**Lecture topic is…**

**(Slide 1) Lecture 3**

**Autonomic nervous system. Endocrine system.**

**(Slide 2)** Lecture plan:

1. Autonomic nervous system. Its functions.
2. Features of the sympathetic, parasympathetic and metasympathetic divisions of the autonomic nervous system.
3. Physiology of the endocrine glands.
4. Regulation of endocrine functions.

 **(Slide 3)** The autonomic nervous system (abbreviated, the ANS) is understood as a complex of central and peripheral nerve structures providing coordinated activity of internal organs for best adaptation of an organism to the variable environment.

**(Slide 4)** The autonomic nervous system controls internal body processes such as the following:

1. Blood pressure
2. Heart and breathing rates
3. Body temperature
4. Digestion
5. Metabolism (thus affecting body weight)
6. The balance of water and electrolytes (such as sodium and calcium)
7. The production of body fluids (saliva, sweat, and tears)
8. Urination
9. Defecation
10. Sexual response

**(Slide 5)** The ANS is divided into three parts: sympathetic, parasympathetic and metasympathetic (enteric). Activity of sympathetic and parasympathetic divisions, as well as of somatic nervous system, is based on reflexes. However, an autonomic reflex differs from a somatic one.

**Watching the video…**

**(Slide 6) Video.**

**The slide shows ..**

**(Slide 7)** Difference between Somatic and Autonomic Reflexes

1. Localization of the interneuron and effector neuron. In the somatic reflex both the interneuron (the 1st neuron) and effector neuron (the 2nd neuron) are located within the gray matter of the CNS (in our case – in the gray matter of the spinal cord). In the autonomic reflex the 1st neuron (the interneuron) is located in the gray matter of the CNS, and the 2nd neuron is located in the ganglion outside the CNS. This results in different consequences of cutting ventral roots of somatic and autonomic nerves. Somatic nerves degenerate, whereas autonomic nerves do not degenerate and continue performing their functions.

2. Exit of the nerve fibers from the CNS. Somatic fibers leave the brainstem and the spinal cord from different segments and supply organs from three adjacent segments. Autonomic fibers leave the CNS in relatively isolated regions: the brainstem (mesencephalon and medulla oblongata), thoracic, lumbar and sacral sections of the spinal cord.

3. Distribution (arrangement) of somatic and autonomic nerves in the periphery. Somatic nerves are mainly arranged in segments, whereas autonomic nerves are mainly diffused.

4. Morphological characteristics of somatic and autonomic nerve fibers. Somatic nerve fibers are primarily covered with myelin which enables propagation of excitation at speeds as high as 100-120 m/s. Autonomic nerve fibers carry little or no myelin at all. Because of this they conduct excitation at much lower speeds: 0.5 – 2 m/s.

**(Slide 8)** Ganglionic synapses of both sympathetic and parasympathetic divisions of the autonomic nervous system use acetylcholine as a neurotransmitter, that is, they are cholinergic. Effector receptors of postsynaptic membranes may be sensitive not only to acetylcholine, but also to nicotine alkaloid extracted from tobacco leaves. (Alkaloids are nitrogen-containing organic compounds of natural plant origin, possessing properties of bases). For this reason they are called nicotinic, or N-receptors. A particular feature of these receptors is their ability to be blocked by ganglion-blocking agents (benzohexon, perylene).

**(Slide 9)** Physiological peculiarities of ganglionic synapses

1) considerable delay in propagation of excitation (5 times that of central synapses);

2) longer duration of postsynaptic potentials;

3) expressed and long-lasting hyperpolarization.

**(Slide 10)** Effector synapses of the parasympathetic nervous system are cholinergic, since they use acetylcholine as a neurotransmitter. Effector receptors of postsynaptic membranes of these synapses are sensitive not only to acetylcholine, but also to muscarine alkaloid, extracted from a red fly-agaric mushroom, and therefore are called muscarinic, or M-receptors. M-receptors can be blocked by atropine. Depending on the second messenger which couples an activated receptor with the processes in the cytoplasm, and on the type of process induced in the cell, M-receptors are classified into M1 and M2 receptors. Interaction of acetylcholine with M1 receptor induces excitation in a cell, whereas activation of M2 receptors induces inhibition.

**(Slide 11) Video.** **Parasympathetic nervous system.**

**(Slide 12)** Neurotransmitters released at effector synapses of the sympathetic nervous system are typically norepinephrine (noradrenaline) and epinephrine (adrenaline). Effector receptors of the postsynaptic membrane may be either α- and β-adrenergic receptors. Interaction of neurotransmitter with α-adrenoreceptors causes excitation in an effector cell, and interaction with β-adrenoreceptors causes inhibition (for instance, in smooth muscle cells of vessel wall). Some sympathetic effector neurons release other kinds of neurotransmitters (acetylcholine, serotonin, dopamine) that interact with the corresponding synaptic receptors.

