

LECTURE № 2

Metabolic disease. Morphology of pathologic accumulation of endogenous and exogenous pigments. Morphology of mineral metabolism disease

Pathologic accumulation of endogenous pigments

- rather often is represented in metabolic disease of complex proteins – chromoproteins,
- nucleoproteins,
- glucoproteins and
- lipoproteins.
- They are observed in parenchyma, as well as in stroma of tissues and organs.
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Chromoproteins

- or colored proteins, are endogenous pigments:
- hematogenous,
- proteinogenous and
- lipidogenous

Endogenous pigments

- lipofuscin,
- melanin,
- and certain derivatives of hemoglobin
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Iron metabolic disease and metabolic disorder of hematogenous pigments

- Ferritin,
- hemosiderin,
- bilirubin - may be accumulated in organism at physiological conditions

hematogenous pigments at pathologic conditions

- hematoïdin,
- hematin,
- porphyrin
- are pigments which are formed only at pathologic processes.
- They are generated from hemoglobin at destruction (hemolysis) of erythrocytes.

Ferritin

- There are two form of ferritin:
- 1- *anabolic form* is generated from iron absorbed in bowels
- 2- *catabolic form* is generated from hemoglobin at intensive intravascular hemolysis of erythrocytes
- When there is a local or systemic excess of iron, ferritin forms hemosiderin granules

Ferritin

- At conditions of hypoxia ferritin is restored into an active form (*SH-ferritin*) which is an adrenalin antagonist, that's why it acts vasoparesically, i.e. as vasodilator.
- An active ferritin is accumulated at incompatible blood transfusion and collapse of vessels is observed, then a syncope takes place.

Hemosiderin

- Hemosiderin is a hemoglobin-derived, golden-yellow to brown, granular or crystalline pigment in which form iron is stored in cells. It is normally stored in association with a protein, apoferritin, to form ferritin micelles.
- Hemosiderin is generated from hemoglobin only in macrophages (intracellularly). It appears outside the cell only after cell destruction. It looks like small brown seeds; tissue acquires brown coloration at evident *hemosiderosis*.

hemosiderosis.

- One can distinguish
- local and
- extensive process

hemosiderosis.

- Common hemosiderosis is developed at intensive intravascular hemolysis of erythrocytes
- (incompatible blood transfusion,
- hemolytic poisoning).

hemosiderosis.

- the vessels by macrophages, in which hemoglobin turns into hemosiderin.
- An example of Topical hemosiderosis arises at areas of extravasation. Erythrocytes are absorbed outside topical hemosiderosis is pulmonary hemosiderosis which is developed at venous plethora of lungs accompanied by diapedetic extravasations

Hemochromatosis

- It is a peculiar disease closely related to common hemosiderosis.
- There could be primary and secondary one. Primary (hereditary) hemochromatosis is referred to storage diseases, caused by a hereditary defect of small intestine ferments.
- A secondary one is conditioned by acquired enzymatic deficiency of systems providing food iron metabolism.

Bilirubin

- is the normal major pigment found in bile. It is derived from hemoglobin but contains no iron.
- Its normal formation and excretion are vital to health, and jaundice is a common clinical disorder due to excesses of this pigment within cells and tissues.

JAUNDICE

- One can distinguish :
- hemolytic jaundice,
- hepatocellular jaundice and
- obstructive (mechanical) jaundice.

Hemolytic jaundice

- arises at infectious diseases,
- intoxications,
- isoimmune and autoimmune conflicts,
- massive hemorrhage,
- as well as erythrocytopathy and hemoglobinopathy.

Hepatocellular jaundice

- arises at liver diseases of various aetiology, in case defective hepatocytes are not able to capture bilirubin, its conjugation to glucuronic acid and excretion are disturbed.

Obstructive (mechanical) jaundice

- arises at retention of bile outflow from liver.
- Clinical jaundice appears when bilirubin is elevated in blood and is deposited in tissues

Hematoidin

- is a pigment which doesn't contain iron.
- It is accumulated in central areas of hemorrhage in the distance of living tissues.

Hematin

- It is an oxidized form of haem.
- The following pigments are referred to:
- malarial pigment** which is generated from hemoglobin under influence of malarial plasmodia,
- muritic hematin** which is generated at hemoglobin interaction with intestinal juice ferments and hydrochloric acid (it colours erosions and bottom of bleeding ulcer into black and brown),
- formalin pigment** which occurs in histologic specimen fixed by acid formalin.

