Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

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METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Endocrine disorders and diseases”

Duration: 3 hours

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EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To study the definition, classification, etiology, pathogenesis, morphology, clinical manifestations, complications, and outcomes of endocrine disorders and diseases. To analyze pathology of the pituitary gland: adenomas (prolactinoma, somatotroph adenoma – acromegaly/gigantism, corticotroph adenoma – Cushing disease, thyrotroph adenoma, gonadotroph adenoma), panhypopituitarism (Sheehan syndrome), diabetes insipidus (central and nephrogenic). To examine thyroid pathology: goiter (diffuse nontoxic, multinodular, toxic – Graves disease), thyroiditis (Hashimoto – autoimmune, subacute – De Quervain, Riedel), benign and malignant neoplasms (follicular adenoma, papillary carcinoma – most common, follicular carcinoma, medullary carcinoma, anaplastic carcinoma). To analyze parathyroid pathology: primary hyperparathyroidism (adenoma, hyperplasia, carcinoma) and hypoparathyroidism. To examine adrenal gland pathology: adrenal cortical hyperfunction (Cushing syndrome – adenoma/carcinoma/hyperplasia, Conn syndrome – aldosteronoma, adrenogenital syndrome), adrenal cortical insufficiency (Addison disease – autoimmune, tuberculosis, metastases), pheochromocytoma (medullary tumor – rule of 10s). To discuss pancreatic endocrine pathology: diabetes mellitus type 1 (autoimmune destruction of beta cells, insulitis, amyloid deposition in islets) and type 2 (insulin resistance, islet amyloid polypeptide, beta-cell dysfunction). To describe the complications of diabetes: microvascular (diabetic nephropathy – Kimmelstiel-Wilson nodules, retinopathy, neuropathy) and macrovascular (atherosclerosis, coronary artery disease, stroke, peripheral vascular disease). To examine the morphology of endocrine neoplasms and the MEN syndromes (multiple endocrine neoplasia types 1, 2A, 2B).

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

***Know*:**

- The morphological features of common pituitary, thyroid, parathyroid, and adrenal disorders;
- The classification and morphology of thyroid neoplasms (papillary, follicular, medullary, anaplastic carcinoma);
- The pathology of diabetes mellitus type 1 and type 2 and their complications;
- The morphological changes in diabetic nephropathy (Kimmelstiel-Wilson nodules);
- The MEN syndromes and associated tumors.

Be able to:

- Identify histological features of papillary thyroid carcinoma (orphan Annie nuclei, psammoma bodies, nuclear grooves);
- Recognize islet pathology in diabetes mellitus (insulitis, amyloid deposition);
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body.

***Master*:**

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Endocrine disorders and diseases affect millions of people worldwide and have significant impacts on metabolism, growth, development, and overall health. Diabetes mellitus is a global epidemic, leading to devastating complications including renal failure, blindness, neuropathy, and cardiovascular disease. Thyroid diseases (nodules, goiter, cancer, thyroiditis) are extremely common in clinical practice. Understanding the morphological basis of endocrine disorders is essential for endocrinologists, internists, surgeons, pathologists, and primary care physicians for accurate diagnosis, treatment, and prevention of complications.

QUESTIONS

1. Growth hormone pathology: acromegaly, nanism. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.
2. Adrenogenital syndrome. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.
3. Waterhouse-Friderichsen syndrome (WFS). Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.
4. Addison’s disease. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.

5. Cushing’s syndrome. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.

6. Thyroid pathology. Goiter. Thyroiditis. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations.

7. Diabetes mellitus. Definition. Etiology. Pathogenesis. Morphology. Clinical manifestations. Causes of death of patients with diabetes mellitus.

COURSE OF THE SESSION

The endocrine system is a complex network of glands and organs responsible for **producing and regulating hormones**, which are chemical messengers that control various physiological processes within the body. The central nervous system (CNS), comprised of the brain and spinal cord, plays a crucial role in regulating the endocrine system through a process known as **neuroendocrine regulation**. This intricate mechanism involves the release of specific hormones from the **hypothalamus** and **pituitary gland**, which act on target glands to stimulate or inhibit the production of hormones, thereby maintaining homeostasis.

