Волгоградский государственный медицинский университет

Кафедра патологической анатомии

LECTURE:
Reversible and irreversible injury. Accumulation of lipids and carbohydrates. Pigments depositions.

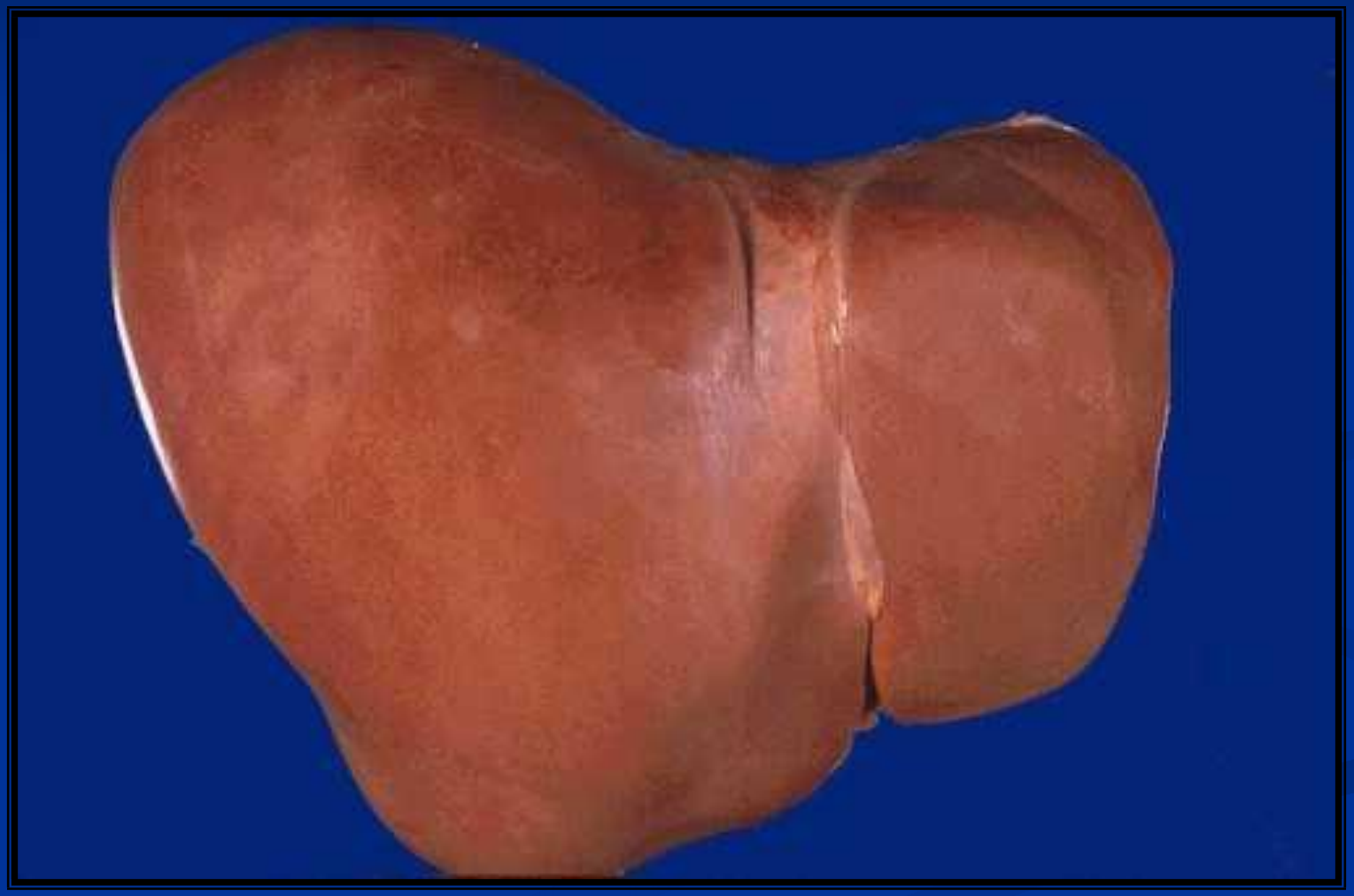
STEATOSIS (FATTY CHANGE)

The terms "steatosis" and "fatty change" describe abnormal accumulations of triglycerides within parenchymal cells.

The causes of steatosis include toxins, protein malnutrition, diabetes mellitus, obesity, and anoxia. In industrialized nations, by far the most common cause of significant fatty changes in the liver (fatty liver) is alcohol abuse.

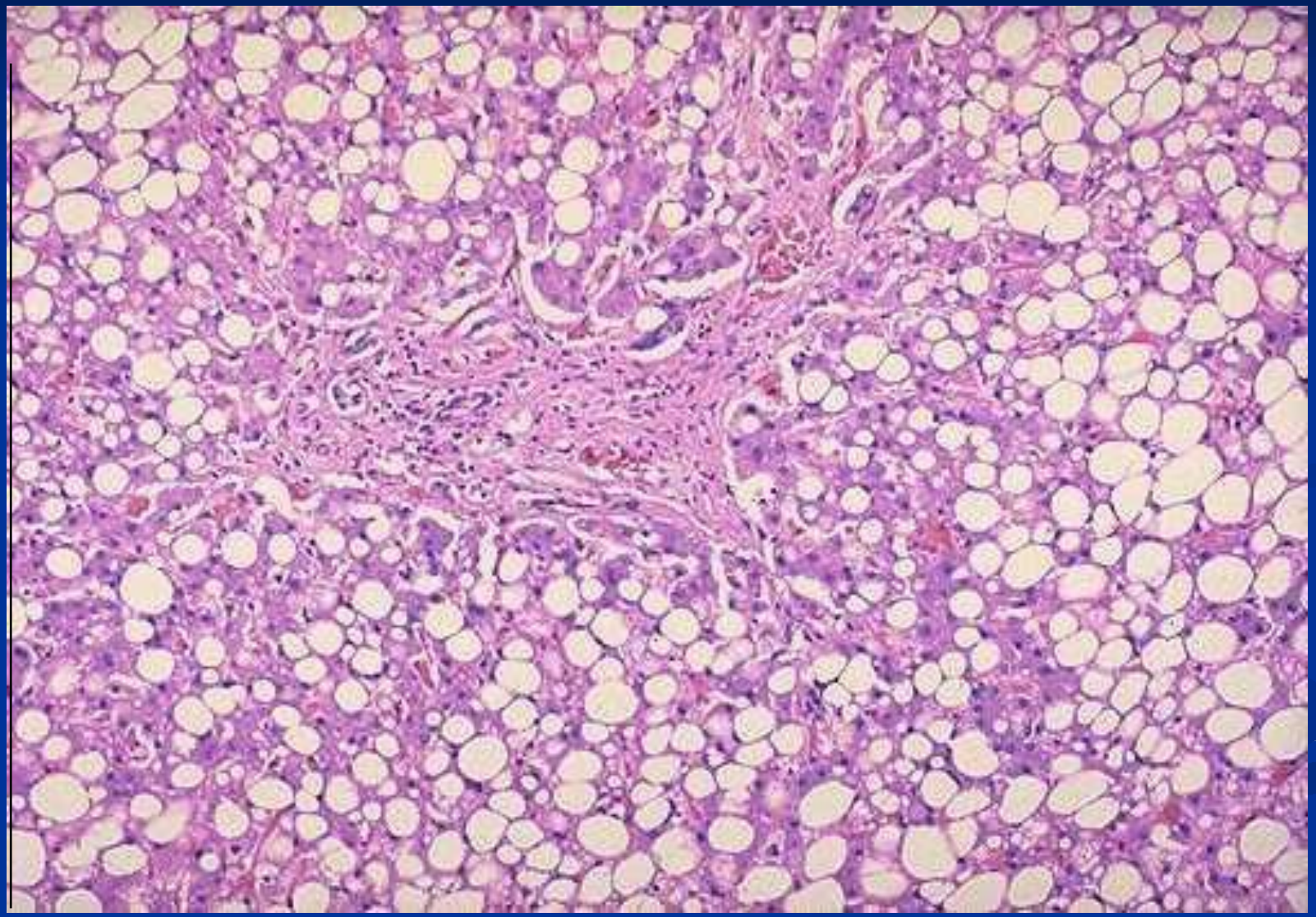
Liver. In the liver, mild fatty change may not affect the gross appearance. With progressive accumulation, the organ enlarges and becomes increasingly yellow until, in extreme instances, the liver may weigh 3 to 6 kg and be transformed into a bright yellow, soft, greasy organ.

Normal Liver



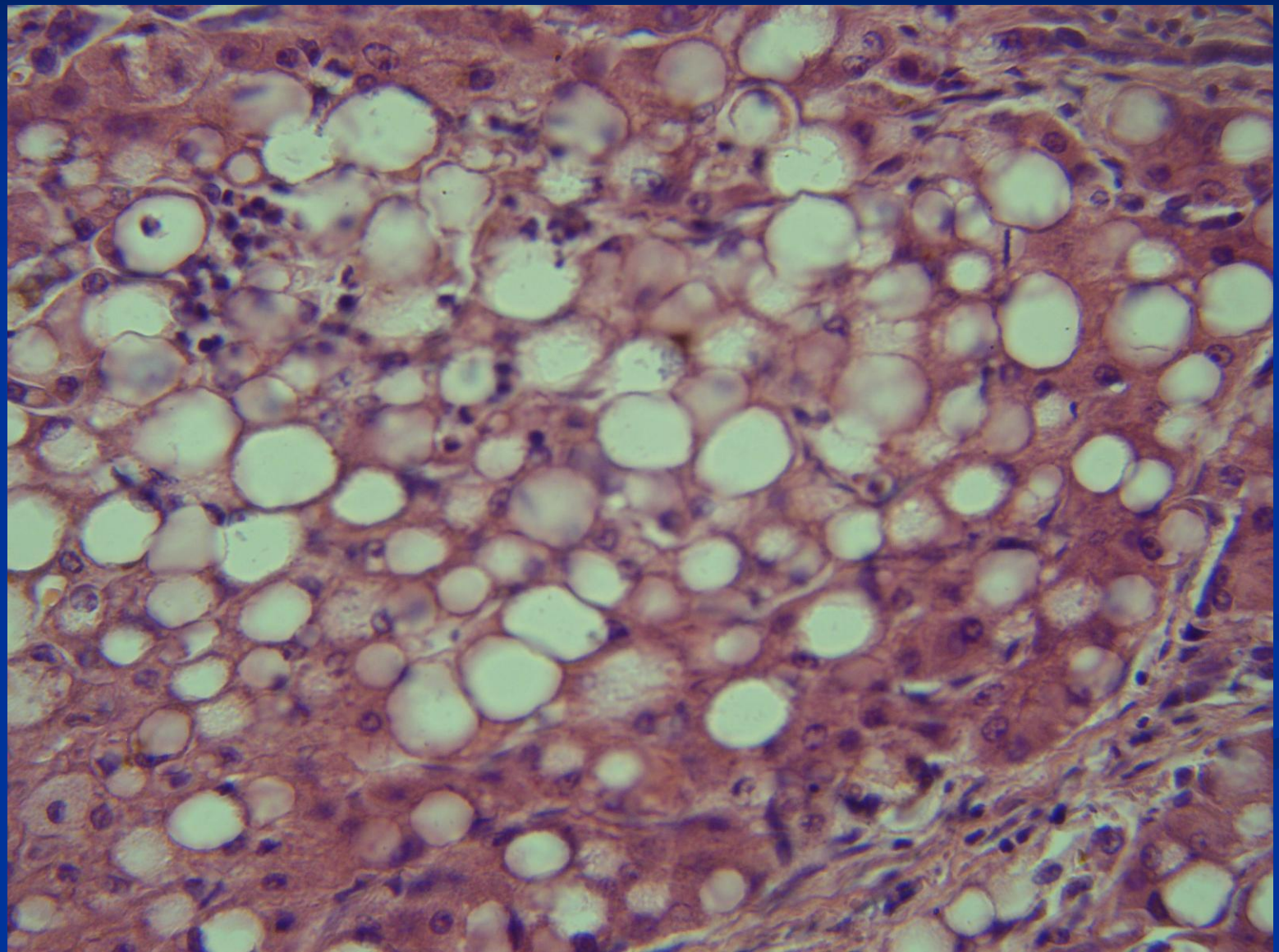
- Fatty change begins with the development of minute, membrane-bound inclusions closely applied to the endoplasmic reticulum. It is first manifested light microscopically by the appearance of small fat vacuoles in the cytoplasm around the nucleus. As the process progresses, the vacuoles coalesce, creating cleared spaces that displace the nucleus to the periphery of the cell. Occasionally, contiguous cells rupture, and the enclosed fat globules coalesce, producing so-called fatty cysts.