Hematoporphyrin

- It is a pigment which is a melanin antagonist.
- Its small quantity is contained in blood, urine and stool, it heightens light sensibility of skin. Excess accumulation of this pigment is called **porphyria**.
- It could be caused by congenital defect of porphyrin metabolism or acquired one: lead or barbiturate poisoning, avitaminosis PP, etc.

Metabolic disorder of proteinogenous pigments. Melanin chromogenesis disorder.

- Melanin,
- as well as adrenochrome and
- pigment of enterochromaffin cell granules are referred to proteinogenous (tyrosinogenous) pigments which are tyrosine and tryptophan metabolic derivatives.

Melanin

- It is a brown-black pigment which determines color of skin, hair and eyes.
- Melanin could appear in increase or decrease in skin.
- There could be local or extensive process.
- There could be congenital or acquired pathology.

hypomelanosis

- Extensive hypopigmentation or (albinism) appears as a result of hereditary deficiency of tyrosinase.
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Local hypomelanosis

- (vitiligo, leukoderma) appears as a result of disorder of neuroendocrine control of melanogenesis at
- leprosy,
- diabetes mellitus, hyperparathyroidism,
- Hashimoto's thyroiditis,
- syphilitic skin affection.

Extensive acquired hypermelanosis

- declares itself in excessive accumulation of melanin in skin (melanoderma) and is observed at emaciation, Addison's disease, endocrine disorders, pellagra, scurvy

Extensive congenital hypermelanosis

- declares itself in spotted skin pigmentation, hyperkeratosis and edema – pigmentary xeroderma.

Local congenital hypermelanosis

- is represented by birthmarks or nevus,
- acquired one is observed at pregnancy,
- pituitary adenoma,
- lentigo,
- melanosis coli at constipation.

Lipofuscin

- Lipofuscin is as insoluble pigment, also known as *lipochrome* and "wear-and-tear" or *aging* pigment.
- Lipofuscin is composed of polymers of lipids and phospholipids complexed with protein

Lipofuscin

- Accumulations
- in the liver, heart, brain
- of aging patients or patients with severe malnutrition and cancer cachexia. It is usually accompanied by organ shrinkage (brown atrophy).

Lipochrome

- colours lipocytes,
- adrenal gland cortex,
- blood serum,
- yellow body of ovary into yellow. At pathologic conditions the quantity of lipochromes is increased in fatty tissue at diabetes mellitus, lipidic-vitaminous metabolic disorder, drastic emaciation.

Metabolic disorder of nucleoproteids

- It could be often observed at excessive formation of uric acid and its salts which determines development
- of podagra,
- urolithiasis,
- uric acid infarct.
- At most cases pathology is determined by congenital purine metabolic disorder.

Pathologic Calcification

- Pathologic calcification implies the abnormal deposition of calcium salts, together with smaller amounts
- of iron,
- magnesium,
- and other mineral salts.

Calcium metabolic disorder

- It could declare itself in increase or decrease of calcium concentration in blood (hypocalcemia and hypercalcemia).
- Calcium metabolic disorder results in development of calcifications (calcinosis) – calcium salts deposits in intercellular substance or cells, that's why calcifications are divided into intercellular and extracellular ones.

Calcium metabolic disorder

- According to development mechanism there are
- metastatic,
- dystrophic,
- metabolic calcifications.
- Calcifications also could be
- systemic or
- local.

Metastatic calcifications

- are more often systemic and appear at hypercalcemia caused by the following:
- disorder of endocrine control of calcium metabolism
- hyperproduction of parathyroid hormone,
- calcitonin deficiency),
- excessive vitamin D content;

Metastatic calcifications

- intensive calcium excretion from bones (multiple fractures,
- myelomatosis,
- tumor deposits of bones,
- osteomalacia,
- hyperparathyroidic osteodystrophy);

Metastatic calcifications

- disorder of calcium excretion from organism (colonic involvement,
- chronic dysentery,
- mercuric chloride poisoning,
- kidney diseases: polycystic renal disease, chronic nephritis).

Metastatic calcifications

- Most often there are calcium salts deposits in lungs,
- mucous coat of stomach, kidneys, miocard, walls of arteries.

