Ministry of health Republic of Belarus
Establishment of education “Gomel state medical university”

Department of histology, cytology and embryology

MANUAL

for 1-st year students of faculty of foreign students on gynecology

Topic: 3:

HISTOPHYSIOLOGY OF THE CENTRAL ORGANS OF THE ENDOCRINE SYSTEM

Duration 4 hours

Authors:

Associate Professor Ph.D. Kravtsova I.L.

Associate Professor Ph.D. Solodova E.K.

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THE MOTIVATIONAL CHARACTERISTIC OF THE THEME

Regulation and coordination of functions of an organism is provided with action nervous and endocrine systems. Endocrine systems (Glands of internal secretion) make it a part of the regulating system intended for maintenance of a homeostasis in an organism. They carry out the function by means of hormones allocated in blood. Change of functional activity of these tissues is accompanied by reorganization of their structure and, on the contrary, infringement of structure of tissues and organs.

The knowledge, got on the given theme, is necessary for understanding of morphological displays of frustration of hormonal regulation.

THE PURPOSE

Studying of a microscopic and ultramicroscopic structure and histophysiologies of endocrine system central organs.

PROBLEMS

The student should know:

1) The general characteristics and classification of endocrine glands.
2) Structures of hypothalamus. It̒s participation in regulation endocrine functions.
3) Hypothalamo-hypophyseal systems.
4) Development and structure of a hypophysis.
5) Epiphysis. Development, structure.

The student should be able:

1) To identify endocrine systems at a microscopic level.
2) To characterize embryonic development and the general laws of its structure.
3) To explain mechanisms hypothalamic control of the endocrine functions.
4) To explain the morphology and the structures of hypothalamus, hypophysis and epiphysis.
5) To use methods of the microscopic and ultramicroscopic analysis for judgement about their functional activity.

REQUIREMENTS TO THE INITIAL LEVEL OF KNOWLEDGE

For full mastering a theme it is necessary for student to repeat from the general biology endocrine and humoral regulation of systems of bodies.

CONTROL QUESTIONS FROM RELATED SUBJECTS

1) Features of structure and mechanisms of cells secretion.
2) Differentiations between exocrine and endocrine glands.
3) The structure and classification of capillaries.

CONTROL QUESTIONS ON THE THEME

1. A general characteristic and the basic structural components of endocrine systems.
2. Hypothalamus. Structure and functional role.
3. A hypophysis. Sources of development, a structure, blood supply and functions.
4. Development, a structure and functions of epiphysis.

THE PRACTICAL PART

1) Hormones and targets cells – to give definition (Exercise № 1 in album)

2) The organization of endocrine systems – (Exercise № 2 in album)

3) The Structure of a hypophysis – to designate in figure (Exercise № 3 in album)

4) Microscopy of histological preparations (Exercise № 4, 7, 8,10and 11 in albums)

5) Hypothalamus-neurohypophysial system – to specify names (Exercise № 5 in album)

6) Hypothalamus-adenohypophysial system – to specify names Exercise № 6 in album)

7) To study diagrams

SLIDES

1. Hypopysis
2. Epiphysis

QUESTIONS FOR SELF-CHECKING KNOWLEDGE

1. Basic characteristic and basic structural components of endocrine glands.
2. Hypothalamus: structure, functions.
3. Hypophysis: source of development, structure, blood supply and histophysiology.
4. Hypothalamus – adenohypophysal system. Principle of feedback mechanisms.
5. Hypothalamus – neurohypophysal system.
6. Neurohemal organs.
7. Epiphysis: development, structure, functions.

HISTOPHYSIOLOGY OF THE CENTRAL ORGANS OF THE ENDOCRINE SYSTEM

Two communication systems – the autonomic nervous system and the endocrine system – coordinate and control the metabolic activities and maintain homeostasis of our multicellular organism.

The nervous system communicates through neural impulse transmission and the local release of neurotransmitters in the immediate vicinity of the target cell. It induces a rapid and localized response. The endocrine system communicates through the release of *hormones. The hormones are* secretions of endocrine cells that pass into the blood and travel to target cells whose functioning they may influence profoundly. It induces a slower and less localized response. Each hormone acts on cells that bear specific receptors for it. That cells are called target cells. Some hormones act only on one organ or on one type of cell, while other hormones may have widespread effects. Classically, endocrine glands have been defined as being ductless glands, because they release their secretory products directly into the blood or lymph.