Fatty Liver



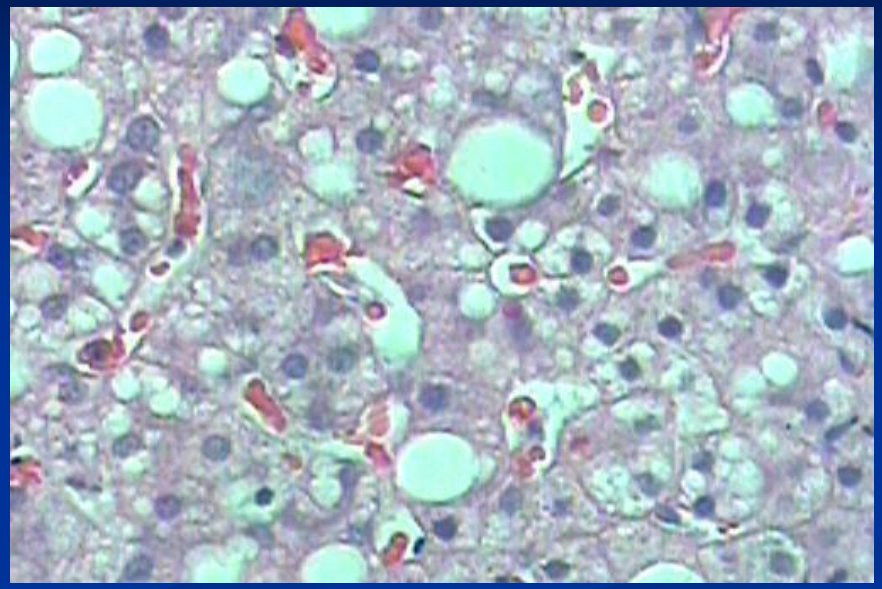
Fatty Liver.

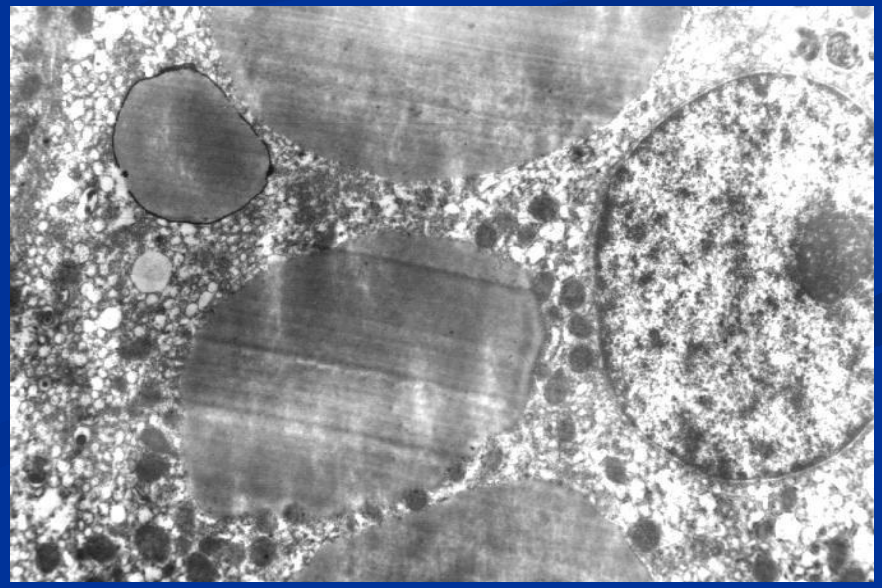
H & E. X 400.



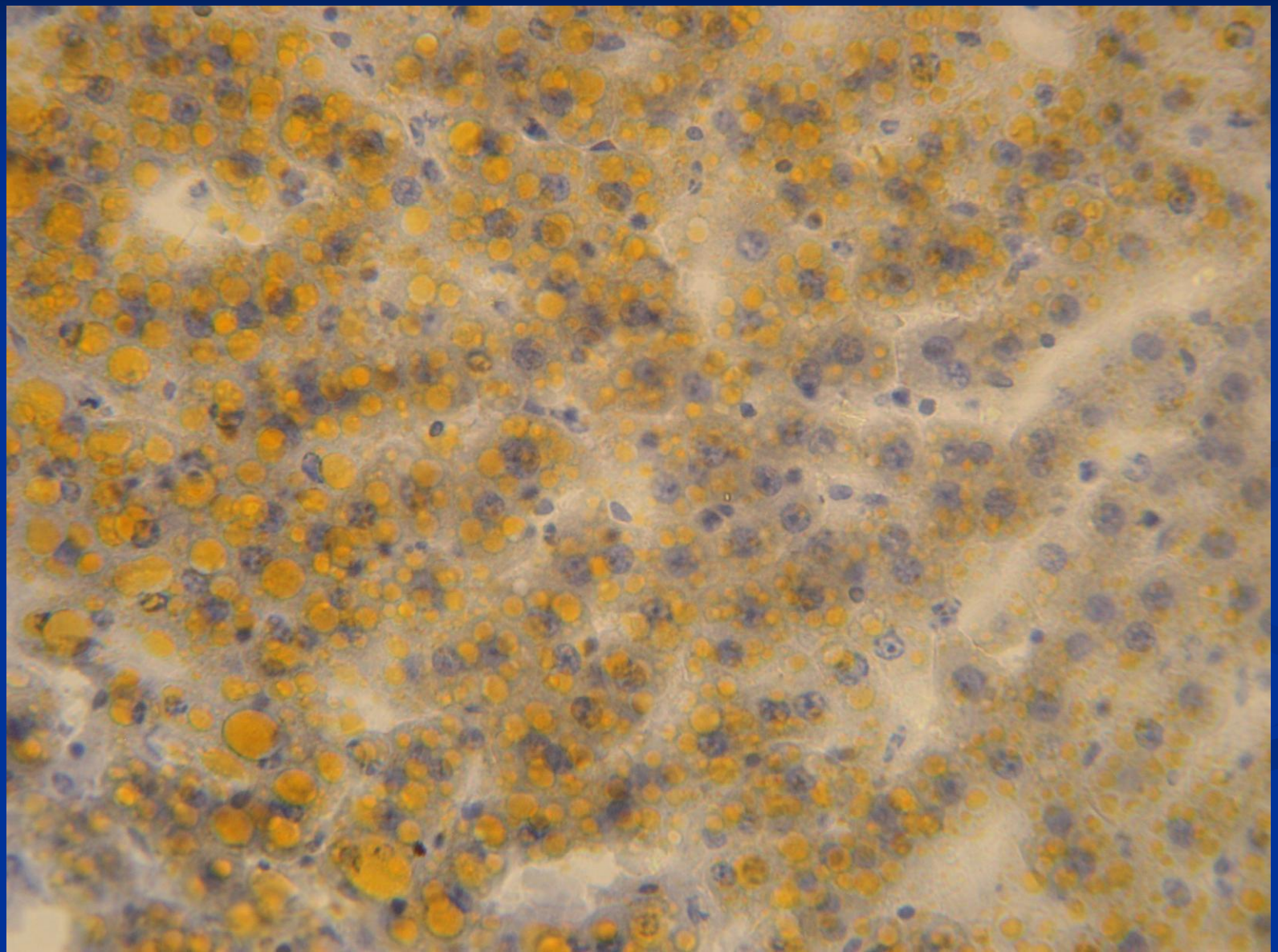
•Cell Injury: Histological expressions

- Fat (neutral fat, triglyceride) in liver cells: indicates some defect in lipid metabolism or lipoprotein synthesis or unusual quantities of adipose or dietary lipid brought to liver. Also referred to as "steatosis".

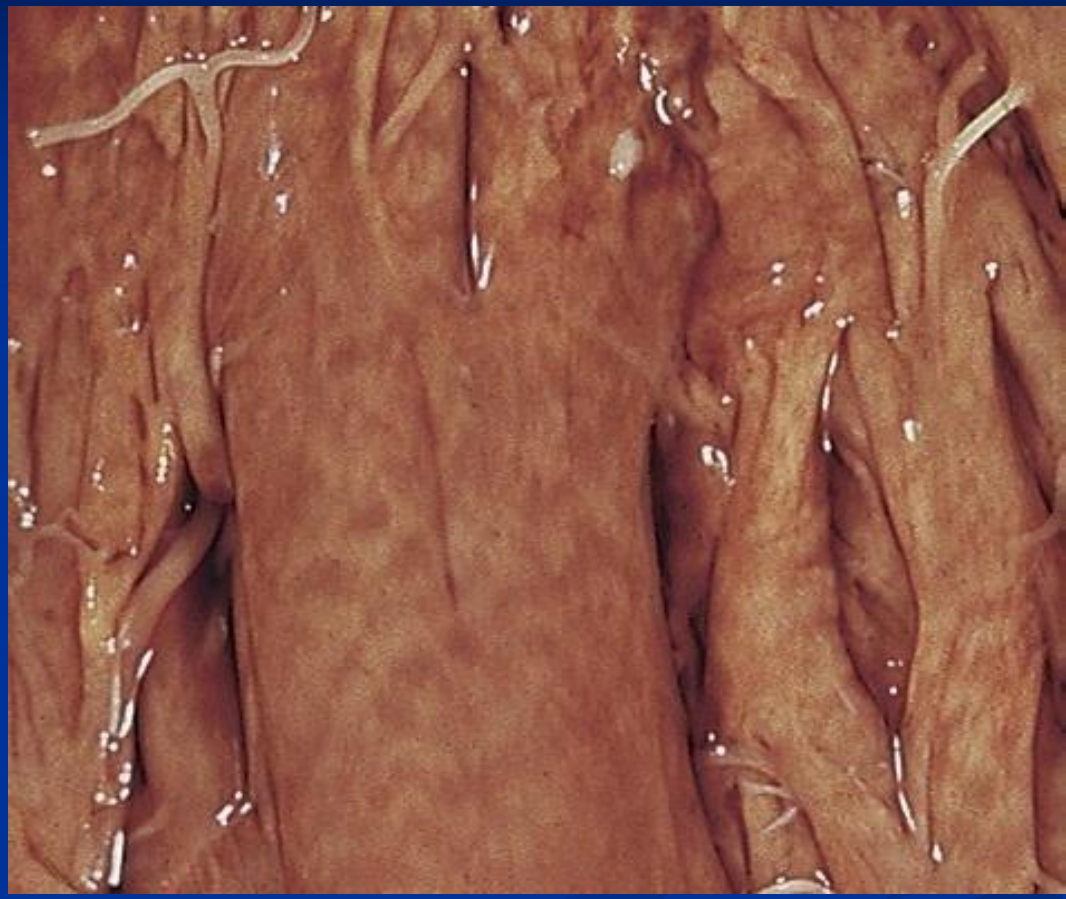




Fatty Liver.
Sudan III (frozen section). X 400.



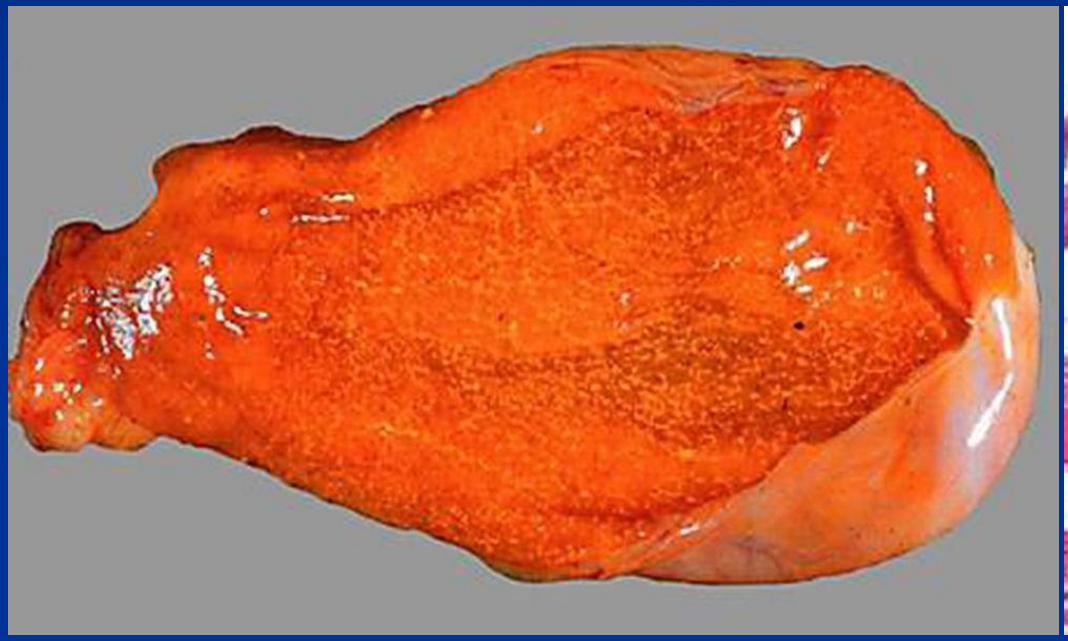
Heart. Lipid, as a neutral fat, is sometimes found in heart muscle in the form of small droplets. It occurs in two patterns. In one, prolonged moderate hypoxia, such as that produced by profound anemia, causes intracellular deposits of fat, which create grossly apparent bands of yellow myocardium alternating with bands of darker, red-brown, uninvolved myocardium (tigered effect). In the other pattern of fatty change produced by more profound hypoxia or some forms of myocarditis the myocardial cells are uniformly affected.

