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: “Mixed degenerations. Pigments accumulations”

Duration: 3 hours

Approved at the meeting of the Department of Pathological Anatomy
(Minutes No. 1 dated 30.08.2025)

2025

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

Educational Goal:

- To equip students with scientific knowledge regarding mixed degenerations, as well as the necessary skills and abilities for studying the etiopathogenesis and structural-functional features of mixed degenerations. This will be achieved by analyzing the general characteristics of the degenerative process and its classification based on the predominant type of metabolic disorder (protein, fat, carbohydrate), the localization of changes (cellular, extracellular, mixed), and the prevalence of the process (systemic and local). This will foster students' understanding of the initial mechanisms underlying the development of pathological processes.

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 causes, mechanisms, and morphological features of typical general pathological processes;
- The etiology, pathogenesis, and morphology of diseases at different stages of their development (morphogenesis), the structural basis of recovery, complications, outcomes, and long-term consequences of diseases, as well as the causes and mechanisms of dying (thanatogenesis).

Be able to:

- Identify major general pathological processes and diseases using histological specimens under light microscopy;
- 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:

The vital activity of any tissue occurs as a result of continuous metabolism. In some cases, metabolic disorders cause qualitative changes in tissues or organs, whereby the content of natural metabolites increases in the cell and intercellular substance, or substances of a different chemical or physical composition appear. Mixed degenerations are represented by structural changes associated with disorders of complex protein and mineral metabolism, which may manifest in a number of diseases: jaundice, gout, nephrolithiasis and cholelithiasis, disorders of melanin metabolism, and the like. Mastering the materials of this topic is a necessary prerequisite for understanding the patterns of morphological reactions and their clinical manifestations during the development of pathological processes and diseases. This is also essential for the future professional activity of a physician for the clinical evaluation of conclusions made by a pathologist, for the clinical diagnosis and treatment of diseases, as well as for analyzing the sources of diagnostic errors in clinical practice.

During the session, students are invited to study the structural-pathogenetic changes in organs and tissues in mixed degenerations; analyze the morphogenetic aspects of the development of specific types of mixed degenerations.

QUESTIONS

1. Pathology of proteinogenic (tyrosinogenic) pigments (melanin): hyperpigmentation and hypopigmentation.
2. Pathology of hemoprotein-derived (hemoglobinogenic) pigments. Hemosiderosis. Etiology. Pathogenesis. Morphology. Staining. Clinical examples. Outcomes.
3. Hemochromatosis. Etiology. Pathogenesis. Morphology. Staining. Clinical examples. Outcomes.
4. Porphyria. Etiology. Pathogenesis. Morphology. Staining. Clinical examples. Outcomes.
5. Pathology of bilirubin metabolism. Jaundice. Etiology. Pathogenesis. Morphology. Clinical examples.
6. Pathologic calcification. Classification. Localization. Causes. Morphology. Outcomes.
7. Disturbances of nucleoproteins metabolism. Gout. Morphology. Clinical examples. Outcomes.
8. Metabolic disorders of copper. Morphology. Clinical examples. Outcomes.

COURSE OF THE SESSION

Mixed degenerations are pathological processes that affect **both the stroma and parenchyma** of tissues.

This type of degeneration involves disturbances in the metabolism of various biochemical substances, including **nucleoproteins**, **lipoproteins**, **mineral substances**, and **chromoproteins** (pigments).

Pigments are colored substances found in most living organisms, including humans.

They can be classified into two broad categories: **endogenous** and **exogenous**.

Pigments classification

1) **Endogenous Pigments** (Chromoproteins): These pigments are either normal constituents of cells or accumulate under certain conditions.

- **Melanin**: The pigment responsible for skin, hair, and eye color.
- **Ochronosis**: A condition where a pigment called homogentisic acid accumulates in connective tissues, often due to a metabolic disorder.
- **Haemoprotein-Derived Pigments**: Such as hemosiderin, which is derived from hemoglobin breakdown.
- **Lipofuscin**: Known as the "wear-and-tear" pigment, it accumulates in cells as a result of aging and oxidative stress.