Chemically, hormones can be divided into four classes:

amino *acid derivatives* (adrenalin, thyroxine);

glands: thyroid and adrenal medulla;

small peptides (vasopressin);

proteins (insulin, parathormone, prolactin);

protein hormones and peptides are produced by cells that originate from endoderma (glands: hypophysis (or pituitary), thyroid, parathyroid, and pancreas. Peptide hormones are also secreted by cells of *diffuse endocrine system);*

steroids (progesterone, oestrogens, testosterone and cortisol). *Steroid hormones* are produced by cells that originate from embryonic mesoderma. Glands: ovaries, testes, and adrenal cortex.

Two main mechanisms of the hormones activity are known. Large protein molecule of hormone bonds to transmembrane's receptor and changes its conformation cause

There are several types of intercellular communications.

Autocrine control. Cell release hormones for itself.

Paracrine control. Endocrine cells may influence the activity of adjacent target cells through the extracellular space.

Endocrine control involves the circulatory system to transport the hormone.

Nervous control.

Neuroendocrine mechanism combines endocrine and nervous controls [1, 2].

Origin of the endocrine cells is different. Mostly they are epithelial cells. But they may originate from neural cells (eurohypophysis, pineal gland, medulla of the adrenals), connective tissue's cells, muscle cells (for example, endocrine cells of the kidney and heart).

Endocrine cells have well developed synthetic apparatus. If cells release protein hormones they have an extensive endoplasmic reticulum and large Golgi complex. Steroid-secreting cells have abundant smooth endoplasmic reticulum, mitochondria with tubular cristae, large numbers of lipid droplets. Usually endocrine cells are characterized by the presence of abundant membrane-limited granules containing the hormonal secretory product. The secretory pole of an endocrine cell is towards the wall of a capillary (or sinusoid).

The components of the endocrine system vary greatly in their organization and include:

1. The discrete endocrine glands – hypophysis, thyroid, parathyroid, adrenal, and pineal; They are large parenchymal organs, covering connective tissue's capsule. A common structural feature of these ductless glands is an exceptionally rich blood supply. Fenestrated or sinusoidal capillaries provide the transport of the released hormones. Endocrine glands are formed by glandular epithelium or nervous tissue.

2. Groups of endocrine cells may be present in organs that have other functions. They include the islets of the pancreas, the follicles and corpora lutea of the ovaries, the placenta.

3. Scattered cells with endocrine function, known as the *diffuse endocrine system.*

They include the interstitial cells of the testes, and some cells in the kidneys and thymus and also the *cells of APUD system.* Recent studies have shown that many cells produce amines that have endocrine functions. Many of these amines also act as neurotransmitters or as neuromodulators. These widely distributed cells have similar metabolism and structure and are grouped together as the neuroendocrine *system* or the *APUD cell system.* Such isolated endocrine cells are present in the epithelial lining of an organs of the digestive, respiratory, urinary, and reproductive systems but they are seen most typically in the gut. *APUD cell system* include also Merkel's cells of the skin, parafollicular cells of the thyroid gland, medulla of the adrenals et al. [1 – 3].

The nervous system and the endocrine system are closely interrelated and may overlap in their function. They are integrated to united neuroendocrine system. The interaction of these systems is coordinated at the hypothalamus, which is one of the major controlling centers for the autonomic nervous system.

Hypothalamus

The hypophysis, or pituitary gland, is a compound endocrine gland suspended from the hypothalamus and located in the sella turcica. The region, surrounding of the floor of the third ventricle forms hypothalamus. A short stalk, the *infundibulum,* attaches the pituitary to the hypothalarnus.

The hypophysis consists of the **pars distalis** or **anterior lobe, posterior lobe**, which is composed of the pars nervosa and the pars intermedia, and a cranial part, **the pars tuberalis,** which surrounds the infundibulum.

The hypophysis is developed from two separate sources: the neural tube and the oral ectoderm. Therefore it may be divided into a glandular portion which has epithelial characteristics and a neural portion. The part that arises **from** ectoderm is known as the **adenohypophysis.** It is derived from an outpocketing (called Rathke's pouch) of the ectoderm of the primitive oral cavity. This diverticulum later becomes cut off from the stomatodaeum. The anterior wall of Rathke's pouch forms large **anterior lobe.** Some cells grow upwards along and form a pars tuberalis. The posterior wall remains thin and forms the pars intermedia, that closely fuse with the pars nervosa. Narrow cavity **of Rathke's** pouch remains between the **anterior lobe** and pars intermedia [4 – 6].