**(Slide 13) Video.** **Sympathetic nervous system.**

**(Slide 14)** It was shown by many researchers that hollow muscle organs taken out from the body and placed into a suitable nutrient medium at the appropriate temperature, continue performing their functions without any visible changes, for example, an isolated frog’s heart continues beating, and an isolated frog’s gut continues peristalsis. This functional autonomy (independence) can be attributed to existence of the network of ganglia in the walls of the internal organs which alongside other mechanisms participate in control of functional activity of these organs. This system of ganglia within the walls of hollow internal organs is considered to be a relatively independent part of the ANS. In Russian physiology this part of the ANS is called metasympathetic part of the ANS.

**(Slide 15)** Functions of Metasympathetic ANS:

1. The metasympathetic division of the autonomic nervous system is an independent structure providing nervous control on the local level.

2. The metasympathetic division of the autonomic nervous system can act as an effector regulatory structure that mediates influence of the higher-lying centers of the CNS.

**(Slide 16)** Features of the metasympathetic system:

1. It has its own sensory link and afferent path.
2. Innervates only the muscles of the internal organs.
3. Receives signals from the sympathetic and parasympathetic systems through incoming synapses.
4. There is no direct connection with the efferent link of the somatic reflex.
5. Those internal organs in which the metasympathetic nervous system (MHC) is disturbed lose their coordinated motor function.
6. The network has its own neurotransmitters.

**(Slide 17) Concept of Humoral Regulatory Mechanisms**

In the evolution of multicellular organisms a need arose in some mechanisms that could provide interrelations both between individual cells of tissues and between individual organs in the whole organism. In result of evolutionary selection two mechanisms of integration of elements into one whole have been formed – mechanisms of nervous and humoral regulation. Mechanisms of nervous regulation have already been discussed above. **Humoral regulation** is a complex of physiological, biochemical and biophysical mechanisms that act through chemical compounds of the internal environment and induce changes in conditions of the individual cells, tissues, organs and systems of an organism.

The concept of the internal environment was introduced by outstanding French physiologist Claude Bernard. He understood the internal environment as a complex of biological fluids – blood, lymph and tissue fluid.

**There exist three classes of chemical substances** that participate in humoral regulatory mechanisms:

1) water-soluble salts, or electrolytes;

2) products of metabolism, or metabolites;

3) biologically active substances including hormones.

The 1st group includes compounds of potassium, sodium, calcium and magnesium. However, in a human organism there may be found almost all currently known chemical elements. Therefore, a decrease or increase in the amount of any of these compounds in the internal environment of the body may affect condition of cells, tissues, organs and systems.

The 2nd group of chemical compounds includes CO2, carbonic acid (H2CO3), lactic acid, pyruvic acid, products of ATP cleavage (ADP, inorganic phosphorus, etc.).

**(Slide 18)** The 3d group includes hormones and parahormones (tissue hormones). The term “hormone” was proposed by English physiologists W. Bayliss and E. Starling in 1905. It originates from the Greek word hormao meaning urging on.

**(Slide 19)** Hormones are highly active chemical substances produced in small amounts by specialized cells, tissues or organs, and released into the internal environment of the body.

Hormones differ from other humoral substances in the following way:

1) they are produced by specialized cells;

2) they act distantly, address their action to all cells but interact only with target cells;

3) they are characterized by extremely high biological activity. For example, epinephrine increases the rate and strength of heart contractions. According to calculations, 1 g of epinephrine is capable of activating 100 000 000 of isolated frogs’ hearts. 1 g of insulin hormone that participates in glucose metabolism can decrease the blood glucose level in 125 000 rabbits.

**(Slide 20) Video.** **Endocrine System and Hormones**

**(Slide 21)** Hormones are produced by:

1) specialized endocrine glands, e.g., thyroid gland, adrenals, parathyroid gland;

2) endocrine tissue of an organ, e.g., endocrine tissue of pancreas containing α- and β-cells;

3) diffused cells possessing endocrine function, e.g., G-cells of the pyloric part of the stomach which secrete gastrin hormone;

4) cells that besides their specialized function, also perform endocrine function. For example, nerve cells of the hypothalamus (diencephalon) function not only as nerve cells (generation of action potentials and propagation of them to other nerve cells), but are also capable of synthesizing and releasing hormones, such as antidiuretic hormone (vasopressin) and oxytocin. The former regulates the amount of urine excreted into the external environment, and the latter regulates the contractile activity of smooth muscle of uterus.