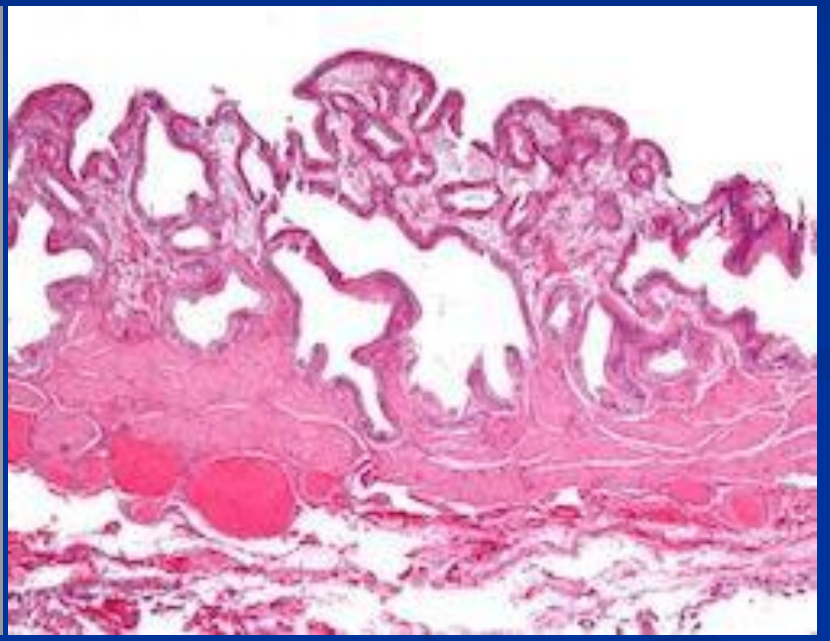


Cholesterol and Cholesterol Esters.

1. Atherosclerosis.
2. Xanthomas. Intracellular accumulation of cholesterol within macrophages is also characteristic of acquired and hereditary hyperlipidemic states. Clusters of foamy cells are found in the subepithelial connective tissue of the skin and in tendons producing tumorous masses known as xanthomas.
3. Inflammation and necrosis. Foamy macrophages are frequently found at sites of cell injury and inflammation, owing to phagocytosis of cholesterol from the membranes of injured cells, including parenchymal cells, leukocytes, and erythrocytes. Phospholipids and myelin figures are also found in inflammatory foci. When abundant, the cholesterol-laden macrophages impart a yellowish discoloration to such inflammatory foci.

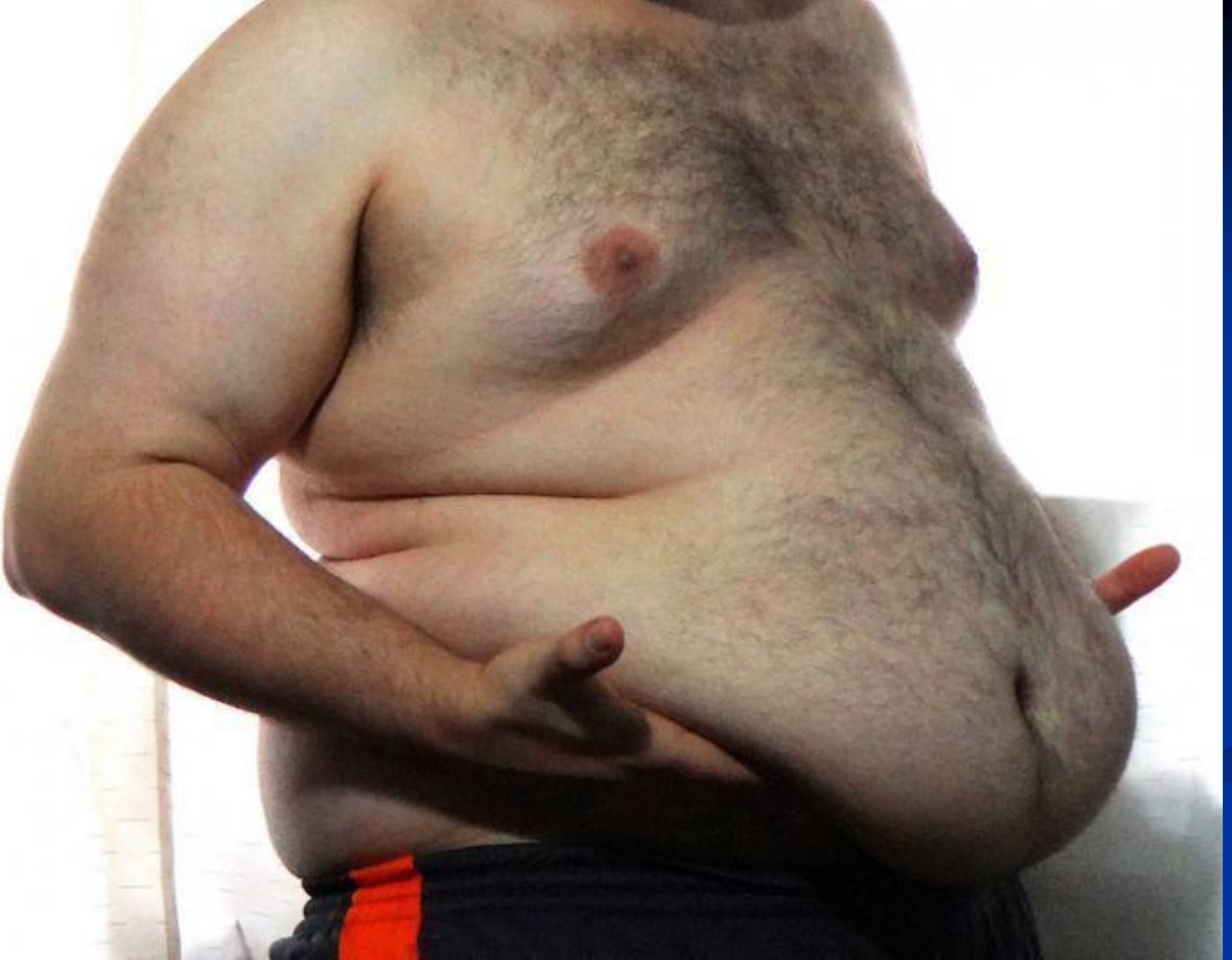
4. Cholesterolosis. This refers to the focal accumulations of cholesterol-laden macrophages in the lamina propria of the gallbladder. The mechanism of accumulation is unknown.