The part of the pituitary that develops from nerve tissue is the **neurohypophysis.** **T**he neurohypophysis arises from an outpocketing of the neuroectoderm of the primitive brain (specifically, the diencephalon). It forms the pars nervosa and the infundibulum.

So, the adenohypophysis is divided into a pars distalis, a pars tuberalis, and a pars intermedia. The neurohypophysis is divided into a pars nervosa and the infundibulum. The infundibulum is composed of the **stem** and **median eminence.**

Additionally, the pars distalis and pars tuberalis are considered to be the anterior lobe of the gland, and the pars nervosa and pars intermedia are called the posterior lobe.

The residual cleft (remain of cavity **of Rathke's** pouch) separates The embryological development of the hypophysis explains the presence of two distinct tissue types.

The anterior lobe constitutes about 75 percent of the hypophysis. It is formed by glandular epithelium and surrounded by a dense connective capsule. The anterior lobe contains cells arranged in cords and clumps, that are separated by numerous sinusoidal fenestrated capillaries. A little connective tissue is present among the cords of cells.

Secretory cells are called adenocytes. Several types of the adenocytes, responsible for the production of different hormones, are present [3].

Using routine staining procedures the adenocytes can be divided into chro*mophil cells* that have brightly staining granules in their cytoplasm; and *chromophobe cells i*n which granules are not prominent. Chromophobes cells make up about 50% of adenocytes. In their cytoplasm. These small cells have long, branching processes. They represent degranulated chromophil cells and stem cells that give rise to new chromophils.

*The chromophils are large cells (*12- 15 mkm). *Its* hormone-containing secretory granules stain strongly. Chromophil cells are further classified as **acidophils** (40%) when their granules stain with acid dyes (like eosin): or **basophils** (10%) when the granules stain with basic dyes (like haematoxylin). The acidophil cells are often called *alpha cells,* and the basophlis are called *beta* celts.

Acidophils predominate at the periphery, whereas chromophobes and basophils show a preference for the more central part of the gland.

The chromophils have a prominent rough endoplasmic reticulum, a large Golgi complex, and numerous membrane-limited granules containing the hormonal secretory product. After appropriate stimulation, the hormone is released by exocytosis and can enter capillary vessels for delivery to the target organs.

Several cell types of the *chromophils* have been identified on the basis of the hormone secreted, staining characteristics and immunocytochemical studies. There are two types of acidophils: (1) somatotropic and (2) lactotropic cells and three types of basophils: (3) gonadotropic (4) thyrotropic cells and (5) adrenocorticofipotropic cells [1 – 4].

The acidophils cells secrete simple proteins. They are smaller cells, containing large granules with protein hormones.

1) The *somatotrops* are the most common type of acidophilic cells. They are small, rounded cells with numerous large round granules and central nuclei.

The somatotropic cells secrete growth hormone (GH); It influences many metabolic processes, but its most marked effect is to stimulate the growth of the epiphyseal cartilages of long bones. This is not a direct action, for somatotropin acts on the liver and kidney to elicit the production of several peptides called somatomedins that act on epiphyseal cartilages). It controls body growth, especially before puberty.

Acromegaly (only growth of the extremities of the body (mandible, nose, fingers, etc) and gigantism are pathology which associated with this hormone.

(2) Mammotropic or lactotropic cells are small and irregular in **shape** except during pregnancy, when they enlarge considerably. Lysosomes are more numerous when secretion is **inhibited.** The lactotropic cells secrete prolactin (LTH), which stimulates activity of the mammary gland and secretion progesterone by the corpus luteum (it's also called luteotropic hormone). Prolactin also stimulates maternal behavior [4 – 6]

The basophils secrete glycoproteins. In the basophils the carbohydrate portion of the hormone molecule is added to the protein moiety both in the endoplasmic reticulum and the Golgi complex. These cells are large, but they have small granules.

(3) The *gonadotrops* are small basophilic cells. They secrete **follicle-stimulating hormone (FSH) and luteinizing hormone (LH),** increase in number at puberty, and demonstrate subtle changes in women during the menstrual cycle; FSH stimulates the growth of ovarian follicles and the secretion of oestrogens in the female. In the male it stimulates spermatogenesis. LH stimulates the maturation of the corpus luteum in the female. In the male LH stimulates the production of androgens. According to some Investigators the two classes of gonadotropic hormones are produced by different cells, but other workers hold that the same cells can produce both the hormones.