One of the key players in the neuroendocrine regulation of the endocrine system is the hypothalamus, a small region of the brain located just below the thalamus. The **hypothalamus** serves as the primary link between the nervous system and the endocrine system, **secreting several releasing and inhibiting hormones** that control the function of the pituitary gland.

Thyrotropin-releasing hormone (TRH) is a hormone produced by the hypothalamus that stimulates the release of **thyroid-stimulating hormone** (TSH) from the anterior pituitary gland. TSH, in turn, acts on the thyroid gland to stimulate the production and release of **thyroid hormones**, which regulate metabolism and energy expenditure.

Prolactin-inhibiting factor (PIF), also known as dopamine, is another hormone produced by the hypothalamus that **inhibits the release of prolactin** (PRL) from the anterior pituitary gland. PRL is primarily involved in lactation and plays a role in reproductive function.

Corticotropin-releasing hormone (CRH) is secreted by the hypothalamus in response to stress or low blood cortisol levels. CRH stimulates the release of **adrenocorticotropic hormone** (ACTH) from the anterior pituitary gland, which, in turn, stimulates the adrenal glands to produce cortisol, a stress hormone involved in the body's response to stress and regulation of metabolism.

Growth hormone-releasing hormone (GHRH) is produced by the hypothalamus to stimulate the release of growth hormone, also known as somatotropin, from the anterior pituitary gland. Growth hormone plays a crucial role in growth, development, and metabolism.

Gonadotropin-releasing hormone (GnRH) is secreted by the hypothalamus to regulate the release of gonadotropins — **follicle-stimulating hormone** (FSH) and **luteinizing hormone** (LH) — from the anterior pituitary gland. FSH and LH are essential for the development and function of the gonads (ovaries and testes) and are involved in the regulation of reproductive processes such as ovulation, sperm production, and sex hormone production.

Growth hormone (GH) pathology encompasses a spectrum of disorders characterized by abnormal secretion or action of growth hormone, leading to disturbances in growth and development. This pathology can manifest in various

forms, including **growth hormone deficiency** (GHD) and growth hormone excess, commonly known as **acromegaly** or **gigantism**.

Growth Hormone Deficiency (GHD) refers to a condition where there is **insufficient secretion of growth hormone** from the anterior pituitary gland. This results in impaired growth and development, particularly during childhood.

Acromegaly is a disorder caused by **excess secretion of growth hormone**, usually due to a pituitary adenoma. It leads to abnormal growth of bones and soft tissues, particularly in the extremities and face.

Growth Hormone Deficiency (GHD) refers to a condition where there is **insufficient secretion of growth hormone** from the anterior pituitary gland. This results in impaired growth and development, particularly during childhood.

GHD can be **congenital** or **acquired**. Congenital GHD may result from **genetic mutations** affecting the synthesis or secretion of growth hormone, while acquired GHD can occur due to **damage to the hypothalamus** or pituitary gland, radiation therapy, or certain medical conditions.

The pathogenesis of GHD involves dysfunction at various levels of the hypothalamic-pituitary axis. **Genetic mutations affecting genes encoding growth hormone** or its receptors can disrupt synthesis, secretion, or signaling pathways. Acquired GHD may result from damage to the hypothalamus or pituitary gland, leading to **impaired stimulation of growth hormone secretion**.

Morphological changes associated with GHD are often subtle and may include **decreased muscle mass**, **delayed skeletal maturation**, and **proportional short stature**.

Radiographic imaging may reveal **delayed bone age** and reduced growth velocity.

Clinical manifestations of GHD vary depending on the age of onset and severity of deficiency. In children, GHD presents as short stature, delayed growth milestones, and decreased growth velocity. Adults with GHD may experience reduced muscle mass, increased adiposity, fatigue, and decreased bone mineral density.

Acromegaly is a disorder caused by **excess secretion of growth hormone**, usually due to a pituitary adenoma. It leads to abnormal growth of bones and soft tissues, particularly in the extremities and face.

Acromegaly typically arises from a **benign pituitary adenoma**, although **ectopic production of growth hormone** from non-pituitary tumors can also occur. Rarely, excess GH secretion may result from hypothalamic disorders or genetic predisposition.