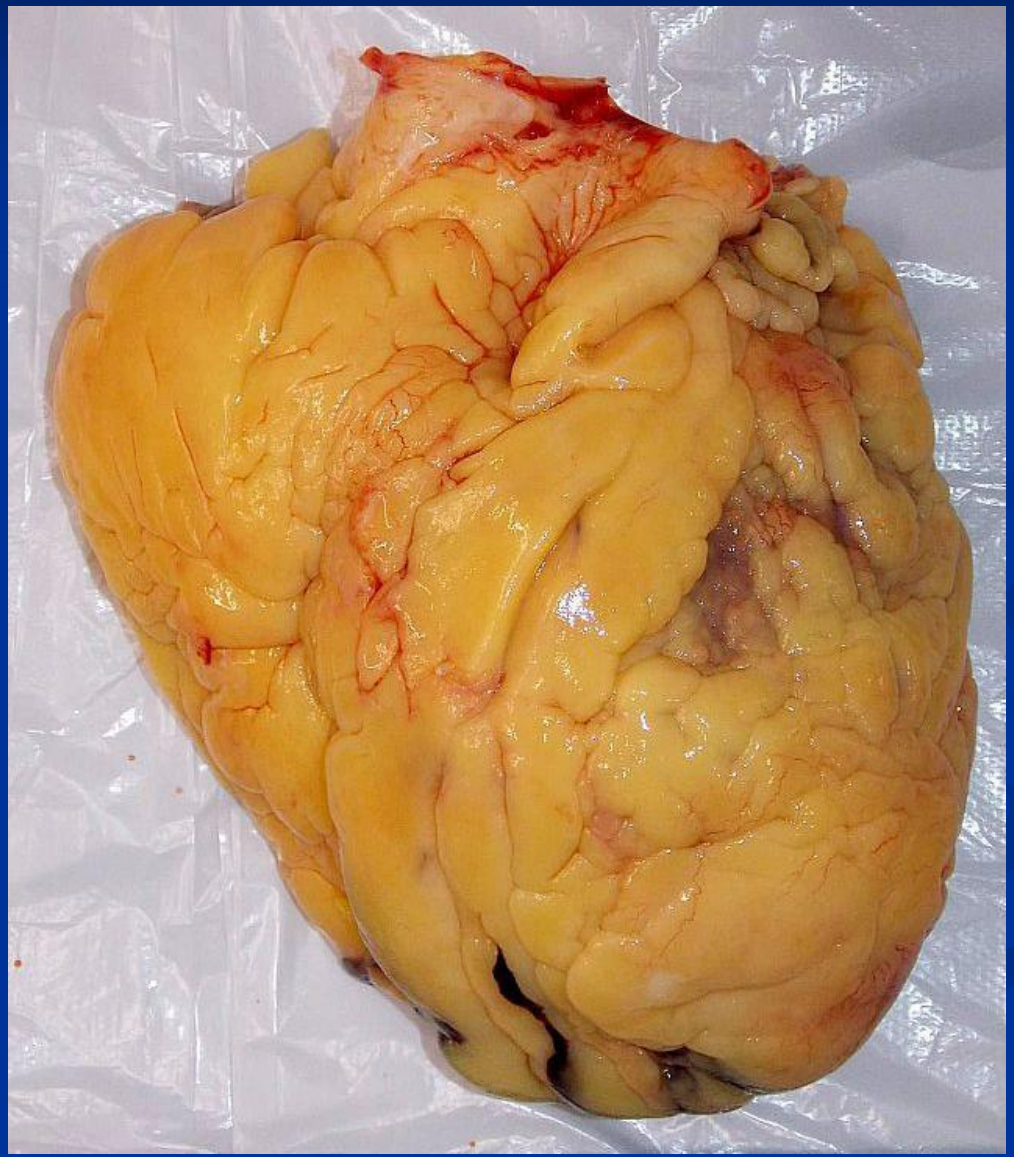


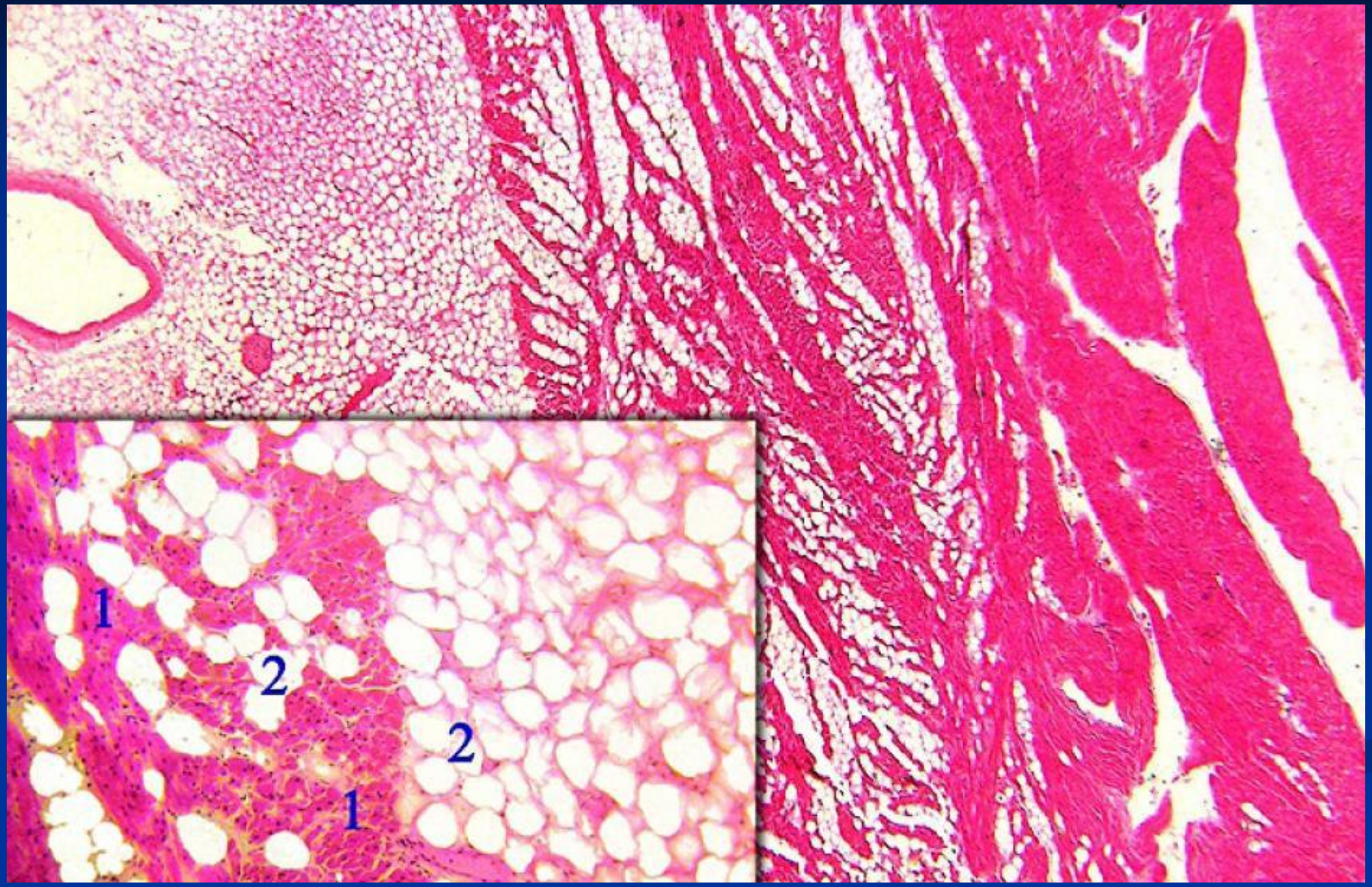
- **STROMAL INFILTRATION OF FAT OR FATTY INGROWTH**
- This is a form of accumulation of lipids that has a mechanism and connotation completely different from those of intracellular fatty accumulation. Fatty ingrowth refers to the accumulation of lipids within stromal connective tissue cells.
- Fatty ingrowth is most commonly encountered in the heart and pancreas, where adult adipose cells appear within the connective tissue stroma. The stromal adipose tissue does not damage the adjacent myocardial cells. In the pancreas, the fat is found in the connective tissue septa of the pancreatic lobules.

Weight Categories	BMI (kg/m2)
Underweight	< 18.5
Healthy Weight	18.5 - 24.9
Overweight	25 - 29.9
Obese (Class I)	30 - 34.9
Severely Obese (Class II)	35 - 39.9
Morbidly Obese (Class III)	40 - 49.9
Super Obese (Class IV)	>50



Fatty dystrophy of heart.

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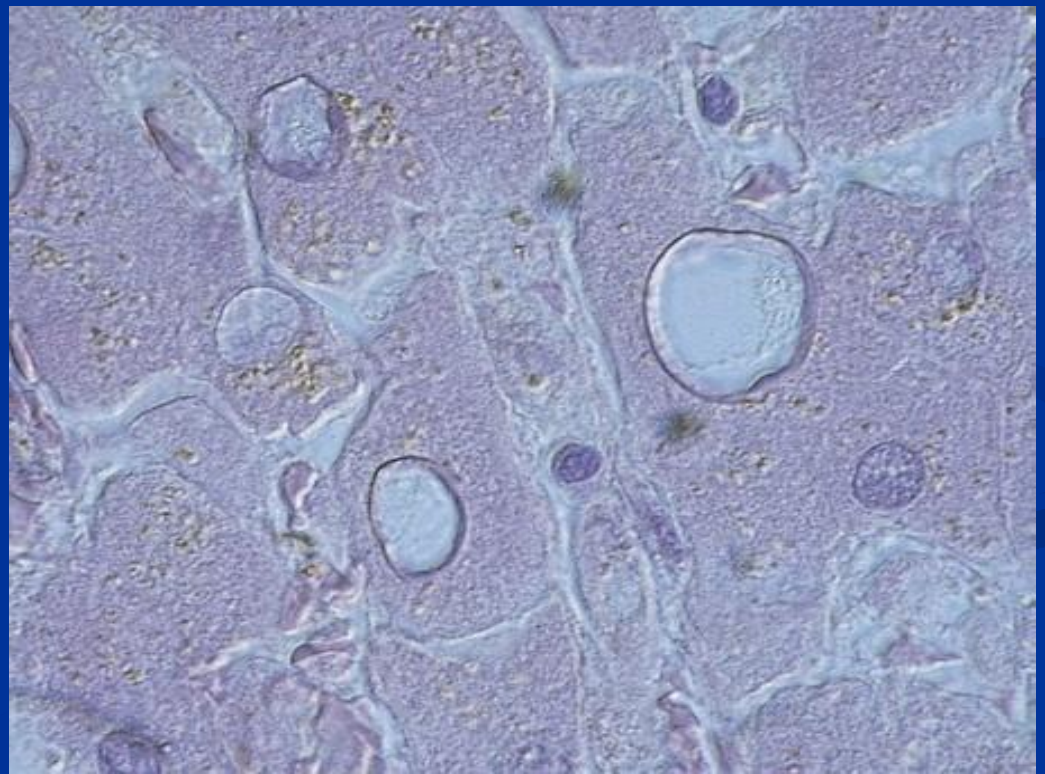
GLYCOGEN

- Excessive intracellular deposits of glycogen are seen in patients with an abnormality in either glucose or glycogen metabolism. Whatever the clinical setting is, the glycogen masses appear as clear vacuoles within the cytoplasm. Glycogen is best preserved in nonaqueous fixatives; for its localization, tissues are best fixed in absolute alcohol. Staining with Best's carmine or the PAS reaction imparts a rose-to-violet color to the glycogen, and diastase digestion of a parallel section before staining serves as a further control by hydrolyzing the glycogen.

Diabetes mellitus

- Diabetes mellitus is the prime example of a disorder of glucose metabolism. In this disease, glycogen is found in the epithelial cells of the distal portions of the proximal convoluted tubules and sometimes in the descending loop of Henle as well as within liver cells, beta cells of the islets of Langerhance, and heart muscle cells.



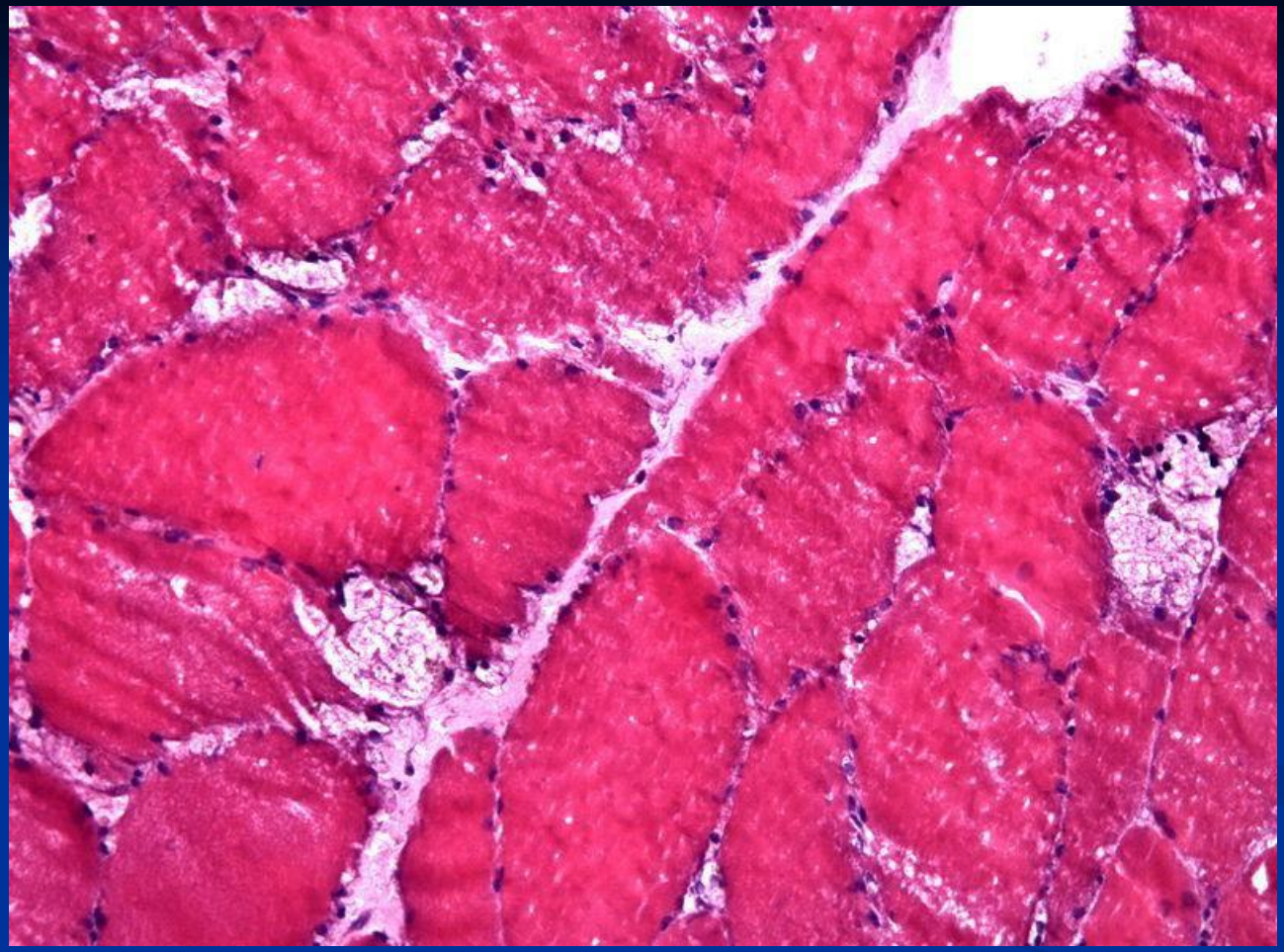
Glycogenoses

Table 21.1 Glycogen-storage diseases

Type	Defective enzyme	Organ affected	Glycogen in the affected organ	Clinical features
Von Gierke	Glucose 6-phosphatase or transport system	Liver and kidney	Increased amount; normal structure.	Massive enlargement of the liver. Failure to thrive. Severe hypoglycemia, ketosis, hyperuricemia, hyperlipemia.
II Pompe	α-1,4-Glucosidase (lysosomal)	All organs	Massive increase in amount; normal structure.	Cardiorespiratory failure causes death, usually before age 2.
III Cori	Amylo-1,6-glucosidase (debranching enzyme)	Muscle and liver	Increased amount; short outer branches.	Like type I, but milder course.
IV Andersen	Branching enzyme (α-1,4 → α-1,6)	Liver and spleen	Normal amount; very long outer branches.	Progressive cirrhosis of the liver. Liver failure causes death, usually before age 2.
V McArdle	Phosphorylase	Muscle	Moderately increased amount; normal structure.	Limited ability to perform strenuous exercise because of painful muscle cramps. Otherwise patient is normal and well developed.
VI Hers	Phosphorylase	Liver	Increased amount.	Like type I, but milder course.
VII	Phosphofructokinase	Muscle	Increased amount; normal structure.	Like type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure.	Mild liver enlargement. Mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives. Type VIII is sex-linked.