(4) The *thyrotrops* are large, irregularly shaped basophilic cells confined to central part of the gland. Their small granules content thyroid-stimulating hormone (TSH, also

called **thyrotropin**). Thyrotropin stimulates the synthesis and liberation of the thyroid hormones.

(5) Adrenocorticotipotropic cells are weakly basophilic (The stain of these cells are intermediate between acidophlls and basophlis), polygonal in **shape,** with round **eccentric** nuclei, a well-developed Golgi complex, and rough endo-plasmic reticulum that tends to be located at the periphery of the cytoplasm. Their granules are the largest. The granules contain a complex molecule *of pro-opiomelonocorticotropin.* This is broken down into adrenocorticotropic hormone (ACTH; Corticotropin), which stimulates production of glucocorticoids by cells of the adrenal cortex.

Other corticotropic hormones that have been identified are lipotropin, melanotropin and endorphin [1].

The hypophysis is one of the most important endocrine glands. It produces several hormones some of which profoundly influence the activities of other endocrine glands. Its own activity is influenced by the hypothalamus.

Hypothalamic secretory neurons, located in the medio-basal zone (preoptic and arcuate nuclei), secrete specific releasing factors for each tropic hormone of the **adenohypophysis. This** factors can stimulate (liberins) or inhibit (statins) secretion of adenohypophysal hormones. The following hypophysiotropic hormones are recognized at present:

- **Somatostatin** inhibits secretion of GH.
- Prolactin-releasing factor (**Prolactostatin**) inhibits prolactin secretion.
- Gonadotropin-releasing hormone (**Gonadoliberin**) stimulates secretion of FSH and LH
- Corticotropin-releasing hormone (**corticoliberin).**

Long axons of medial hypothalamic secretory neurons end at the capillaries of median eminence. The hypophysis is supplied by two sets of vessels: from *superior hypophysea! arteries* and a *inferior hypophyseal arteries.* The inferior hypophyseal arteries supply the pars nervosa. The superior hypophyseal arteries supply blood to the median eminence. Here these arteries break up into a **primary capillary plexus** consisting of fenestrated capillaries. Axons of the neurosecretory neurons, containing the liberins or statins, end here, forming axovasal synapses. The capillaries of the primary plexus rejoin to form the long **portal veins** that traverse the pituitary stalk and ultimately break up into a secondary **capillary plexus** between adenocytes. This **hypophyseal portal system** is of the utmost importance in regulating anterior lobe function.

The venous blood leaving the hypophysis carries the hormones to target cells in various parts of the body [1 – 6].

So, hierarchal system (hypothalamus – adenohypophysis – peripheral endocrine glands) exists. It also includes the system of negative feedback control.

For example, as the thyroid hormone blood level rises the production of TRF is stooped, and therefore production of TSH is too stooped and blood levels the thyroid hormones are reduced.

Note, that a great number of physical and psychologic stimuli that reach the central nervous system are integrated at the level of the hypothalamus, which by means of the hypothalamic hormones modifies the secretion of the peripheral endocrine glands [1 – 3].

Pars Intermedia

This is poorly developed in the human hypophysis. It contains basophilic and chromophobic cells. The most conspicuous feature is the presence of colloid filled vesicles (known as Rathke's cysts). The function of the pars intermedia in the human remains unclear. In amphibians, the basophilic cells produce melanocyte-stimulating hormone (MSH), which causes increased pigmentation of the skin. In the human basophilic cells are most likely adrenocortico-lipotrops.

Pars Tuberalis

The *pars tuberalis* forms a sleeve around the infundibular stem.. It is a highly vascular structure with cords of chromophilic and chromophobic cells. Small follicles are scattered in the pars tuberalis. Most of the cells secrete gonadotropins (FSH and LH) [2].

NEUROHYPOPHYSIS

The neurohypophysis consists of the **pars** nervosa, **infundibulum** and the median eminence. The neurohypophysis consists mainly of unmyelinated axons from hypothalamic neurons. The cell bodies of these of neurosecretory **cells** are located in the paraventricular and supraoptic nuclei of the hypothalamus. Two hormones are associated with neurohypophysis.

Vasopressin is produced mainly in the supraoptlc nucleus, and **oxytocin** in the paraventrlcular nucleus. These hormones (which are bound with a protein called neurophysin) produced in the neuronal perikaryon move along the axons through the infundlbulum into the neural lobe. Here neurosecretory granules are stored at the dilated blind endings of the axons (known as Herring bodies). The released hormones are freed from the neurophysin, transverse the perivascular space, enter the fenestrated capillaries, and are distributed to target organs, tissues, and cells via the systemic circulation.