2) **Exogenous Pigments**: These pigments are introduced into the body from external sources, typically through inhalation, ingestion, or inoculation.

- **Carbon** (Coal Dust): Inhaled by individuals working in certain industries, leading to conditions like pneumoconiosis.
- **Tattoo Ink**: Introduced into the skin through inoculation.
- **Carotenoids**: Ingested through food, contributing to the color of the skin.

Classification by Structure

1) **Proteinogenic (Tyrosinogenic) Pigments**:

Origin: These pigments are derived from the amino acid tyrosine.

Key Pigment and Function: Melanin. It provides color to the skin, hair, and eyes, and plays a critical role in protecting the skin from ultraviolet (UV) radiation.

Types of Melanin:

- Eumelanin: Brown-black pigment found in high concentrations in individuals with darker skin and hair.
- Pheomelanin: Red-yellow pigment, more prevalent in individuals with lighter skin and red or blonde hair.
- Neuromelanin: Found in the brain, particularly in the substantia nigra, and is involved in neurological functions.

2) **Hemoprotein-Derived (Hemoglobinogenic) Pigments**:

Origin: These pigments are derived from hemoglobin and other related hemoproteins.

Key Pigments:

- Hemosiderin: An iron-storage complex that forms from the breakdown of hemoglobin, typically seen in conditions involving excessive iron accumulation, such as hemosiderosis and chronic hemorrhage.
- Bilirubin: A yellow pigment formed by the breakdown of heme in red blood cells. It is excreted in bile and urine; elevated levels lead to jaundice.
- Bilineurin and Hematin: Pigments related to the breakdown and conversion of hemoglobin, seen in various stages of bruising and in certain pathological conditions.

3) **Lipidogenic Pigments**:

Origin: These pigments are associated with the metabolism of lipids and the aging process.

Key Pigments:

- Lipofuscin: A yellow-brown "wear-and-tear" pigment that accumulates in various tissues, particularly in aging cells, and is considered a marker of oxidative stress.

Ceroid: Similar to lipofuscin but accumulates under pathological conditions, such as in certain storage diseases and chronic inflammatory states.

Generalized hyperpigmentation

Generalized hyperpigmentation refers to an increase in skin pigmentation that affects large areas of the body. It is associated with various conditions and can be a key clinical indicator of underlying systemic diseases.

a) **Addison's Disease:**

Overview: Known as primary adrenal insufficiency, is characterized by the inadequate production of cortisol and aldosterone by the adrenal glands.

Hyperpigmentation:

- *Mechanism*: The hyperpigmentation occurs due to elevated levels of adrenocorticotropic hormone (ACTH), which stimulates melanocytes to produce more melanin.
- *Distribution*: The pigmentation is most pronounced in areas exposed to light (e.g., face, hands), as well as in regions of friction (e.g., elbows, knees), and on the buccal mucosa. It may also appear in scars, skin folds, and pressure points.

b) **Chloasma (Melasma):**

Overview: Chloasma, also known as melasma, is a condition characterized by dark, hyperpigmented patches on the skin.

Associated with Pregnancy:

- *Influence of Hormones:* During pregnancy, elevated levels of estrogen and progesterone stimulate melanocyte activity, leading to increased melanin production.
- *Distribution:* The hyperpigmentation commonly affects the face, particularly the forehead, cheeks, and upper lip, as well as the nipples and genitalia.

Other Causes:

- *Oral Contraceptives:* Women taking oral contraceptives may experience similar hyperpigmentation due to hormonal influences that mimic pregnancy.

c) **Chronic Arsenical Poisoning:**

Overview: Chronic exposure to arsenic, often through contaminated water or occupational exposure, can lead to a range of systemic effects, including skin changes.