Acromegaly is primarily caused by excessive secretion of growth hormone from a pituitary adenoma. These **adenomas are monoclonal in origin** and arise from somatotroph cells of the anterior pituitary gland. The tumor produces and secretes excess growth hormone, which **stimulates the liver to produce insulin-like growth factor 1** (IGF-1), mediating the clinical manifestations of acromegaly.

In acromegaly, the excess secretion of growth hormone leads to characteristic morphological changes, including **soft tissue swelling**, **coarse facial features**, **enlarged hands and feet** (acral enlargement), and **prognathism**. Skeletal changes may manifest as thickened bones and joint deformities. Pituitary imaging typically shows a pituitary adenoma.

Acromegaly presents with gradual onset and progressive enlargement of soft tissues and bones. Common **clinical manifestations** include acral enlargement, coarse facial features (such as frontal bossing, prominent supraorbital ridges, and prognathism), thickened skin, deepening of voice, joint pain, headaches, and visceromegaly. **Complications** of acromegaly include cardiovascular disease, hypertension, diabetes mellitus, and neoplasms.

The syndrome often arises from structural or functional **damage to the hypothalamus**, commonly due to tumors, trauma, infections, or vascular lesions affecting this region of the brain. Tumors of the hypothalamus or nearby structures, such as craniopharyngiomas or gliomas, are frequent causes. Additionally, congenital malformations or genetic disorders affecting hypothalamic development can contribute to the development of Fröhlich's syndrome.

The pathogenesis of Fröhlich's syndrome involves **disruption of hypothalamic regulation of appetite**, **metabolism**, and **reproductive function**. Damage to the hypothalamus can impair the secretion or action of various hormones, including growth hormone-releasing hormone (GHRH), leading to abnormalities in growth, metabolism, and sexual maturation. Dysfunction of the hypothalamic-pituitary-gonadal axis results in hypogonadism, (reduced production of sex hormones and impaired reproductive function).

Clinical manifestations of Fröhlich's syndrome

1) **Obesity**: Patients with Fröhlich's syndrome often present with early-onset and severe obesity, which may be disproportionate and resistant to conventional weight loss interventions. This obesity is primarily central in distribution, with an increased accumulation of adipose tissue around the trunk and face (truncal obesity).

2) **Hypogonadism**: Hypogonadism manifests as delayed or incomplete sexual maturation, with underdeveloped secondary sexual characteristics and impaired fertility. In males, this may include small testes, reduced muscle mass, and diminished libido, while in females, it may present as absent or irregular menstruation and infertility.

3) **Developmental Abnormalities**: Children with Fröhlich's syndrome may exhibit developmental delays, intellectual impairment, or behavioral disturbances due to the underlying hypothalamic dysfunction.

4) Other Endocrine Dysfunction: In addition to obesity and hypogonadism, patients with Fröhlich's syndrome may experience other endocrine abnormalities, such as **growth hormone deficiency**, **thyroid dysfunction**, or **adrenal insufficiency**, depending on the extent of hypothalamic involvement.

Waterhouse-Friderichsen syndrome (WFS) is a rare but **life-threatening condition** characterized by **acute adrenal insufficiency** due to bilateral adrenal

hemorrhage, often associated with severe bacterial infection, most commonly meningococcal septicemia.

The primary etiology of Waterhouse-Friderichsen syndrome is **severe bacterial infection**, most commonly due to Neisseria meningitidis (meningococcus). Other infectious agents implicated in WFS include Streptococcus pneumoniae, Haemophilus influenzae, and other gram-negative bacteria. The main mechanisms leading to adrenal hemorrhage are **endothelial damage** and **coagulopathy** induced by bacterial endotoxins.

The pathogenesis of Waterhouse-Friderichsen syndrome involves a complex interplay of bacterial virulence factors, host immune response, and coagulation abnormalities. In meningococcal septicemia, bacterial endotoxins trigger a **systemic inflammatory response**, leading to endothelial damage, disseminated intravascular coagulation (**DIC**), and **microvascular thrombosis**. This endothelial damage, coupled with DIC-induced coagulopathy, predisposes to hemorrhage within the adrenal glands, resulting in acute adrenal insufficiency.

On gross examination, adrenal glands affected by Waterhouse-Friderichsen syndrome typically exhibit **bilateral hemorrhage**, leading to **enlargement and discoloration of the glands**. Microscopically, there is evidence of adrenal hemorrhage with extravasation of blood into the adrenal cortex and medulla. Associated findings may include acute **inflammation**, **necrosis of adrenal cells**, and thrombosis of adrenal vasculature.