Dystrophic calcifications

- or petrifications are of local character and result in calcium salts deposits formation in necrosis areas or areas of severe dystrophic changes of tissues (tuberculosis,
- gumma,
- infarction,
- atherosclerosis of vessel wall,
- mitral valve at endocarditis,
- dead parasites).

Stone formation

- is an appearance of solid concrements in caval organs or excretory ducts of glands.
- Stones appear in biliary and urinary tracts,
- excretory ducts of pancreas and salivary glands,
- bronchi and bronchiectasis, as well as in vessels and bowels.

Stone formation

- Stone formation is caused by acquired or hereditary metabolic diseases (metabolic disorders of carbohydrates, fats, nucleoproteins, minerals).
- Among local factors there are
- secretion disorder,
- secretion congestion,
- inflammation.
- Depending on localization and form of organ in which stones appear there are solitary, multiple, round, oval stones, stones with processes, cylindrical, smooth and shaggy stones.
- Cholelithic disease and urolithiasis, pressure bedsores, perforation of organs, fistulas, inflammation of walls of caval organs, jaundice, hydronephrosis are the consequences of stone formation.

Lecture

- Cells and tissues damage and death.
- Necrosis and apoptosis.

Necrosis classification by etiology

- trophoneurotic,
- toxic,
- traumatic,
- vascular,
- allergic

Trophoneurotic necrosis

occurs under central nervous system and peripheral nerves injury

Traumatic necrosis

- occurs in the result of physical,
- electrical,
- chemical,
- thermal trauma direct action.

Toxic necrosis

- occurs in the result of toxins,
- mostly of bacterial origin influence on tissues.

Allergic necrosis

- develops on condition of tissues hypersensitivity (sensibilization).

Vascular (ischemic) necrosis

- occurs in the result of tissues blood supply significant decrease or termination.

Clinicopathologic classification of the necrosis

- coagulation,
- colliquative,
- infarction,
- gangrene,
- decubitus,
- sequester.

Coagulation (dry) necrosis

- is characterized with sphacelus portion deauration and induration.
- It includes cheesy (caseation) necrosis under tuberculosis,
- lues,
- lymphogranulomatosis as well as cereous myonecrosis under abdominal and flea-borne typhus, cholera, fibrinoid necrosis under allergic and lymphocytic diseases, malignant hypertension as well as adiponecrosis which is distributed into ferment, which occurs under pancreatitis and non-ferment caused by trauma.

Colliquative (wet) necrosis

- is characterized with necrotic tissue rarefaction and fusion in the result of hydrolytic processes activation.
- It is developed in tissues rich with moisture,
- for example in cerebrum.

Infarction

- It is necrosis caused by blood supply deficiency.
- Occurs in the result of
- thrombosis,
- embolism,
- long term arteriostenosis and long term, functional overexertion of organ in hypoxia conditions.

Gangrene

- It is death of tissues contacting with air (bowel, extremities).
- Under the influence of air ferric sulphide is formed from hemoglobin, and this ferric sulphide colors necrotic portion in black.
- Dry and wet gangrenes are differentiated.

Decubitus

- is a kind of gangrene.
- It is caused by blood supply and nervous trophism disturbance of subiculum in the place of squeezing (sacral bone, bladebones, calx) under seriously ill patient long term decubitus, for example, cerebrovascular accident.

Sequestrum

- is sphacelus which is not subject for autolysis for a long time.
- As a rule sequestra are observed in bones under osteomyelitis.

Apoptosis

- It is genetically programmed death of unnecessary or defective cells in living body and the following causing these cells destruction in the process of embryogenesis and physiologic involution: cutaneous epithelium, white and red corpuscles extinction.

Apoptosis

- Apoptosis differs from necrosis in:
- inflammation absence,
- only several cells or their groups are involved in the process,
- cell membrane is saved,
- cellular breakdown is done not by activated hydrolytic ferments, but in participation of special calcium-magnesium dependent endonucleases which cut nucleus into numerous fragments,
- formed cells fragments (apoptosis corpuscles) phagocytized by parenchymatous or stromal cells which are situated nearby.

Apoptosis

- Apoptosis morphogenesis develops in several stages:
- chromatin condensation and margination, nucleus becomes fragmented,
- intracellular organelles condensation and cells shrinkage,
- apoptosis corpuscles formation,
- apoptosis corpuscles phagocytosis with parenchymatous cells or macrophages .