Hyperpigmentation:

- *Characteristic Appearance:* One of the hallmark signs is "rain-drop" pigmentation, where the skin develops small, dark, irregularly distributed spots resembling raindrops.
- *Distribution:* This pigmentation is often seen on the trunk and extremities and can be accompanied by other skin changes, such as keratoses.

Focal hyperpigmentation

Focal hyperpigmentation refers to localized areas of increased pigmentation, often associated with specific genetic conditions, syndromes, or pathological changes. These pigmentary changes can serve as important clinical markers for underlying diseases.

a) **Café-au-lait Spots:**

Description: Café-au-lait spots are light brown to dark brown pigmented patches that are usually oval-shaped and can vary in size.

Associated Conditions:

- *Neurofibromatosis:* Multiple café-au-lait spots are a diagnostic feature of neurofibromatosis type 1 (NF1), a genetic disorder characterized by the growth of benign nerve sheath tumors.
- *Albright's Syndrome:* Also known as McCune-Albright syndrome, this condition includes café-au-lait spots, often with irregular borders (resembling the "coast of Maine") and is associated with fibrous dysplasia of the bone and endocrine abnormalities.

b) **Peutz-Jeghers' Syndrome:**

Description: Peutz-Jeghers syndrome is a genetic disorder characterized by the development of benign polyps in the gastrointestinal tract and distinctive hyperpigmented macules.

Focal Pigmentation: The pigmentation typically appears as dark blue or brown spots around the mouth (perioral region), on the lips, and sometimes on the hands and feet.

c) **Melanosis Coli:**

Description: Melanosis coli is a condition characterized by the dark pigmentation of the colonic mucosa.

Cause: It is often associated with the prolonged use of anthraquinone-containing laxatives, such as senna or cascara.

Clinical Significance: While generally benign and reversible, the presence of melanosis coli can be an indicator of chronic laxative use.

d) **Melanotic Tumors:**

- *Pigmented Nevus:* Commonly known as moles, these benign tumors are composed of melanocytes and are typically brown or black in color due to increased melanogenesis.

- *Melanoma:* A highly aggressive skin cancer arising from melanocytes, melanoma is associated with increased melanogenesis. It often presents as a dark, irregularly shaped lesion that can spread rapidly.

Clinical Note: Early detection of melanoma through changes in size, shape, or color of pigmented lesions is critical for successful treatment.

e) **Lentigo:**

Description: Lentigo refers to small, well-defined, hyperpigmented macules on the skin, often in sun-exposed areas.

- *Lentigo Simplex:* A benign form often seen in childhood, not related to sun exposure.
- *Solar Lentigo:* Commonly known as "age spots" or "liver spots," these occur due to chronic sun exposure and are more common in older adults.

Generalized hypopigmentation

Albinism is a genetic condition characterized by an extreme degree of **generalized hypopigmentation**. It results from a genetic defect that impairs the activity of tyrosinase, an enzyme crucial for melanin production in melanocytes.

The defect in tyrosinase activity prevents the synthesis of melanin, the pigment responsible for coloration in skin, hair, and eyes.

Individuals with albinism typically have very light-colored hair, often appearing blonde or white. The skin is very pale and lacks the usual pigmentation. Vision problems are common, including poor vision and severe photophobia (sensitivity to light), due to the lack of melanin in the retina.

People with albinism are highly sensitive to sunlight due to the absence of melanin, which normally provides some level of protection against UV radiation. Chronic exposure to sunlight can lead to an increased risk of developing precancerous lesions and skin cancers, including squamous cell carcinoma and basal cell carcinoma.

Localized hypopigmentation

1) **Vitiligo** is a common condition characterized by localized loss of skin pigmentation. Vitiligo involves the destruction of melanocytes in the affected areas, leading to well-defined, white patches on the skin. Common sites include the hands, face, and around body orifices.

2) **Acquired Focal Hypopigmentation** refers to the loss of pigment in specific areas of the skin due to various external or internal factors.