Table 21.1
Biochemistry, Seventh Edition

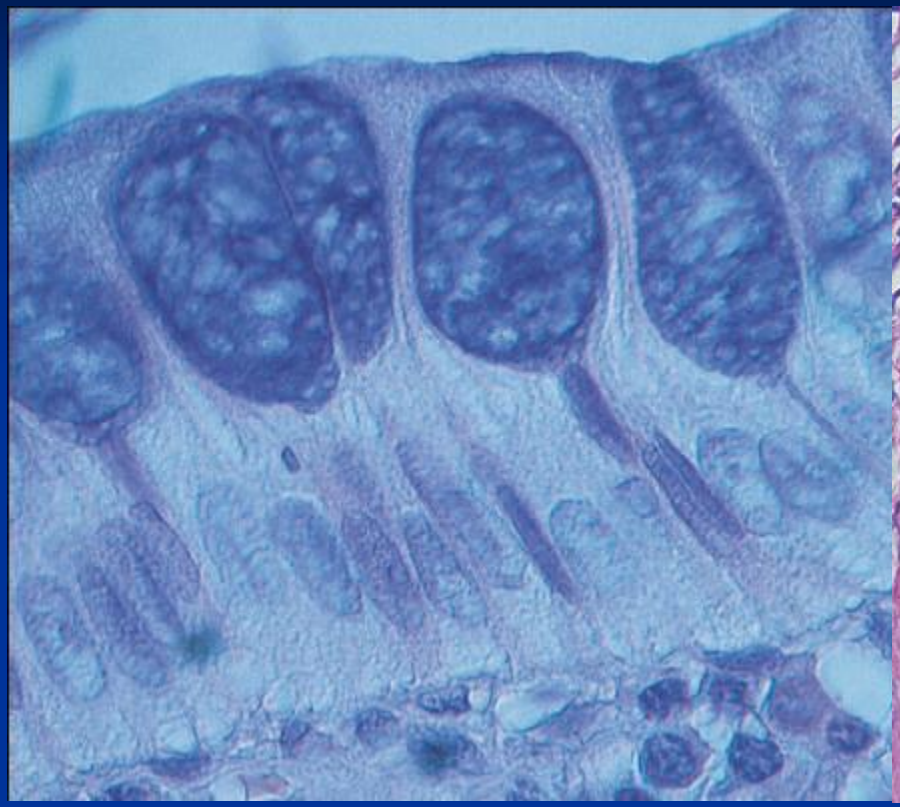


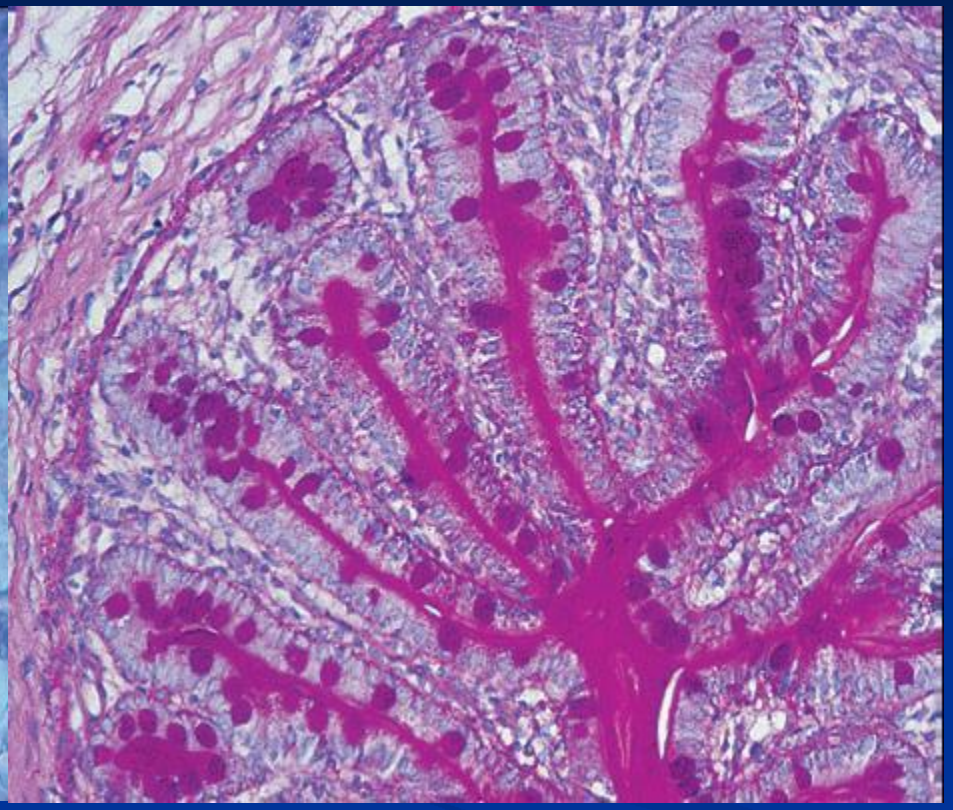
Muscle biopsy showing large vacuoles in a case of Pompes disease: α-1,4-glucosidase (acid maltase) deficiency (HE stain, frozen section).

Proteoglycan Secretion Disorders

- Cystic Fibrosis Synonym: mucoviscidosis.
- Definition: Hereditary defect of an anion channel that transports chloride ions. The defect results in dysfunctional exocrine secretion, creating excessively viscid mucus in the respiratory and digestive tracts. Accumulation of mucus in tissue results.

- Causal pathogenesis: The disorder is caused by a single-point mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) protein, a membrane protein forming the chloride channel.
- Formal pathogenesis: The CFTR protein is only formed by certain epithelial cells.
- The lack of a choroid channel prevents normal reabsorption of Cl, for example from sweat in the glandular lumen. This results in a high concentration of salt in secreted sweat (a clinical sign of the disease) and reduced Cl conductivity.
- It also causes secretion of viscid mucus by the submucosal glands of the respiratory tree, the sublingual glands, the intestinal mucosa, the pancreas, and the bile ducts. This results in obstruction of the excretory duct by plugs of mucus and secretions.





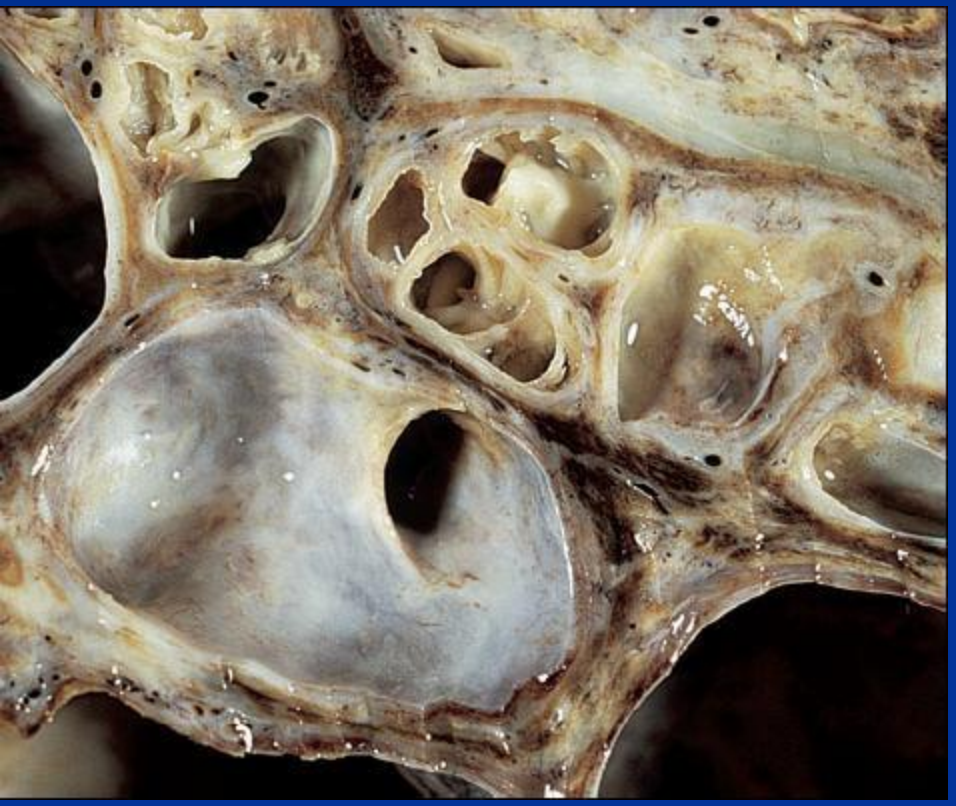
- **Mucus accumulation in goblet cell of bronchi** (HE) x 200

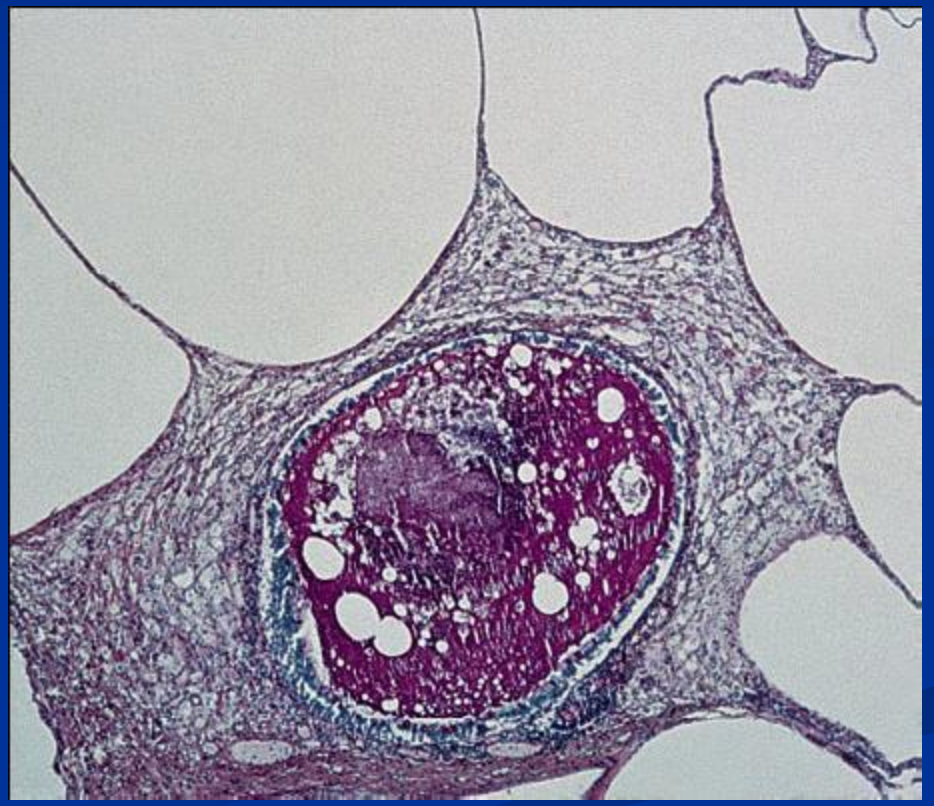
Mucus accumulation in colon crypts (PAS) x 250

Sequelae of Cystic Fibrosis

- Bronchiectasis: Mucus accumulation in the goblet cells and glands, and ciliary hypomotility with defective mucociliary action, result in accumulation of secreted mucus.
- This leads to bronchitis, which in turn results in abnormal, irreversible expansion of the bronchi; the lumen is partially filled with thickened whitish secretion. The result is persistent peribronchial inflammation.