**(Slide 22) Classification of Hormones**

By chemical composition, hormones fall into three groups:

A) derivatives of amino acids. For example, epinephrine, a hormone of adrenal medulla, is a derivative of tyrosine. Iodine-containing thyroid hormones are also derivatives of tyrosine;

B) hormones of protein origin further classified into three subgroups:

a) oligopeptides – low-molecular-weight proteins, e.g., antidiuretic hormone (vasopressin), oxytocin, gastrin, etc.;

b) proteins proper (insulin, glucagon, etc.);

c) glucoproteins, e.g., follicle-stimulating hormone, leuteinizing hormone;

C) steroid hormones (hormones of adrenal cortex, sex hormones).

**(Slide 23)** By mechanism of action hormones are classified into two groups:

a) hormones of membrane action (insulin, glucagon). Receptors sensitive to these hormones, are built into the biological membranes of target cells. A hormone “finds” a receptor on the membrane of a target cell and interacts with it. After that a hormone-receptor complex activates second messengers that couple processes occurring on the membrane and processes in the cytoplasm. Second messengers may be substances that participate in synaptic transmission:

- adenylate cyclase – cyclic adenosine monophosphate (cAMP)

- guanilate cyclase – cyclic guanosine monophosphate (cGMP)

- phospholipase C – inositol-3-phosphate;

- Ca++- calmodulin;

b) hormones of intracellular (cytosolic) action. This group includes steroid hormones and reproductive hormones. Receptors sensitive to these hormones are located inside cells. Therefore, to be able to act on a cell a hormone must first enter a cell and interact with the receptor. Hormones of cytosolic action realize their effect through hereditary apparatus of the cell located in the nucleus.

**(Slide 24)** By physiological effect hormones are classified into:

a) effector hormones acting on target cells in tissues and organs;

b) tropic, or regulatory hormones. Hormones of this group are synthesized in the anterior pituitary (adenohypophysis) and include adrenocorticotropic hormones, thyrotropic hormones and gonadotropic hormones. Their primary function is to regulate the activity of pituitary-dependent endocrine glands;

c) neurohormones (regulators of regulators). This group includes releasing hormones (liberins and statins) produced in the hypothalamic region. The main function of this group of hormones is to regulate production of tropic hormones by the anterior pituitary.

**(Slide 25)** Hormones are continuously synthesized by the endocrine glands. The intensity of synthesis is determined not only by controlling signals, but also by the amount of produced hormone. The principle of inhibition by the end product known in biochemistry, means suppression of hormone synthesis if it accumulates in the producer cells. Release of hormone from producer cells causes increase in its synthesis.

Activity of endocrine cells may also be determined by concentration of a hormone in the internal environment. With high concentration of hormone the activity of producing cells decreases. This phenomenon requires a special care in use of hormones for practical purposes. For example, recently some anabolics of steroid nature have been widely used in sports due to their ability to build up muscle mass. But, since the chemical structure of anabolics of this group is similar to that of male reproductive (sex) hormones, their use may suppress the function of reproductive glands in males with their further hypotrophy and even atrophy.

**(Slide 26)** And, at last, in some cases the amount of synthesized and released hormones depends on the amount of substrates controlled by the given hormone in the internal environment. For example, activity of pancreatic β-cells to synthesize and release insulin into the internal environment depends on the concentration of glucose, and increase in the latter enhances synthesis and secretion of insulin by β-cells.

Effect of Hormones on Target Cells

**(Slide 27)** 1) Metabolic effect. In this case hormones cause changes in metabolism in target cells. These changes may be associated with increase in permeability of biological membranes, with synthesis of some enzymes or with a change in their activity. For example, thyroid hormones possess a pronounced metabolic effect.

**(Slide 28)** 2) Morphogenetic effect. Here, hormones induce changes in the target cells in the individual development of a human. For example, somatotropin, a hormone of adenohypophysis, influences growth of an individual. Sex hormones participate in formation of the secondary sex signs.

**(Slide 29)** 3) Kinetic effect. This effect is associated with the ability of hormones to evoke physiological processes. For example, oxytocin (a hormone produced in the hypothalamic region) activates contraction of smooth muscles of uterus, and antidiuretic hormone stimulates reabsorption in kidneys.

**(Slide 30)** 4) Corrective effect. This effect of hormones is associated with their ability to modify the current activity of target cells, tissues and organs. An example is the influence of epinephrine on the heart rate.

**(Slide 31)** 5) Reactogenic effect. This effect is associated with the ability of hormones to modify response of cells, tissues and organs to different stimuli including other hormones. For example, gastrin and cholecystokinin modify excitability of feeding and satiety nerve centers located in the hypothalamic region.

3. Concept of Endocrine Glands. Classification of Endocrine glands

Endocrine glands have no excretory ducts for excretion of biologically active substances synthesized by them. Endocrine glands release the synthesized substances directly into the internal environment of the body for spreading throughout the body.