Owing to the present of axovasal synapses both **pars** nervosa and median eminence are called **neurohemal** organs.

About 25% of the volume of the neurohypophysis consists of a specific type of glial cell called a pituicyte**.** Pituicytes are highly branched cells with processes that partially or completely surround neuroseeretory cell axons. The cytoplasm of these cells may contain lipid droplets and pigment.

Oxytocin stimulates contraction of the smooth muscle of the uteri l during childbirth and contraction of myoepithelial cells that surround the alveoli and ducts of the mammary glands. The neurohormonal reflex triggered by nursing is called the **milk** ejection **reflex.**

Vasopressin promotes the contraction of smooth muscle of blood vessels, raising the blood pressure. The main effect of vasopressin is to increase the reabsorption of water by kidney tubules. It helps to regulate the osmotic balance and called antidiuretic hormone (ADH). Individuals producing low levels of ADH (diabetes insipidus) excrete large amounts of dilute urine and suffer from extreme thirst.

So, hypophysis and hypothalamus form common *hypothalamohypophyseal system.*

Cells of the adrenal cortex do not store their secretory products in granules; rather, they synthesize and secrete steroid hormones only upon demand. Steroids, being low-molecular-weight, lipid-soluble molecules, can freely diffuse through the plasma membrane and do not require the specialized process of exocytosis for their release [2].

PINEAL GLAND

The pineal gland (or pineal body, or *epiphysis cerebri*} is a small neuroendocrine organ present in relation to the posterior wall of the third ventricle of the diencephalic. The pia mater covers its surface and forms a capsule from which connective tissue septa containing fenestrated blood vessels, penetrate into the gland dividing it into poorly denned lobules.

The pineal gland consists of two basic cell types: *pinealocytes,* which are in the majority and are arranged in clumps or cords within the lobules, and *glial cells (interstitial cells*).

Each *pinealocyte* has a polyhedral body containing a large irregular nucleus. The ceil body gives off long processes with expanded *terminal buds* that end in relation to the wall of capillaries. Dense-cored, membrane-bound granules and large numbers of microtubules arranged in parallel bundles within the cytoplasmic processes. The cell bodies of pinealocytes contain both granular and agranular endoplasmic reticulum, a well developed Golgi complex, and many mitochondria, lipid droplets.

An organelle of unusual structure made up of groups of microfibrils may be present *(canaliculate lamellar bodies).*

Dark and light pinealocytes are present.

Small numbers of glial cells are surrounding the clumps or cords of pinealocytes. The glial cells that resemble astrocytes in structure, have small, often elongate nuclei that stain more intensely than those of the pinealocytes [3].

The human pineal gland contains calcified concretions, known as *corpora arenacea,* or *brain sand,* which form in the organic matrix of the substance secreted by the pinealocytes. These concretions, consisting of calcium phosphates and carbonates, have an irregular shape. It has been postulated that polypeptide hormones of the *pinealocytes* first exist in the form of complexes with a carrier protein called *neuroepiphysin.* When hormones are released from the complex the carrier protein combines with calcium ions and is deposited as brain sand.

The pinealocytes produce a number of hormones. These hormones have an important regulating influence (chiefly inhibitory) on many other endocrine organs: the adenohypophysis, the neurohypophysis, the thyroid, the parathyroids, the adrenal cortex and medulla, the gonads, and the pancreatic islets.

The best-known hormone of the pineal gland is the amino acid *melatonin* (so called because it causes changes in skin color in amphibians). Serotonin is a precursor of melatonin. M*elatonin* inhibits the steroidogenic activity of the gonads. Clinically, it is important to note that diseases of the pineal, which are rare, are often associated with abnormal gonadal function. Children with tumors that destroy the pineal parenchyma demonstrate precocious (or early onset of) puberty.

The synthesis of melatonin and the gland's activity is influenced by changes in the external lighting, that is, by periods of light and darkness. The pineal glands are most active in darkness. Therefore, the pineal gland may act as a kind of biological clock which may produce circadian rhythms. The pineal gland, through the secretion of melatonin, influences the gonads in response to light, modulating their daily physiological activity

It has been suggested that the suprachiasmatic nucleus of the hypothalamus plays an important role in the cyclic activity of the pineal gland. This nucleus receives fibres from the retina. Light entering the eye stimulates neurons to transmit impulses to the pineal gland that inhibit the secretion of melatonin [1 – 3].

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