- Leprosy
- Healing of Wounds
- Discoid Lupus Erythematosus (DLE)
- Radiation Dermatitis

Hemoprotein-derived pigments

Hemoproteins are crucial endogenous pigments derived from hemoglobin, cytochromes, and their breakdown products. Understanding disorders related to hemoproteins requires a fundamental knowledge of normal iron metabolism and transport. Disruptions in iron metabolism and transport lead to the accumulation of

various hemoprotein-derived pigments, including hemosiderin, hematin, bilirubin, and porphyrins.

Normal Hemoprotein-Derived Pigments:

1) **Ferritin:** Ferritin is an iron-storage complex composed of iron and apoferritin. It can be visualized using electron microscopy and is primarily located in the liver, spleen, bone marrow, and lymph nodes. Ferritin exists in two forms:

- **Inactive Ferritin:** This form of ferritin stores iron and is not actively involved in physiological processes.
- **Active Ferritin:** Formed under conditions of low oxygen, it has vasoparalytic and hypotensive actions and acts as an antagonist to adrenaline.

2) **Hemosiderin:** Hemosiderin is a pigment formed from the aggregation of ferritin and appears golden-yellow to brown under light microscopy. It accumulates in tissues where there is increased breakdown of red blood cells or iron overload. Hemosiderin deposition can result from:

- **Primary Causes:** Hereditary hemochromatosis.
- **Secondary Causes:** Conditions such as thalassemia, sideroblastic anemia, alcoholic cirrhosis, and multiple blood transfusions.

Pathological Hemoprotein-Derived Pigments:

1) **Hematoidin:** This pigment is derived from the breakdown of hemoglobin. It is typically found in areas of hemorrhage.

2) **Hematin:** Hematin is a derivative of hemoglobin, resulting from the oxidation of heme.

3) **Porphyrins:** These are pigments involved in the synthesis of heme, and their abnormal accumulation can lead to porphyrias, which are disorders characterized by the overproduction of porphyrins and their precursors.

Hemosiderosis is a pathological condition characterized by the excessive accumulation of hemosiderin in tissues. This can occur due to increased breakdown of red blood cells or systemic iron overload, which might be primary (e.g., hereditary hemochromatosis) or secondary to conditions such as thalassemia, sideroblastic anemia, or repeated blood transfusions.

1) **Local Hemosiderosis** refers to the accumulation of hemosiderin in specific tissues or organs following localized hemorrhage. When hemorrhage occurs, red blood cells break down, releasing hemoglobin. This hemoglobin is then phagocytosed by macrophages, where it is degraded and stored as hemosiderin.

- **Tissue Hemorrhage:** In any localized bleeding event, such as trauma or a hematoma, hemosiderin deposits form as a result of the breakdown and storage of hemoglobin by macrophages.
- **Brown Induration of the Lungs:** This condition is associated with chronic pulmonary congestion, often seen in mitral stenosis and left ventricular failure. Repeated small hemorrhages in the lungs lead to the accumulation of hemosiderin in the lung tissue, causing a characteristic brown discoloration.

2) **Generalized Hemosiderosis** involves systemic iron overload, leading to widespread deposition of hemosiderin in organs such as the liver, pancreas, kidneys, and heart.

- **Hemochromatosis:** Genetic disorder causing excessive intestinal iron absorption.
- **Hemolytic Anemia:** Increased red blood cell breakdown releases more iron.
- **Excessive Dietary Iron:** Example: Bantu's disease, where iron pots contribute to high dietary iron intake.
- **Repeated Blood Transfusions or Parenteral Iron Therapy:** Introduces excess iron into the body.

Reticuloendothelial Deposition: Occurs mainly due to repeated blood transfusions or parenteral iron therapy, leading to iron accumulation in macrophages in the liver, spleen, and bone marrow.

Idiopathic hemochromatosis

This is an **autosomal dominant disease** characterized by excessive absorption of iron.