1) By localization endocrine glands are classified into central and peripheral. Central glands include epiphysis, hypothalamic region, pituitary. Peripheral glands include thyroid, parathyroid, adrenals, thymus, pancreatic islets, reproductive glands and others.

2) By controlling mechanism endocrine glands are categorized to pituitary-dependent and non-pituitary-dependent. The pituitary-dependent glands include thyroid, adrenal cortex, reproductive glands, epiphysis. The non-pituitary-dependent glands include parathyroid glands, thymus, pancreatic islets and adrenal medulla.

4. Regulation of Activity of Endocrine Glands

Activity of the endocrine glands is regulated by deviation (quantity) and by stimulation (input). The mechanism of regulation by deviation has been considered in discussion of regulation of the activity of hormone-producing cells.

The second type of regulation is by “stimulation”. Regulation of endocrine glands by stimulation is realized through neural and humoral mechanisms. An example of neural mechanism is activation of the adrenal medulla through stimulation of the sympathetic nervous system with participation of dorsal hypothalamic nuclei of the diencephalon.

Humoral mechanism of activation of pituitary-dependent endocrine glands also starts in the hypothalamic region with secretion of the appropriate releasing hormones (liberins) which stimulate the anterior pituitary (adenohypophysis) to produce tropic hormones, which in turn activate pituitary-dependent endocrine glands. This mechanism is used for activation of adrenal cortex.

Action on an organism of a strong stimulus activates not only sympatho-adrenal complex, but also the neurosecretory activity of the hypothalamus, in particular, secretion of corticoliberin hormone which reaches the anterior pituitary where it activates synthesis and secretion of adrenocorticotropic hormones. The latter are transported throughout the body and “find” the target cells in the adrenal cortex, which responds to it by activation of synthesis and secretion of corticosteroids, in particular, of hydrocortison.

Both mechanisms of regulation of the activity of endocrine glands supplement each other at different stages of adaptation of the body to changes in the environment.

In each cell there usually function different kinds of receptors to one hormone (for example, both α- and β-adrenoreceptors). Besides, a cell is usually sensitive to 7-10 different endocrine regulators (neurotransmitters, hormones, prostaglandins, growth factors). Each of these regulators is characterized by specific duration and amplitude of regulatory signal, and each regulator is characterized by a certain proportion of activities of second messenger generation systems in the cell or by certain variations in the membrane potential. On the level of effector systems of the cell there may occur both potentiation and mutual extinction of different regulator signals.

Besides, in each cell there also function special biochemical mechanisms that regulate sensitivity of a cell to a hormone. This mechanism may be considered on an example of a receptor coupled with G-proteins. The level of hormones that act through this system of transmembrane signalization (which, besides substances mentioned above, include prostaglandins, pituitary hormones, angiotensin II, bradykinin, vasopressin, oxytocin, histamine, dopamine, enkephalin, endorphin, serotonin, endothelin, cholecystokinin, gastrin, parathyroid hormone) usually rises for several minutes. This period is sufficient for formation of the required quantity of the second messengers (cyclic AMP, Ca2+, diacylglycerole), which activate the respective protein kinases with subsequent phosphorylation of proteins. But if the level of hormones stays high for dozens of minutes or several hours (as in hyperfunction of the endocrine gland or due to pharmacological intervention), the desensitization of the respective receptor results. At first the receptor becomes phosphorylated by protein kinase present in the plasma membrane practically of all cells, with the result of 2-5-times decrease in their affinity to the given hormone.

Protein kinase may phosphorylate only hormone+receptor complex; therefore the longer the hormone remains bound to the receptor, the higher the probability for this receptor to be phosphorylated. If such phosphorylation is unable to suppress the hormone signal, then in 15-30 minutes the receptor becomes phosphorylated by protein kinase that is activated by the respective second messenger (for example, by cAMP-dependent protein kinase in case of β-adrenergic receptors that activate adenylate cyclase; or by protein kinase C in case of α1-adrenergic or M1- and M3-cholinergic receptors that activate phospholipase C). Phosphorylation of receptors by protein kinases dependent on second messengers deranges coupling with G-proteins that weakens activating or inhibiting influence of hormones acting through receptors on adenylate cyclase or K+ channels. If the level of the hormone keeps high within hours, and the above mentioned desensitization mechanisms fail to suppress the regulatory signal, the hormone+receptor complexes undergo endocytosis, with receptosomes appearing inside cells. If the level of hormone decreases within the first 2-3 hours, the complexes may again build into the plasma membrane. If the level does not decrease, they fuse with the lysosomes, after which receptors are destroyed. It is clear that restoration of the sensitivity of the cell to this hormone will require new synthesis of hormones.

Finish for today

The full lecture is at the indicated website.

**Thank you for attention**