action	Hypoglycemic effect	Indications
Sulphonilureics			
Biguanides			
Thiazolidindinones			
Meglitinides			
GLP-1 aginists			
DPP-IV inhibitors			
Tetrazaharides			
Aldoreductase			

inhibitors			
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8) Clinical case:

The patient has irritability, increased excitability, sweating, tachycardia, sleep disorder, exophthalmia and a progressive weight loss. The doctor, after a thorough examination, indicated a medicine. All signs of disease have diminished, but the patient has reported fatigue, muscular cramps, increasing in the volume anterior region of the throat. Repeated examination of the patient revealed leukopenia.

What drug was indicated to the patient?

What was the cause of enlarged volume of the anterior region of the neck?

What was the cause of leukopenia?

What is required to indicate to the patient for prophylaxis of the detected complications?

HORMONES AND THEIR ANTAGONISTS (part II). DRUGS AFFECTING THE TONUS AND CONTRACTIBILITY OF MYOMETRIUM.

A. Actuality. There are many pathological conditions that appear as a result of insufficiency or hyperfunction of endocrine glands. It is obvious that in the first case hormones are administered as substitution therapy, but in the second case, antihormonal drugs are indicated. Hormonal medications are also used in the treatment of some non-endocrine diseases as pathogenic therapy.

Drugs that stimulate the smooth muscles of the uterus have wide use in obstetrics and gynecology to induce and support the labor process, to provoke an abortion and prevent postnatal hemorrhages. Preparations that reduce uterine contractility are useful for the prophylaxis and treatment of imminence of abortion and premature birth.

B. The purpose of the training is to study the pharmacology of hormonal drugs and their antagonists, the principles of drug selection in a specific pathology and the correct prescription of drugs according to the indications. Introduce the students to the pharmacology of drugs that influence the contractile activity of the myometrium and tonus of the uterine cervix.

C. Learning objectives:

1) The student must **know** the definition and classification of hormonal drugs and their antagonists, uterine stimulants and relaxants, their pharmacokinetics, and pharmacodynamics, names, medicinal forms and ways of administration, general indications and contraindications, side effects.

2) The student must **be able to:** write out hormonal drugs and their antagonists in different medicinal forms, prescribe them according to the pathological state and age of the patient.

D. The initial level of knowledge required for the interdisciplinary integration

Human anatomy. Endocrine glands. Uterus structure. Functional modifications of the uterus. Nerves and vessels of the uterus.

Human physiology. General characteristics of endocrine glands. Hormones. The participation of humoral factors in the integral reactions within the body. Adrenal glands. The importance of steroids in the body. Sexual glands. Sexual hormones and their importance for the body. Parturition. Increased uterine contractability before birth. Influence of oxytocin on the uterus. Stretching of uterine muscles. Beginning of labor – initiation through a positive feedback theory. The mechanism of parturition. Separation and expulsion of the placenta. Involution of the uterus.

Histology. Endocrine system. The structure of endocrine glands. Endocrine system regulation centers. Adrenal glands. Isolated hormone-secreting cells. Male and female reproductive system. Uterus. Development. Structure. Vascularization and innervation of the uterus.

Biochemistry. Glucocorticoids, mineralocorticoids, biosynthesis and secretion regulation. Influence on protein, carbohydrates, lipids, and hydrosalin

metabolism. Sexual hormones: structure, influence on metabolism and function of sexual organs. Prostaglandins. Structure and nomenclature. Biosynthesis and metabolism. Biological action.

Pathophysiology. Pathophysiology of adrenocortical medulla, sexual glands.

Morphopathology. Morphological changes in endocrine pathologies.

Morphopathological modifications of the uterus.

E. Self-training questions

1. Mineralocorticoids: mechanism of action, influence on the body, indications, side effects.
2. Glucocorticoids. Classification according to the route of administration, duration of action, basic effects and potency. Genomic and nongenomic action. Influence on carbohydrates, proteins, lipids, and hydrosaline metabolism, on mesenchymal tissue, cardiovascular system, CNS, muscles and blood. Anti-inflammatory, antiallergic, immunodepressive and antishock action of glucocorticoids.
3. Indications of glucocorticoids. Principles of dosage. Side effects.
4. Estrogens and their derivatives: classification, mechanism of action, effects, indications, side effects.
5. Progestins and their derivatives: classification, mechanism of action, effects, indications, side effects.
6. Antiestrogens: classification, mechanism of action, indications.
7. Antiprogestins: mechanism of action, effects, indications.
8. Contraceptives: classification, mechanism of action, effects, indications, side effects.
9. Androgen medications: classification, mechanism of action, effects, indications, side effects.
10. Androgen antagonists (antiandrogens): classification, mechanism of action, indications.
11. Classification of anabolic drugs. Steroid anabolics: effects, indications, contraindications, side effects.
12. Nonsteroidal anabolics: classification, mechanism of action, effects. Indications. Side effects.
13. Classification of drugs that influence the tone and the contractility of the myometrium.
14. Uterine stimulants (ocitocic drugs): classification, mechanism of action, indications, contraindications and adverse reactions.
15. Tocolytics : classification, mechanism of action, effects, indications, side effects.
16. Drugs that increase the tone of the myometrium (ergot alkaloids): mechanism of action, effects, indications, side effects.
17. Drugs that reduce the tone of the cervix: mechanism of action, effects, indications, side effects.