It is associated with triad of pigmentary **liver cirrhosis**, **pancreatic damage** resulting in diabetes mellitus, and **skin pigmentation**.

On the basis of the last two features the disease has come to be termed as 'bronze diabetes'.

Bilirubin and Jaundice

Bilirubin: A non-iron-containing pigment formed from the breakdown of red blood cells in the reticuloendothelial system.

1) **Non-Conjugated Bilirubin:** Released into the blood from the reticuloendothelial system.

2) **Conjugated Bilirubin:** Transported to the liver, where it binds with glucuronic acid and becomes conjugated.

Conjugated bilirubin is released into the small intestine, where it is converted to **stercobilin** (in stool) and **urobilin** (in urine).

Jaundice is an excessive bilirubin in the body leading to a yellowing of skin and sclerae.

1) **Prehepatic (Hemolytic):** Caused by excessive destruction of red blood cells, leading to increased production of bilirubin.

2) **Posthepatic (Obstructive/Mechanical):** Resulting from obstruction in the bile ducts, preventing the outflow of conjugated bilirubin.

3) **Hepatocellular (Hepatic):** Due to liver cell dysfunction, impairing bilirubin conjugation and transport from the liver to the intestine.

Clinical Manifestations: Bilirubin accumulates in hepatocytes, Kupffer cells, and bile sinusoids, leading to yellowing of the skin and sclerae. In infants, elevated unconjugated bilirubin can cause kernicterus, a toxic brain injury.

Hematin

Hematin is a brown-black hemoprotein-derived pigment with ferric iron. Unlike hemosiderin, it does not stain with Prussian blue.

Types of Hematin:

1) **Muriatic Hematin:** Formed in **gastric erosions and ulcers** from hemoglobin interacting with hydrochloric acid in gastric juice.

2) **Hemomelanin:** A brown pigment from **malarial parasites**, found in the liver and spleen after being taken up by monocytes.

3) **Formalin Pigment:** Appears as dark brown grains in tissues fixed with **acid formalin** (pH < 6.0).

Porphyrins

Porphyrins are tetrapyrrole compounds found in nature, each associated with different metals:

1) **Hem:** Contains iron, essential for oxygen transport in blood.

2) **Chlorophyll:** Contains magnesium, crucial for photosynthesis in plants.

3) **Cobalamin (Vitamin B12):** Contains cobalt, important for DNA synthesis and red blood cell formation.

Porphyria results from **genetic deficiencies** in enzymes involved in heme synthesis, leading to an **accumulation of porphyrins** and their precursors.

This condition can be triggered or exacerbated by various factors, including drug intake.

Types of Porphyria

1) **Erythropoietic Porphyria**: Characterized by defective hem synthesis in erythrocytes, leading to:

- **Congenital Erythropoietic Porphyria**: An inherited condition with severe symptoms from birth, including photosensitivity and red urine.
- **Erythropoietic Protoporphyria**: A less severe form that often presents with skin photosensitivity, usually in childhood or early adulthood.

2) **Hepatic Porphyria**: Involves defects in hem synthesis within the liver and includes:

- **Acute Intermittent Porphyria**: Characterized by acute abdominal pain, neurological symptoms, and possible psychiatric manifestations. It can be triggered by drugs, fasting, or alcohol.
- **Variegate Porphyria**: Associated with both skin symptoms (photosensitivity) and acute attacks similar to acute intermittent porphyria.
- **Hereditary Coproporphyria**: Can present with both acute attacks and skin sensitivity, often triggered by drugs and alcohol.
- **Porphyria Cutanea Tarda**: The most common form, primarily affecting the skin, causing blistering and fragility, often exacerbated by alcohol, hepatitis C, and estrogen use.

Lipidogenic pigments

Lipidogenic pigments include **lipofuscin**, **ceroid**, **lipochrome**, and pigments associated with **vitamin E deficiency**.