Clinical manifestations of WFS are acute and often rapidly progressive. WFS carries a **high mortality rate** if not promptly recognized and treated with aggressive resuscitation:

1) **Hypotension and Shock**: Adrenal insufficiency resulting from bilateral adrenal hemorrhage leads to impaired synthesis and release of cortisol and aldosterone, causing hypotension, shock, and cardiovascular collapse.

2) **Fever**: Patients typically present with high fever due to the underlying severe bacterial infection, such as meningococcal septicemia.

3) **Hypoglycemia**: Adrenal insufficiency can lead to decreased glucose production and impaired glucose utilization, resulting in hypoglycemia.

4) **Nausea, Vomiting, and Abdominal Pain**: Gastrointestinal symptoms may occur secondary to adrenal insufficiency and the systemic effects of severe infection.

5) Multiorgan Dysfunction: Severe bacterial sepsis can lead to **multiorgan dysfunction syndrome** (MODS), including acute respiratory distress syndrome (ARDS), acute kidney injury, hepatic dysfunction, and disseminated intravascular coagulation (DIC).

Addison's disease, also known as **primary adrenal insufficiency** or adrenal insufficiency, is a rare but potentially life-threatening condition characterized by **insufficient production of adrenal hormones**, particularly cortisol and aldosterone, due to damage or dysfunction of the adrenal glands.

The primary etiology of Addison's disease is **autoimmune adrenalitis**, accounting for approximately 70-90% of cases in developed countries. Autoimmune adrenalitis involves the body's immune system mistakenly attacking and destroying

the adrenal cortex, leading to progressive loss of adrenal function. Other less common causes of Addison's disease include **infectious diseases** such as tuberculosis, fungal infections, adrenal tumors, adrenal gland metastasis, and certain genetic disorders affecting adrenal steroidogenesis.

The pathogenesis of autoimmune adrenalitis involves a complex interplay of **genetic predisposition**, **environmental triggers**, and **immune dysregulation**. In susceptible individuals, genetic factors predispose to the development of autoantibodies targeting components of the adrenal cortex, particularly enzymes involved in steroid biosynthesis, such as 21-hydroxylase. Environmental triggers, such as infections or stress, may initiate or exacerbate autoimmune destruction of the adrenal glands.

On gross examination, the adrenal glands in Addison's disease may appear normal or atrophic, depending on the extent of adrenal damage and duration of the disease. Microscopically, autoimmune adrenalitis is characterized by **lymphocytic infiltration and destruction of the adrenal cortex**, predominantly affecting the zona fasciculata and zona reticularis. Histopathological findings may include **adrenal cortical atrophy**, **fibrosis**, and loss of functional adrenal tissue.

Clinical manifestations of Addison's disease

1) **Chronic Fatigue and Weakness**: Patients often experience persistent fatigue, weakness, and lethargy due to inadequate cortisol production and impaired energy metabolism.

2) **Hyperpigmentation**: Hyperpigmentation of the skin and mucous membranes, particularly in sun-exposed areas and skin creases, is a classic feature of Addison's disease, resulting from elevated levels of ACTH stimulating melanocyte production.

3) **Orthostatic Hypotension**: Decreased aldosterone production leads to sodium loss and volume depletion, resulting in orthostatic hypotension, dizziness, and syncope upon standing.

4) **Hyponatremia and Hyperkalemia**: Aldosterone deficiency impairs sodium reabsorption and potassium excretion in the kidneys, leading to hyponatremia, hyperkalemia, and metabolic acidosis.

5) **Hypoglycemia**: Inadequate cortisol secretion impairs gluconeogenesis and glycogenolysis, leading to hypoglycemia, particularly during periods of fasting or stress.

6) **Gastrointestinal Symptoms**: Patients may experience nausea, vomiting, anorexia, weight loss, and abdominal pain due to gastrointestinal disturbances and adrenal insufficiency.

7) **Adrenal Crisis**: Acute adrenal crisis is a life-threatening complication of Addison's disease characterized by severe hypotension, shock, electrolyte abnormalities, hypoglycemia, and altered mental status, often precipitated by infection, trauma, surgery, or stress.