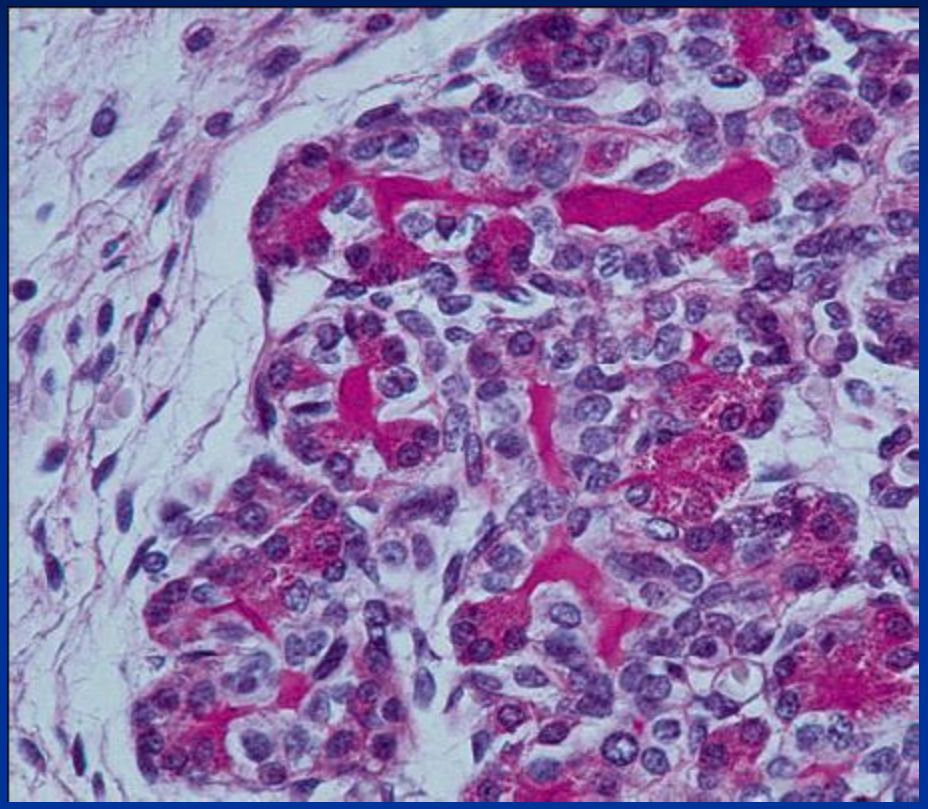
- **Bronchiectasis** **Mucus accumulation in bronchi** (PAS) x 50

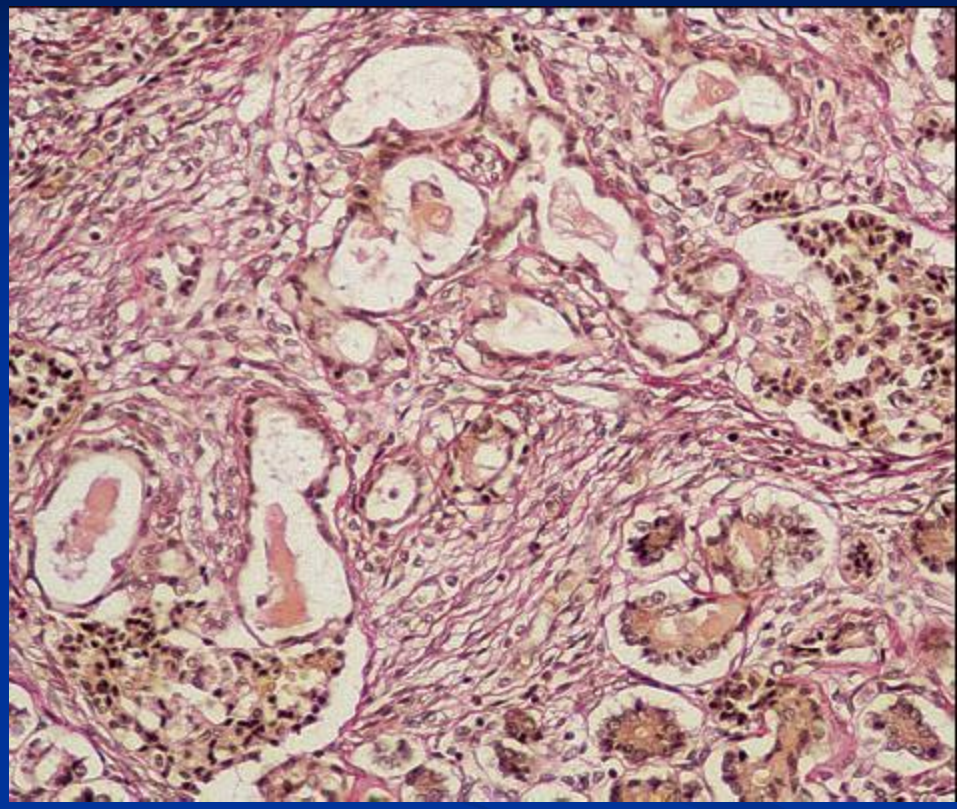




Cystic fibrosis of the pancreas

- Accumulation of thickened mucus in the excretory ducts leads to formation of pancreatic stones and expansion of the excretory duct. Retention cysts form, which are accompanied by periductal resorptive inflammation. The excretory ducts become encased in scar tissue.
- This results in progressive atrophy of the exocrine acinar epithelia, with acinar metaplasia characterized by small cysts and replacement with fatty tissue.





- **Mucus accumulation in pancreas:** (19th week of gestation; PAS) x 60

Cystic mucus accumulation in pancreas (newborn; EvG) x 75

Proteoglycan Lysis Deficiencies

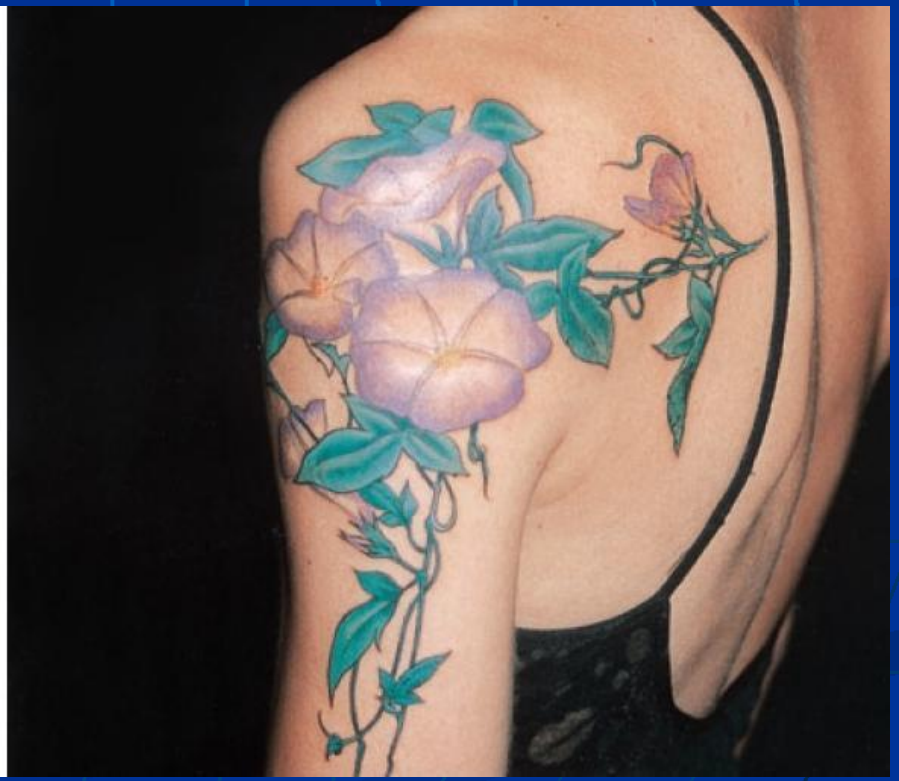
- General definition: Rare hereditary lysosomal disorder involving deficient metabolism of glycosaminoglycan in which mucopolysaccharide breakdown products are stored and excreted.
- General pathogenesis: An autosomal recessive enzyme deficiency (except Hunter's syndrome) prevents complete metabolism of mucopolysaccharides.
- Metabolites are stored in lysosomes, creating a cytoplasmic vacuolization. When the lysosomal storage vacuoles are filled to capacity, mucopolysaccharide metabolites are excreted in the urine, which is how the diagnosis is made.

Pigments

Pigments are substances whose ntrinsic color makes them recognizable in living tissue. They are either synthesized within the body itself (endogenous pigments) or are introduced into the body (exogenous pigments). They may be inert and, ignored by the body, lie on or within tissue. Alternatively, they may act on the body as foreign or poisonous substances, eliciting an inflammatory reaction.

Exogenous pigments

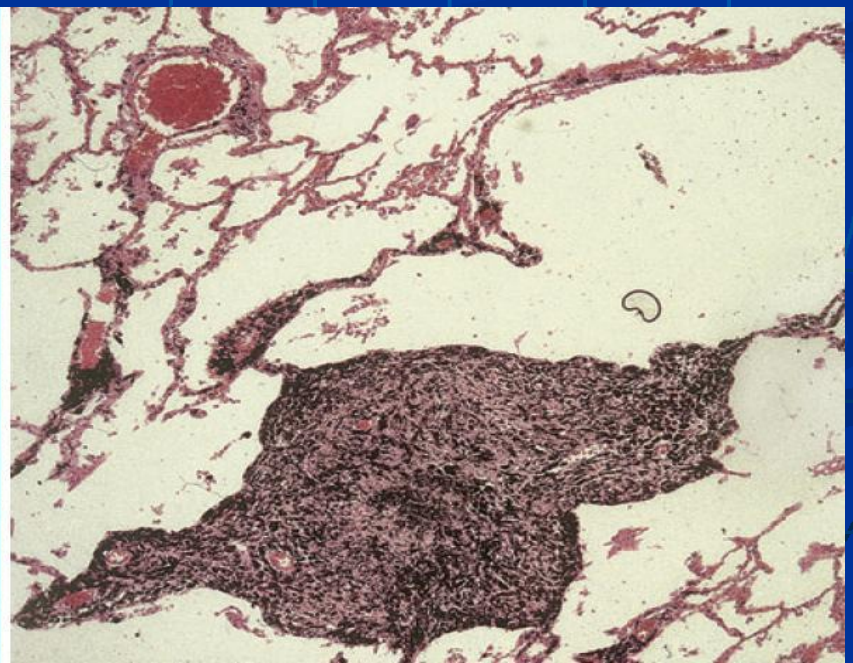
- Exogenous pigments in the form of cosmetic allergens or local discoloration around metallic implants are of secondary importance in a clinical setting.



Tattoos

Occupational Toxin Pigments

Anthracosis: Nodular black discoloration of the lungs with inhaled carbon dust (coal dust or cigarette smoke). The substances are phagocytized by alveolar macrophages and removed via the lymph vessels. The condition is common. The same process occurs with the ferrous dusts inhaled by workers at steel and/or ceramics factories.



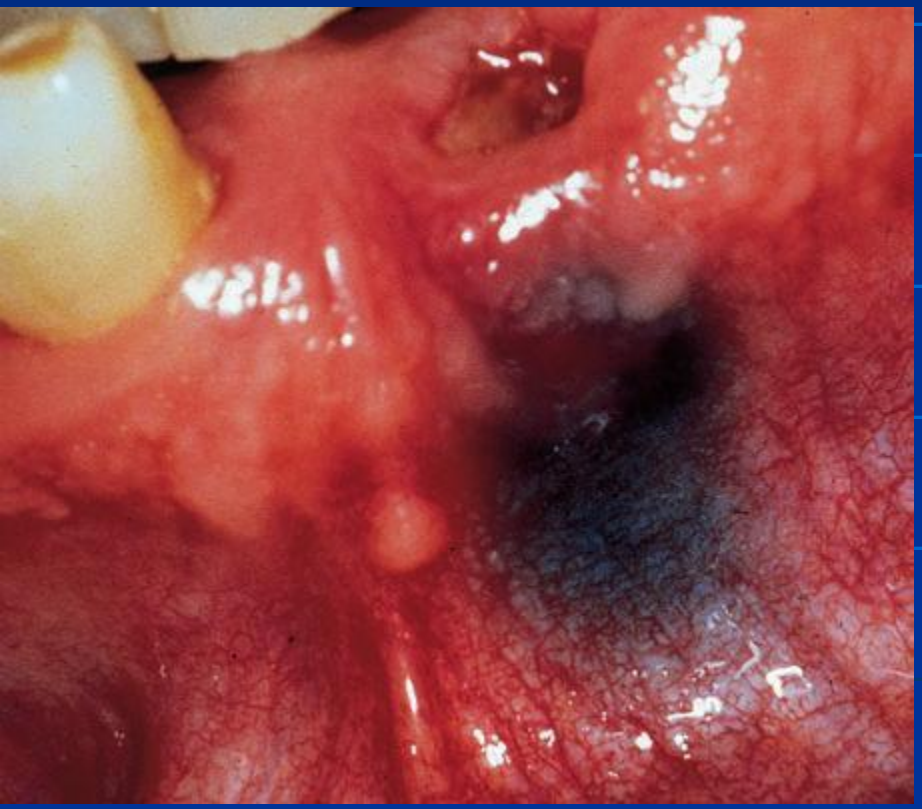
Plumbism: Chronic lead poisoning causes this condition. Pathogens stimulating decomposition in the pockets of the gums (periodontitis) transform lead into lead sulfide, producing a halo-like deposits in the gingiva.

Chalcosis: Exhaust gases containing copper and dusts from the copper processing industry cause green discoloration of the hair. The disorder is rare.