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

1) Brief characteristics of compulsory drugs:

Down: Drug name. 1. Desoxycorticosterone acetate. 2. Hydrocortisone acetate. 3. Prednisolone. 4. Dexamethasone. 5. Fluticasone. 6. Estradiol. 7. Hexestrol. 8. Progesteron. 9. Ethisterone. 10. Methyltestosterone. 11. Trisiston. 12. Clomiphene citrate. 13. Cyproterone. 14. Finasteride. 15. Nandrolone. 16. Dinoprost. 17. Dinoprostone. 18. Ergotamine. 19. Methylergometrine. 20. Fenoterol. 21. Ritodrine.

Subject-related medicines are reviewed in the previous compartments: 1. Oxytocin. 2. Dexamethasone

Across: 1. Medicinal form. 2. Ways of administration. 3. Doses. 4. Mechanism of action. 5. Indications. 6. Contraindications. 7. Side effects.

2) Medical prescriptions

To prescribe: 1. Desoxycorticosterone acetate. 2. Hydrocortisone acetate. 3. Prednisolone. 4. Dexamethasone. 5. Fluticasone. 6. Estradiol. 7. Hexestrol. 8. Progesteron. 9. Ethisterone. 10. Methyltestosterone. 11. Trisiston. 12. Clomiphene citrate. 13. Cyproterone. 14. Finasteride. 15. Nandrolone. 16. Dinoprost. 17. Dinoprostone. 18. Ergotamine. 19. Methylergometrine. 20. Fenoterol. 21. Ritodrine.

Drugs used in (for): ovarian hypofunction, prostate cancer, male genital hypoplasia, myocardial infarction, alimentary-infectious dystrophy in children, Addison's disease, rheumatism, anaphylactic shock, eczema, acute suprarenal failure, brochial asthma, rheumathoid arthritis, status asthmaticus, lupus erythematosus, hemolytic anaemia, inducing and augmenting labor, prevention of unwanted pregnancy, postpartum uterine atony, metrorrhagia, relaxation of the uterine cervix, to induce abortion, postpartum hemorrhages, prophylaxis and treatment of imminent abortion and premature labor.

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

4) Clinical case (Guidelines for Laboratory Work in Pharmacology).

5) Virtual situations (Guidelines for Laboratory Work in Pharmacology).

6) Virtual didactic movie

7) Tables

Table N1

Physiological effects of glucocorticoids

Target organs and tissues		Effects	Effect mechanism
Metabolic effects	Carbohydrate metabolism		
	Protein metabolism		
	Lipid metabolism		
Hydro-electrolytic metabolism	Content in the body:		
	H ₂ O		
	Na ⁺		
	K ⁺		

	Ca ⁺⁺		
Blood system	Content in the blood:		
	Erythrocytes		
	Thrombocytes		
	Neutrophils		
	Eosinophils		
	T - lymphocytes		
Central nervous system			
Cardiovascular system	Blood pressure		
hypothalamo-hypophyseal-suprarenal system			

Table N2

Indications of estrogens

Indications	Estradiol	Ethinyl-estradiol	Hexestrol	Fosfestrol
Ovarian hypofunction (primary and secondary hypogonadism)				
Dysmenorrhea (menstrual cycle disorder)				
Insufficient contractile activity of the myometrium in the natal period				
Substitution therapy in natural or surgical menopause				
Oral contraception (combined with progestogen)				
Prostate cancer				

Table N3

Progestins indications

Indications	Progesterone	Hydroxyprogesterone caproate	Medroxyprogesterone acetate	Norethisterone
Dysmenorrhea (menstrual cycle disorder)				
The imminence of spontaneous abortion (caused by yellow body insufficiency)				
Endometriosis				

Peroral contraception (combined with estrogen)				
Parenteral contraception (injectible)				
Substitution therapy in natural or surgical menopause (combined with estrogen)				
Cancer of the endometrium and mammary gland				

Note. Presence of the effects indicate with “+”

Table N4

Indications of hormonal contraceptives

Group of drugs	Women up to 40 years, without contraindications to hormonal contraception	Women up to 40 years, with contraindications to estrogens usage	Smokers Female older than 35	Women during lactation	Women older than the reproductive period
Combined oral contraceptives					
Contraceptives containing only progestin					

Table N5

Regulation of contractile activity of the myometrium.

Myometrium receptors	Stimulating effect	Depressing effect
Stimulation of alpha – adrenoreceptors		
Stimulation beta 2 - adrenoreceptors		
Stimulation M - cholinoreceptors		
Stimulation of oxytocin receptors		
Stimulation of prostaglandin receptors		

Note. Presence of the effects indicate with “+”

Table N6

Indications of uterine stimulants

Indications	Oxytocin and its analogs	Prostaglandins	Ergot alkaloids
Stimulation of contractile activity of miometrium			
Artificial interruption of pregnancy in its different periods			
Artificial interruption of pregnancy in late period			
Acceleration of uterine involution in postpartum period			
Postpartum hemostasis			

8) Clinical case:

In order to stop bleeding due to postnatal uterine atony, the patient was given a drug to be taken twice a day for 3 days. Contrary to indications, the patient used the preparation 4 times a day for one week. Bleeding stopped but appeared pain in the extremities.

What preparation was prescribed to the patient?

What is the cause of appeared complications?