Lipofuscin is a yellowish-brown intracellular lipid pigment known as the "wear-and-tear" pigment. It accumulates in cells as they age and is often found in

myocardial fibers, hepatocytes, testicular cells, and neurons. Key points about lipofuscin include:

- **Location:** It typically accumulates in the central part of cells around the nuclei.
- **Heart Muscle:** In myocardial fibers, lipofuscin deposition is associated with "brown atrophy," reflecting muscle wasting.
- **Neurons:** In neurons, lipofuscin accumulation is linked to senile dementia, although it can also accumulate rapidly in various cells during wasting diseases unrelated to aging.

Lipofuscin is a result of indigestible material collecting in lysosomes after autophagy, making it an example of residual bodies. It can be stained using fat stains and is unique for being both fluorescent and acid-fast.

Exogenous pigments

Exogenous Pigments are pigments introduced into the body from **external sources**.

They are categorized based on their route of entry:

1) **Inhaled Pigments:**

Common Inhalants: Carbon or coal dust, silica, stone dust, iron or iron oxide, asbestos, and various organic substances.

Occupational Lung Diseases: Inhalation of these substances can lead to pneumoconiosis, including conditions like anthracosis (carbon deposition), coal miners' pneumoconiosis, silicosis, and asbestosis.

Mechanism: Pigment particles are engulfed by alveolar macrophages. Some are expelled via coughing, while others are deposited in lung interstitial tissues and lymph nodes, potentially causing low-grade inflammation, fibrosis, and impaired respiratory function.

2) **Ingested Pigments:**

Argyria: Chronic ingestion of silver compounds leads to a permanent blue-gray discoloration of the skin, mucous membranes, and internal organs.

Lead Poisoning: Chronic exposure to lead is characterized by the appearance of blue lines at the gumline, known as Burton's lines, and may cause systemic issues such as anemia, neuropathy, and abdominal pain.

Carotenemia: Excessive consumption of carotene-rich foods, such as carrots, causes a yellowish-red discoloration of the skin, particularly noticeable on the palms and soles. This condition is typically harmless and reversible.

3) **Injected Pigments (Tattooing):**

Common Pigments: India ink, cinnabar, and carbon.

Process: During tattooing, pigments are introduced into the dermis and taken up by macrophages, remaining permanently in the connective tissue.

Other Examples: Prolonged use of ointments containing mercury, accidental contamination in wounds, and various tattooing inks.

Pathologic calcification

Pathologic calcification involves the deposition of calcium salts in tissues outside the bone or enamel and is categorized into three types:

1) **Dystrophic Calcification:** This occurs in dead or degenerated tissues with normal serum calcium levels and calcium metabolism. It is characterized by calcium deposits in areas of tissue damage.

2) **Metastatic Calcification:** Found in otherwise normal tissues, this type is associated with disrupted calcium metabolism and hypercalcemia. It results from elevated calcium levels in the blood.

3) **Metabolic Calcification:** This is due to imbalances in the buffering systems of blood and tissue fluids, leading to abnormal calcium deposition.

Histologically, these deposits appear as deeply basophilic, irregular, and granular clumps in H&E stained sections, and can be found intracellularly, extracellularly, or both. In some cases, this can lead to heterotopic bone formation or ossification.

Dystrophic calcification

Calcification in **dead tissue**:

1. **Caseous Necrosis:** Seen in tuberculosis, where necrotic tissue becomes calcified.
2. **Liquefaction Necrosis:** Chronic abscesses may undergo calcification.
3. **Fat Necrosis:** Occurs following acute pancreatitis or trauma to fat tissue.
4. **Infarcts:** Necrotic areas of infarcts can sometimes develop dystrophic calcification.
5. **Thrombi:** In veins, thrombi may calcify, forming phleboliths.
6. **Hematomas:** Blood clots near bones may undergo dystrophic calcification.
7. **Dead Parasites:** Such as in hydatid cysts, Schistosoma eggs, and cysticercosis.
8. **Breast Cancer:** Calcification detected in breast tissue via mammography.
9. **Congenital Toxoplasmosis:** Can involve calcification in the CNS.