Cushing's syndrome is a collection of signs and symptoms resulting from chronic exposure to **excessive levels of cortisol**.

Cushing's syndrome can be classified into two main categories based on the source of excess cortisol:

1) **Endogenous Cushing's Syndrome**: This form of the syndrome results from excessive production of cortisol within the body. Common causes include adrenal adenomas, adrenal carcinomas, bilateral adrenal hyperplasia, and ACTH-secreting pituitary adenomas (Cushing's disease). Rarely, ectopic ACTH-producing tumors, such as small cell lung cancer, can also cause endogenous Cushing's syndrome.

2) **Exogenous Cushing's Syndrome**: This type of Cushing's syndrome occurs due to prolonged administration of exogenous glucocorticoid medications, such as prednisone, dexamethasone, or cortisone, for the treatment of various medical conditions, such as asthma, rheumatoid arthritis, or inflammatory bowel disease.

The pathogenesis of Cushing's syndrome involves **dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis**, leading to excessive production of cortisol. In endogenous Cushing's syndrome, overproduction of cortisol may result from primary adrenal pathology (adrenal tumors or hyperplasia) or excessive stimulation of the adrenal glands by ACTH-secreting pituitary adenomas or ectopic ACTH-producing tumors.

The morphological changes associated with Cushing's syndrome depend on the underlying etiology. **Adrenal tumors**, including adenomas and carcinomas, may exhibit gross enlargement and nodularity on imaging studies. **Pituitary adenomas** causing Cushing's disease typically involve enlargement of the pituitary gland, often with a microadenoma or macroadenoma identified on MRI. Histopathological examination of adrenal tumors may reveal **architectural distortion**, **cellular atypia**, and **increased mitotic activity** in cases of **adrenal carcinoma**.

Clinical manifestations of Cushing's syndrome

1) **Central Obesity**: Excess cortisol promotes fat deposition, particularly in the central (truncal) regions of the body, leading to characteristic "moon face" and "buffalo hump" appearance.

2) **Muscle Weakness and Wasting**: Cortisol-induced protein catabolism results in muscle weakness, wasting, and thinning of the extremities.

3) **Skin Changes**: Patients may develop thinning of the skin, easy bruising, striae (purple or red stretch marks), acne, and hirsutism (excessive hair growth), particularly in women.

4) **Metabolic Disturbances**: Hypercortisolism leads to insulin resistance, impaired glucose tolerance, and hyperglycemia, predisposing to diabetes mellitus.

5) **Hypertension**: Excess cortisol promotes sodium retention and potassium excretion, leading to hypertension and electrolyte imbalances.

6) **Osteoporosis**: Chronic hypercortisolism results in increased bone resorption and decreased bone formation, leading to osteoporosis and an increased risk of fractures.

7) **Psychiatric Symptoms**: Patients may experience mood disturbances, including depression, anxiety, irritability, and cognitive impairment.

8) **Menstrual Irregularities**: In women, menstrual irregularities, amenorrhea, and infertility may occur due to cortisol-induced suppression of gonadotropin-releasing hormone (GnRH) and gonadotropin secretion.

9) **Immunosuppression**: Excessive cortisol suppresses immune function, increasing susceptibility to infections and impairing wound healing.

10) **Adrenal Crisis**: Acute adrenal crisis can occur in patients with Cushing's syndrome during periods of stress or following abrupt cessation of exogenous glucocorticoid therapy, leading to hypotension, shock, electrolyte abnormalities, and altered mental status.

Adrenogenital syndrome, also known as congenital adrenal hyperplasia (CAH), refers to a group of genetic disorders characterized by **impaired synthesis of cortisol and aldosterone** by the adrenal glands, leading to **excessive production of androgens**. This results in a spectrum of clinical manifestations affecting the genitalia, growth, and metabolism.

The primary etiology of adrenogenital syndrome is **genetic mutations** affecting enzymes involved in adrenal steroid biosynthesis, particularly **21-hydroxylase deficiency**, which accounts for approximately 95% of cases. Less common forms of adrenogenital syndrome may result from mutations affecting other enzymes, such as **11β-hydroxylase** or **17α-hydroxylase**. These genetic mutations lead to impaired cortisol and aldosterone synthesis and shunting of steroid precursors towards androgen production.