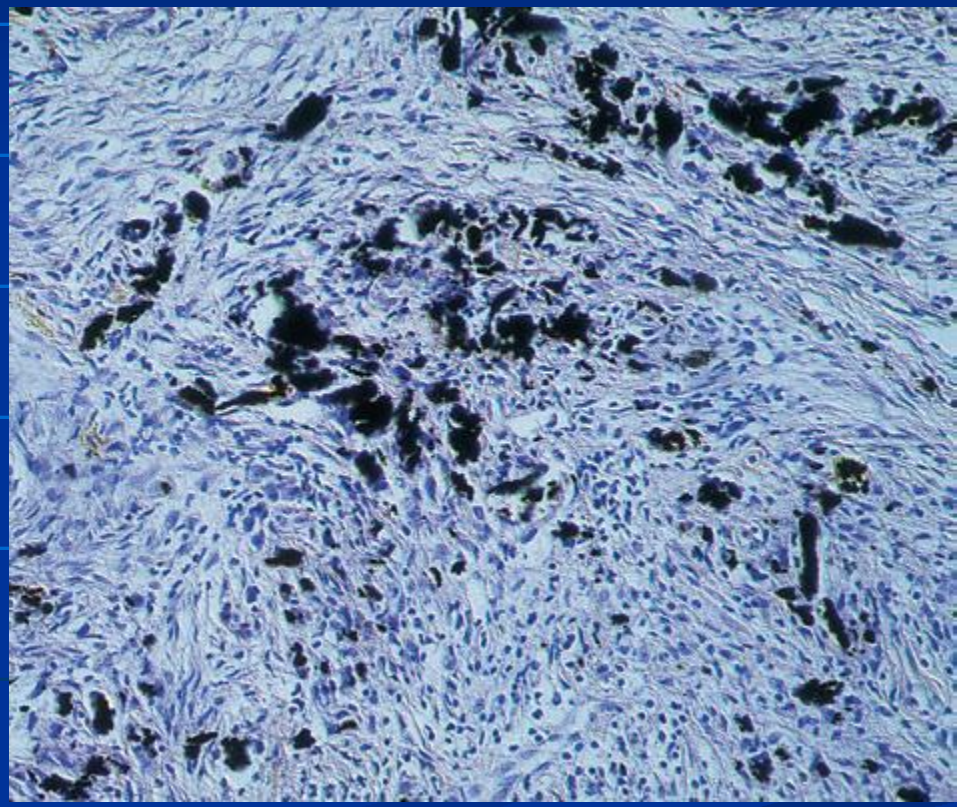
Tetracycline: Integration of the substance in bone and teeth in children leads to irreversible yellow discoloration.

Amalgam: Chronic abrasion of mercury containing tooth fillings produces grayish blue mucosal discoloration with metal deposits in the mucosal stroma. This disorder is common.

- **Gingiva in amalgam carrier**



- **Gingiva in amalgam carrier (HE) x 150**



Endogenous pigments

 Endogenous pigments have important biologic functions. Disorders of their synthesis or breakdown can have far-reaching consequences, as the most important of these substances either catalyze several steps in metabolism or certain steps in sensory physiology. Due to their intrinsic color, their absence or overabundance is a sign of tissue damage.

Hematogenous pigments may contain iron. They can be associated with defective porphyrin synthesis (porphyria), which is accompanied by photodermatosis, liver damage, and occasionally anemia. They can also be associated with blockage of some stage of the metabolism and excretion of bilirubin. The bilirubin accumulation in blood manifests itself clinically as jaundice (icterus). The hematogenous pigments also include the malaria pigment.

Tyrosine derivative pigments in the form of cutaneous melanin act as a natural sunscreen. Neuromelanin defects lead to neurologic and sensory deficits such as Parkinson's disease, retinitis pigmentosa (blindness), and Waardenburg syndrome (inner ear deafness).

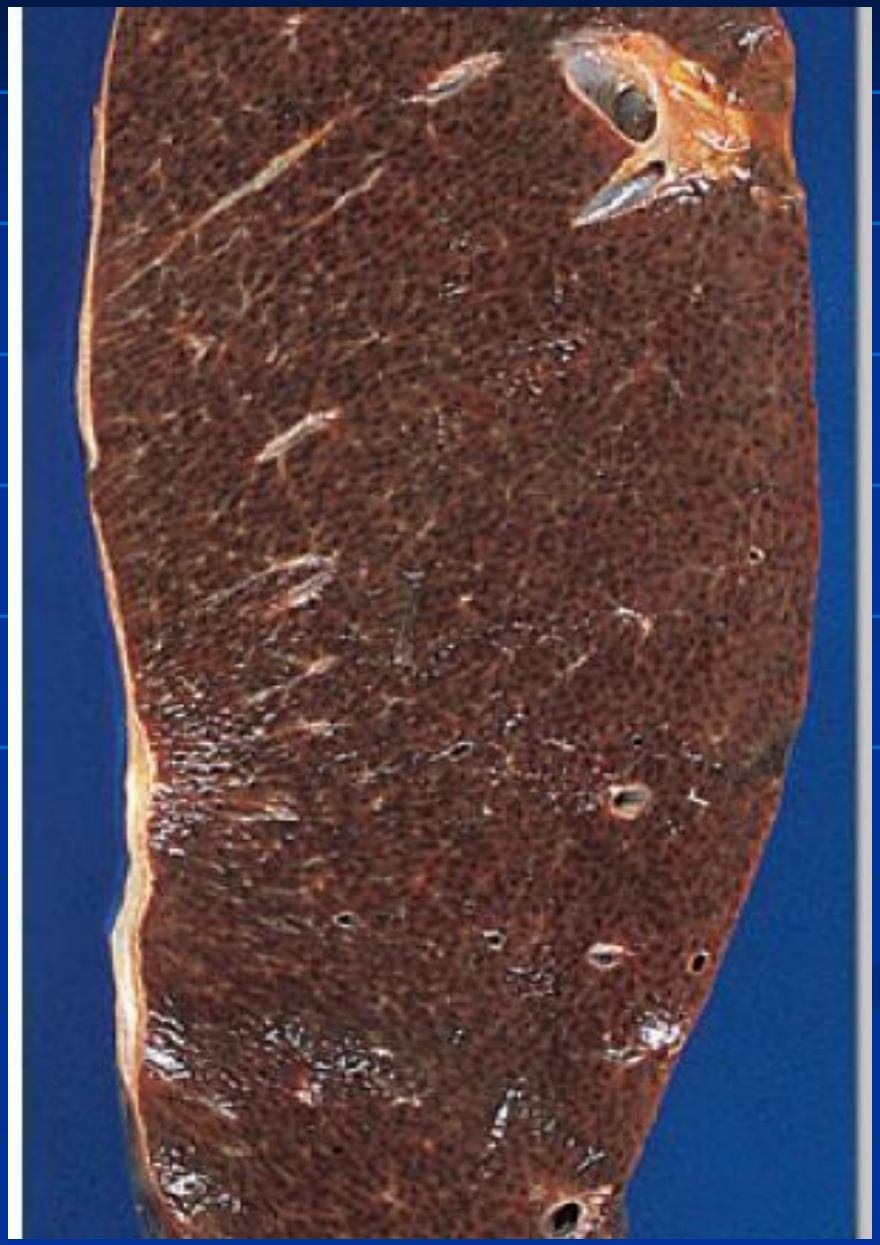
Lipogenous pigments only have potential pathologic significance in the form of visual purple (rhodopsin), whereas lipofuscin and ceroid are color indicators of tissue damage.

Hemoglobin Breakdown Pigments

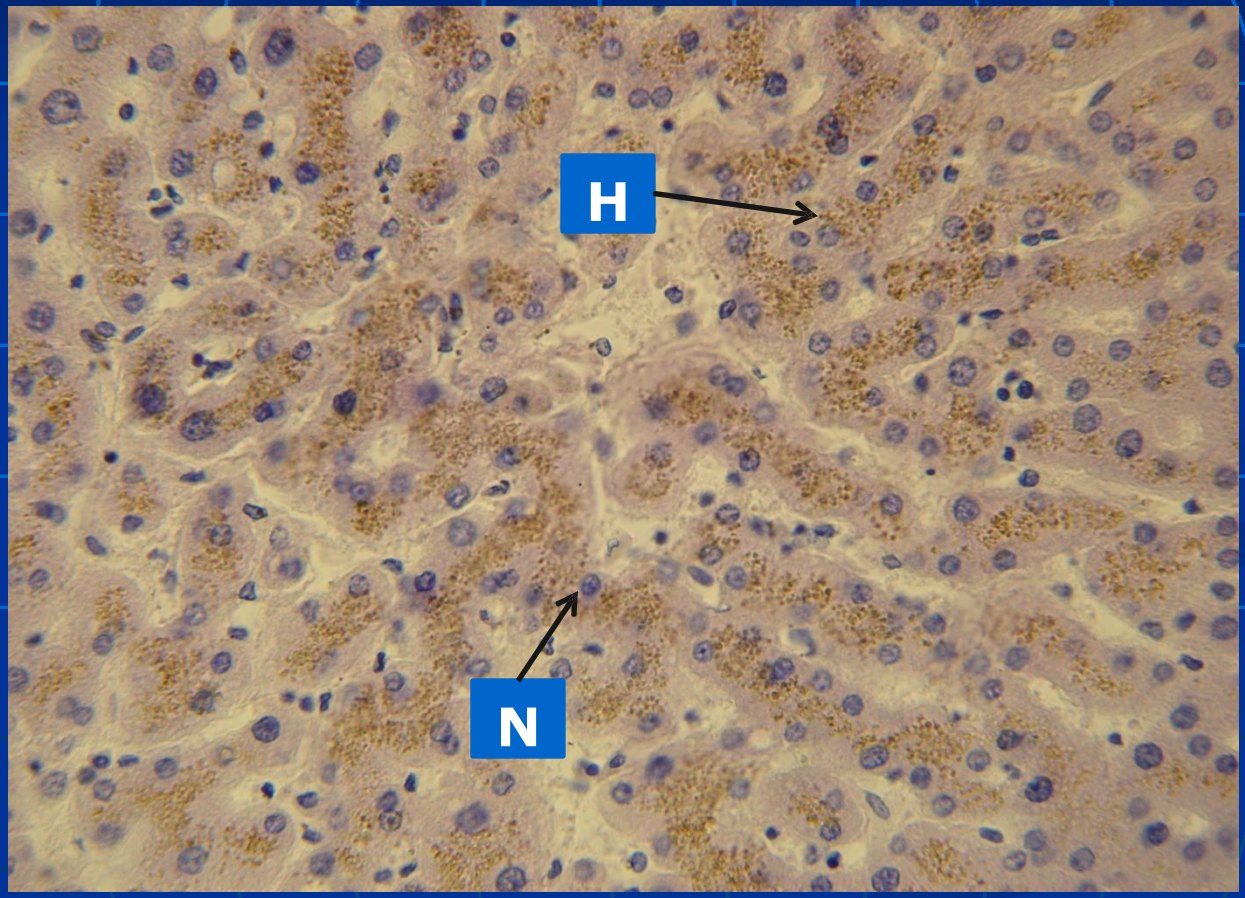
- Hemosiderin:
- Definition: Ferrous, yellowish brown pigment that is free of pyrrole (siderin).
- Pathogenesis: Requiring 2 days to develop, the substance forms only in living cells that also store the phagocytized iron in this form, i.e., cells of the reticuloendothelial system. This produces brown discoloration in the storage tissue