Calcification in **degenerated tissues**:

1. **Old Scars:** May undergo hyaline degeneration followed by calcification.
2. **Atheromas:** Common in the aorta and coronary arteries, leading to calcification.
3. **Monckeberg's Sclerosis:** Characterized by calcification in the tunica media of arteries.
4. **Tumor Stroma:** Includes calcification in uterine leiomyomas and psammoma bodies in meningiomas.
5. **Old Cysts:** May develop calcification over time.
6. **Calcinosis Cutis:** Localized calcification in the skin.
7. **Senile Degeneration:** Dystrophic calcification can occur in costal cartilages, tracheal or bronchial cartilages, and the pineal gland.

Metastatic calcification

Hypercalcemia plays a crucial role in metastatic calcification, where calcium deposits accumulate in otherwise normal tissues due to elevated calcium levels in the blood. This condition is associated with several underlying pathologies:

1) **Excessive Calcium Mobilization:** Conditions like **hyperparathyroidism** (whether primary, such as parathyroid adenoma, or secondary, such as from chronic renal failure) and **bony destructive lesions** (e.g., multiple myeloma, metastatic carcinoma) cause excessive calcium release from bones into the bloodstream.

2) **Increased Gastrointestinal Absorption:** Disorders such as **hypervitaminosis D** or **milk-alkali syndrome** lead to excessive absorption of calcium from the gastrointestinal tract, contributing to elevated blood calcium levels.

Metabolic calcification

Metabolic calcification, or calciphylaxis, is primarily due to instability in the organism's buffer systems, which prevents proper regulation of calcium salts in the blood and interstitial fluid. This leads to the deposition of calcium salts in tissues.

Disturbances of nucleoproteins metabolism

Disturbances in Nucleoprotein Metabolism are characterized by **excessive uric acid production** and its subsequent deposition in tissues, observed in conditions such as gout, urolithiasis, and uric acid infarction of the kidneys.

Gout is marked by the periodic deposition of sodium urate crystals in joints, leading to painful attacks. Patients exhibit elevated levels of uric acid in the blood (**hyperuricemia**) and urine (**hyperuricuria**). Common sites for urate crystal accumulation include the **synovial fluid**, cartilage of the feet and small joints of the hands, the talocrural and knee joints, tendons, and the cartilage of the auricles. These deposits can lead to tissue necrosis and trigger an inflammatory response with giant cell formation around the deposits.

Gout is primarily associated with congenital metabolic disturbances (primary gout), though dietary factors, particularly high consumption of animal proteins, also play a significant role.

Wilson's disease

Wilson Disease is an inherited disorder characterized by the accumulation of **excessive copper** in the liver, brain, and eyes. Symptoms typically begin between ages 6 and 45, often manifesting in the teenage years.

Liver Disease: In affected children and young adults, liver problems are usually the first signs, presenting as **jaundice**, **fatigue**, **loss of appetite**, and **abdominal swelling**. In older individuals, liver symptoms may be milder or absent.

Neurological and Psychiatric Issues: For those diagnosed in adulthood or young adults, neurological and psychiatric symptoms often precede liver disease. These may include **clumsiness**, **tremors**, **difficulty walking**, **speech problems**, **impaired thinking**, **depression**, **anxiety**, and **mood swings**.

Eye Manifestations: A hallmark feature of Wilson disease is the **Kayser-Fleischer ring** — a green-to-brownish ring around the cornea. Other eye abnormalities may include restricted upward gaze.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

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4. Weir & Abrahams' imaging atlas of human anatomy / ed.: J. D. Spratt [and oth.] ; consultant eds.: J. Weir, P. H. Abrahams. – 5th ed. - [S.l.] : Elsevier, 2017. - xvi, 263 p. : ill.

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.

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