The pathogenesis of adrenogenital syndrome involves disruption of adrenal steroidogenesis due to genetic mutations affecting key enzymes in the steroid biosynthesis pathway. 21-hydroxylase deficiency, the most common form of CAH, leads to decreased conversion of 17-hydroxyprogesterone to 11-deoxycortisol, resulting in **elevated levels of adrenal androgens**, such as **testosterone** and **dehydroepiandrosterone** (DHEA). Excessive androgen production leads to virilization of the external genitalia in affected females and may cause ambiguous genitalia in severe cases.

On gross examination, adrenal glands affected by adrenogenital syndrome may appear **hyperplastic** due to chronic stimulation by adrenocorticotropic hormone (ACTH). Microscopically, histopathological examination may reveal **nodular hyperplasia of the adrenal cortex**, particularly in severe cases of adrenogenital syndrome. Adrenal histology may also show evidence of inflammation, fibrosis, and lipid accumulation.

Clinical manifestations of adrenogenital syndrome

1) **Virilization of External Genitalia**: In females, excessive androgens during fetal development can lead to virilization of the external genitalia, resulting in clitoromegaly, fusion of the labioscrotal folds, and enlargement of the phallus. In severe cases, affected individuals may have ambiguous genitalia, making sex determination challenging at birth.

2) **Accelerated Growth** and **Advanced Bone Age**: Excessive androgens can lead to accelerated linear growth and advanced bone age in affected children, resulting in tall stature and premature closure of the epiphyseal growth plates.

3) **Pubertal Precocity**: Androgen excess may result in premature development of secondary sexual characteristics, such as pubic hair growth, acne, and voice deepening, in both males and females.

4) **Menstrual Irregularities**: In adolescent and adult females, irregular menstrual cycles, oligomenorrhea, or amenorrhea may occur due to androgen-mediated suppression of gonadotropin secretion and ovarian dysfunction.

5) **Infertility**: Androgen excess and ovarian dysfunction can lead to infertility in affected females due to anovulation or inadequate follicular development.

6) **Salt-Wasting Crisis**: In severe cases of 21-hydroxylase deficiency, impaired aldosterone synthesis can lead to salt-wasting crises in neonates, characterized by hyponatremia, hyperkalemia, dehydration, and hypotension, which can be life-threatening if not promptly recognized and treated.

7) **Adrenal Insufficiency**: In individuals with severe forms of CAH, adrenal insufficiency may occur due to impaired cortisol synthesis, leading to symptoms such as fatigue, weakness, hypoglycemia, and hypotension, particularly during periods of stress or illness.

A goiter refers to the **abnormal enlargement of the thyroid gland**, resulting in a visible swelling or lump in the neck.

Etiology:

1) **Iodine Deficiency**: In regions where iodine intake is insufficient, the thyroid gland may enlarge in an attempt to compensate for decreased thyroid hormone synthesis, leading to endemic goiter.

2) **Autoimmune Thyroiditis**: Autoimmune thyroid diseases, such as Hashimoto's thyroiditis and Graves' disease, can cause goiter due to chronic inflammation, thyroid cell destruction, and lymphocytic infiltration of the thyroid gland.

3) **Thyroid Nodules**: Benign colloid nodules or adenomas, can lead to goiter formation, particularly when multiple nodules are present or when nodules grow larger in size.

4) **Thyroid Cancer**: Papillary, follicular, and medullary thyroid carcinomas can cause focal or diffuse enlargement of the thyroid gland, resulting in goiter.

5) **Endemic Factors**: Other factors contributing to goiter development include genetic predisposition, hormonal imbalances, medications (e.g., lithium, amiodarone), and environmental factors.

Pathogenesis of goiter

1) **Iodine Deficiency**: Insufficient iodine intake impairs thyroid hormone synthesis, leading to decreased feedback inhibition of thyroid-stimulating hormone (TSH) secretion by the anterior pituitary gland. Elevated TSH levels stimulate thyroid follicular cell proliferation and hypertrophy, resulting in goiter formation.

2) **Autoimmune Thyroiditis**: In autoimmune thyroid diseases, such as Hashimoto's thyroiditis, immune-mediated destruction of thyroid cells leads to chronic inflammation and fibrosis within the thyroid gland, causing diffuse or nodular enlargement of the thyroid gland.

3) **Thyroid Nodules**: Benign thyroid nodules may arise from various etiologies, including follicular adenomas, colloid nodules, or multinodular goiter. These nodules can compress surrounding thyroid tissue, leading to goiter formation.

4) **Thyroid Cancer**: Malignant tumors of the thyroid gland can cause focal or diffuse enlargement of the thyroid gland, resulting in goiter. Thyroid cancer may present as a solitary thyroid nodule or as diffuse enlargement of the thyroid gland with or without associated lymphadenopathy.

Morphology of goiter

1) **Iodine Deficiency Goiter**: Gross examination may reveal diffuse enlargement of the thyroid gland with a nodular or multinodular appearance. Microscopically, thyroid follicles may exhibit **hypertrophy**, **hyperplasia**, or colloid accumulation.

2) **Autoimmune Thyroiditis**: Hashimoto's thyroiditis typically presents with diffuse enlargement of the thyroid gland, often with a firm consistency. Histopathological examination may show **lymphocytic infiltration**, follicular cell destruction, **fibrosis**, and **formation of lymphoid follicles**.

3) **Thyroid Nodules**: Benign thyroid nodules may appear as discrete, well-circumscribed masses within the thyroid gland on gross examination. Microscopically, nodules may exhibit features of **adenomatous hyperplasia**, colloid accumulation, or **follicular proliferation**.

4) **Thyroid Cancer**: Malignant thyroid tumors may present as solitary nodules or as diffuse enlargement of the thyroid gland with areas of necrosis, hemorrhage, or invasion into surrounding tissues. Histological subtypes of thyroid cancer, such as **papillary, follicular, or medullary carcinoma**, exhibit characteristic architectural and cytological features.

Clinical manifestations of goiter

1) **Visible Neck Swelling**: The most common clinical feature of goiter is a visible or palpable swelling in the neck, often described as a "lump" or "mass" in the thyroid region.

2) **Dysphagia** and **Dyspnea**: Large goiters may compress adjacent structures, such as the esophagus or trachea, leading to symptoms of dysphagia (difficulty swallowing) or dyspnea (difficulty breathing).

3) **Hoarseness**: Compression of the recurrent laryngeal nerve by a large goiter may result in hoarseness or changes in voice quality.

4) **Thyroid Dysfunction**: Depending on the underlying etiology, patients with goiter may present with symptoms of hyperthyroidism (e.g., palpitations, heat intolerance, weight loss) or hypothyroidism (e.g., fatigue, cold intolerance, weight gain).

5) **Pain** or **Discomfort**: Some patients with goiter may experience pain or discomfort in the neck region, particularly if the goiter is associated with inflammation or hemorrhage.

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels (hyperglycemia) due to defects in insulin secretion, insulin action, or both. This condition results from dysfunction of the pancreas, insulin

resistance in target tissues, or a combination of both factors. Diabetes mellitus encompasses several subtypes, including type 1 diabetes, type 2 diabetes, gestational diabetes, and other less common forms.

The etiology of diabetes mellitus varies depending on the subtype:

1) *Type 1 Diabetes*: Type 1 diabetes is primarily caused by **autoimmune destruction of pancreatic beta cells**, leading to **absolute insulin deficiency**. Genetic susceptibility, environmental triggers (such as viral infections), and autoimmune factors contribute to the pathogenesis of type 1 diabetes.

2) *Type 2 Diabetes*: Type 2 diabetes results from a combination of **insulin resistance in peripheral tissues** (such as muscle, liver, and adipose tissue) and **impaired insulin secretion by pancreatic beta cells**. Risk factors for type 2 diabetes include obesity, physical inactivity, genetic predisposition, and aging.

Morphology of diabetes mellitus

1) **Pancreatic Changes**: In type 1 diabetes, histological examination of the pancreas may reveal lymphocytic infiltration, fibrosis, and loss of pancreatic beta cells. In type 2 diabetes, pancreatic changes may include amyloid deposition in pancreatic islets (amyloidosis) and hypertrophy of pancreatic alpha cells.

2) **Diabetic Nephropathy**: Kimmelstiel-Wilson nodules are distinctive and characteristic lesions within the glomeruli. They appear as spherical, eosinophilic nodules and range in size from a few micrometers to several millimeters in diameter.

3) **Microvascular Changes**: Chronic hyperglycemia in diabetes mellitus can lead to microvascular complications, including hyalinosis, endothelial dysfunction, and capillary basement membrane thickening in various organs, particularly the kidneys, eyes, and peripheral nerves.

4) **Macrovascular Changes**: Diabetes mellitus is associated with accelerated atherosclerosis and increased risk of cardiovascular disease, including coronary artery disease, peripheral arterial disease, and cerebrovascular disease. Morphological changes in blood vessels may include atherosclerotic plaques, arterial stenosis, and thrombosis.

Clinical manifestations of diabetes mellitus

1) **Polyuria, Polydipsia, Polyphagia**: Classic symptoms of diabetes mellitus include polyuria (excessive urination), polydipsia (excessive thirst), and polyphagia (excessive hunger) due to hyperglycemia-induced osmotic diuresis, dehydration, and cellular starvation.

2) **Weight Loss**: Despite increased hunger and food intake, patients with diabetes may experience weight loss due to catabolic effects of insulin deficiency or resistance, particularly in type 1 diabetes.

3) **Fatigue and Weakness**: Chronic hyperglycemia and metabolic dysregulation can lead to fatigue, weakness, and malaise in patients with diabetes mellitus.

4) **Visual Changes**: Diabetes mellitus is associated with an increased risk of diabetic retinopathy, leading to visual impairment and blindness if left untreated.

5) **Neuropathy**: Peripheral neuropathy is a common complication of diabetes mellitus, characterized by sensory loss, numbness, tingling, and pain in the extremities.

6) **Nephropathy**: Diabetic nephropathy is a leading cause of chronic kidney disease and end-stage renal disease (ESRD) worldwide, characterized by proteinuria, hypertension, and progressive decline in renal function.

7) **Cardiovascular Disease**: Diabetes mellitus significantly increases the risk of cardiovascular disease, including coronary artery disease, myocardial infarction, stroke, and peripheral arterial disease.

Main Causes of Death in Diabetes

1) **Coma** (Diabetic Ketoacidosis or Hyperosmolar Hyperglycemic State): Acute complications of diabetes mellitus, such as **diabetic ketoacidosis** (DKA) or **hyperosmolar hyperglycemic state** (HHS), can lead to coma and death if not promptly recognized and treated. DKA results from severe insulin deficiency, leading to hyperglycemia, ketosis, metabolic acidosis, and dehydration. HHS is characterized by extreme hyperglycemia, hyperosmolarity, and dehydration.

2) **Kidney Failure** (End-Stage Renal Disease): Diabetic nephropathy is a leading cause of end-stage renal disease (ESRD) worldwide. Progressive decline in renal function in patients with diabetic nephropathy can lead to **uremia**, **electrolyte imbalances**, and complications such as volume overload and **hyperkalemia**, ultimately resulting in death if not managed with renal replacement therapy (dialysis or kidney transplantation).

3) **Gangrene** (Peripheral Vascular Disease): Diabetes mellitus is associated with an increased risk of peripheral arterial disease (PAD), which can lead to impaired blood flow to the lower extremities and lower extremity ischemia. Chronic ischemia and impaired wound healing in patients with diabetes increase the risk of foot ulcers, infections, and gangrene, which can necessitate limb amputation and increase mortality risk due to sepsis or cardiovascular complications.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

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ADDITIONAL LITERATURE

1. Sobotta. Atlas of human anatomy. [V. 1]. General anatomy and musculoskeletal system / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 400 p. : ill., col. ill.

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NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

Access mode: http://patan.by/menyu/administrativnyie-proczeduryi.html - The date fccess: 20.03.2022.

ELECTRONIC DATABASES

1. Physician's consultant. Electronic Medical Library = Consultant of the doctor. Electronic medical library [Electronic resource] / Publishing group "GEOTAR-Media", LLC "IPUZ". – Access mode: http://www.rosmedlib.ru/ . – Access date: 03/15/2022.

2. Springer Link [Electronic resource] / Springer International Publishing AG. – Access mode: https:link.springer.com. – Date of access: 03/15/2022.