Normal liver

Hemosiderosis

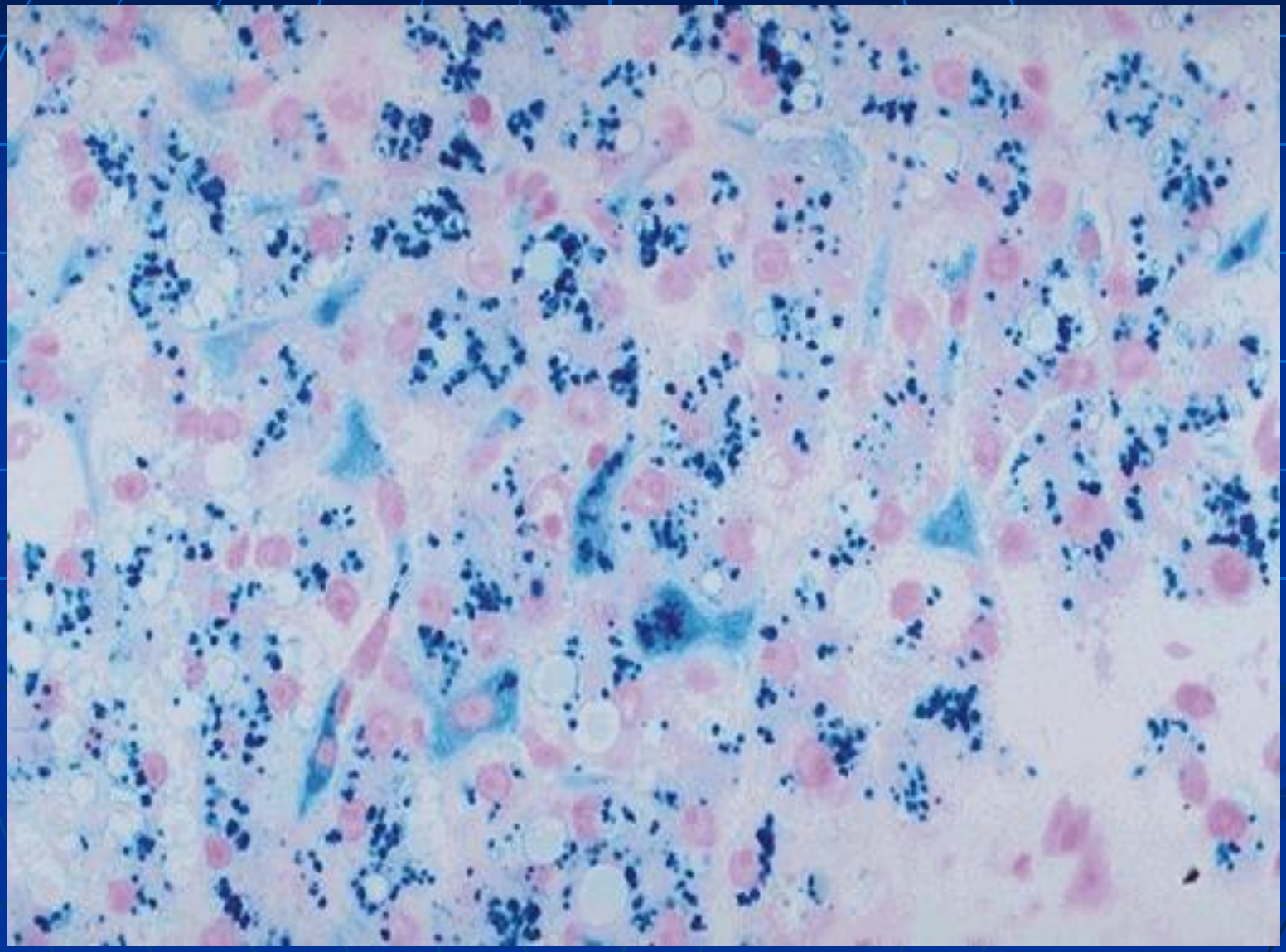


Hemosiderosis of liver. H & E. X 400.



- H – hemosiderin
- N – nucleus of hepatocyte

Hemosiderosis of liver.
Prussian blue. X 520.

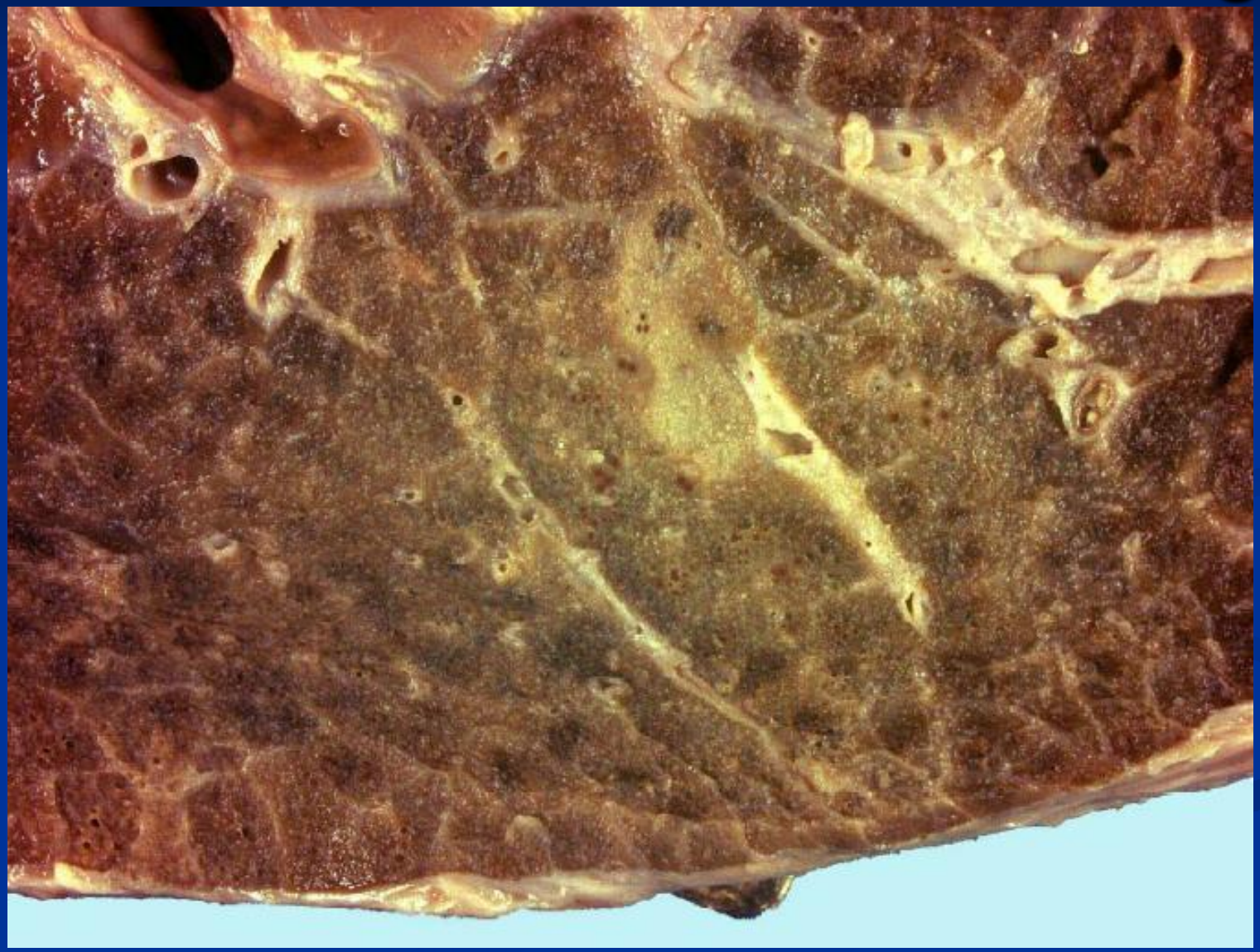


Hemosiderin is deposited in many organs and tissues, a condition called hemosiderosis.

It is seen with

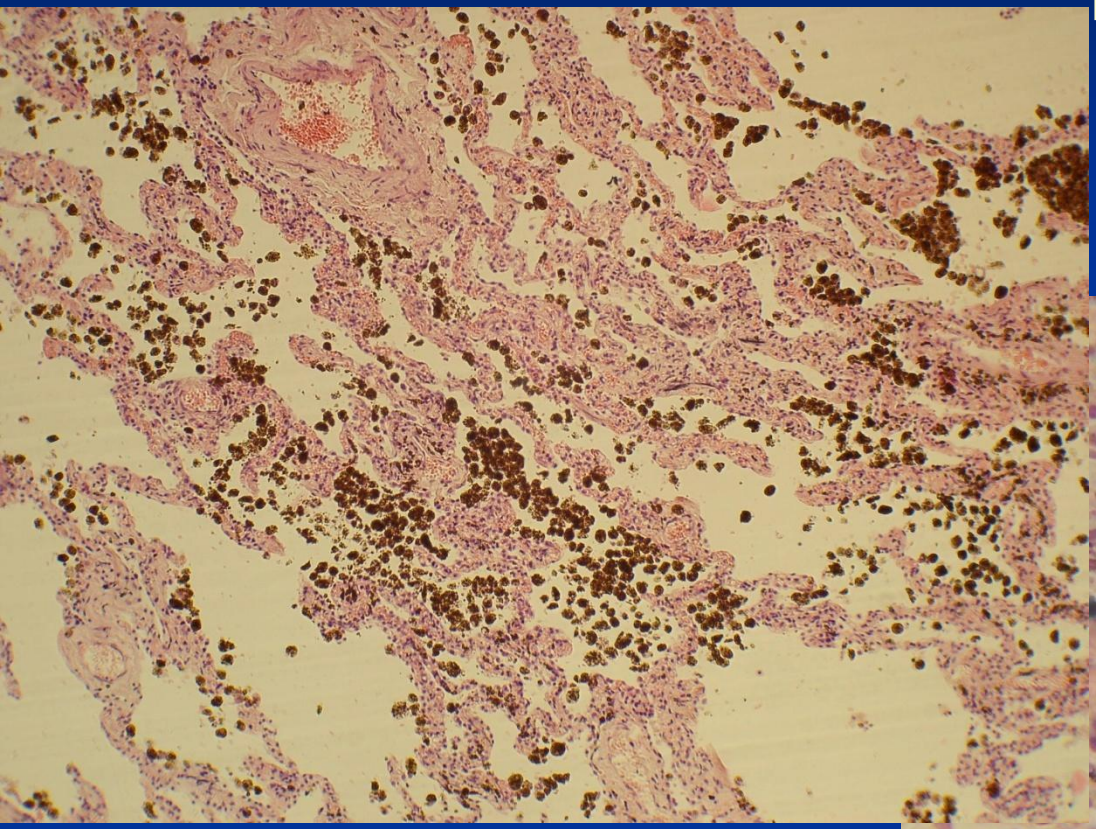
- 1) increased absorption of dietary iron,
- 2) impaired utilization of iron,
- 3) hemolytic anemias,
- 4) transfusions because the transfused red cells constitute an exogenous load of iron.

Brown induration of the lung.

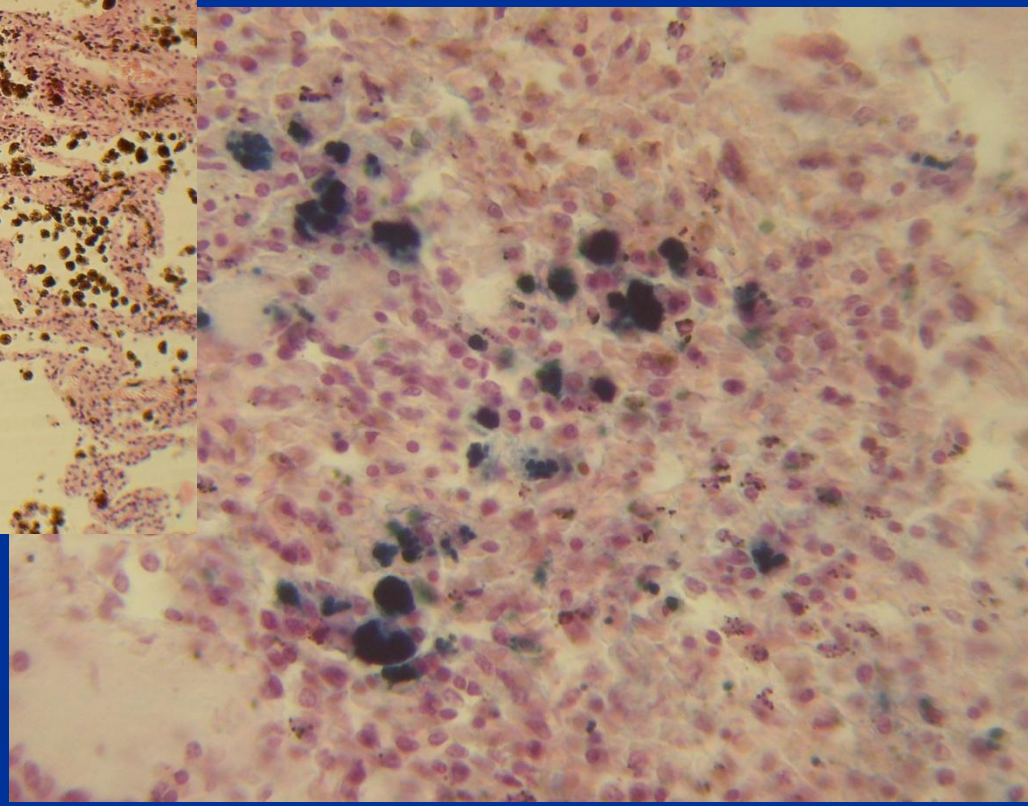


Hemosiderosis of lung.

H & E. X 100.



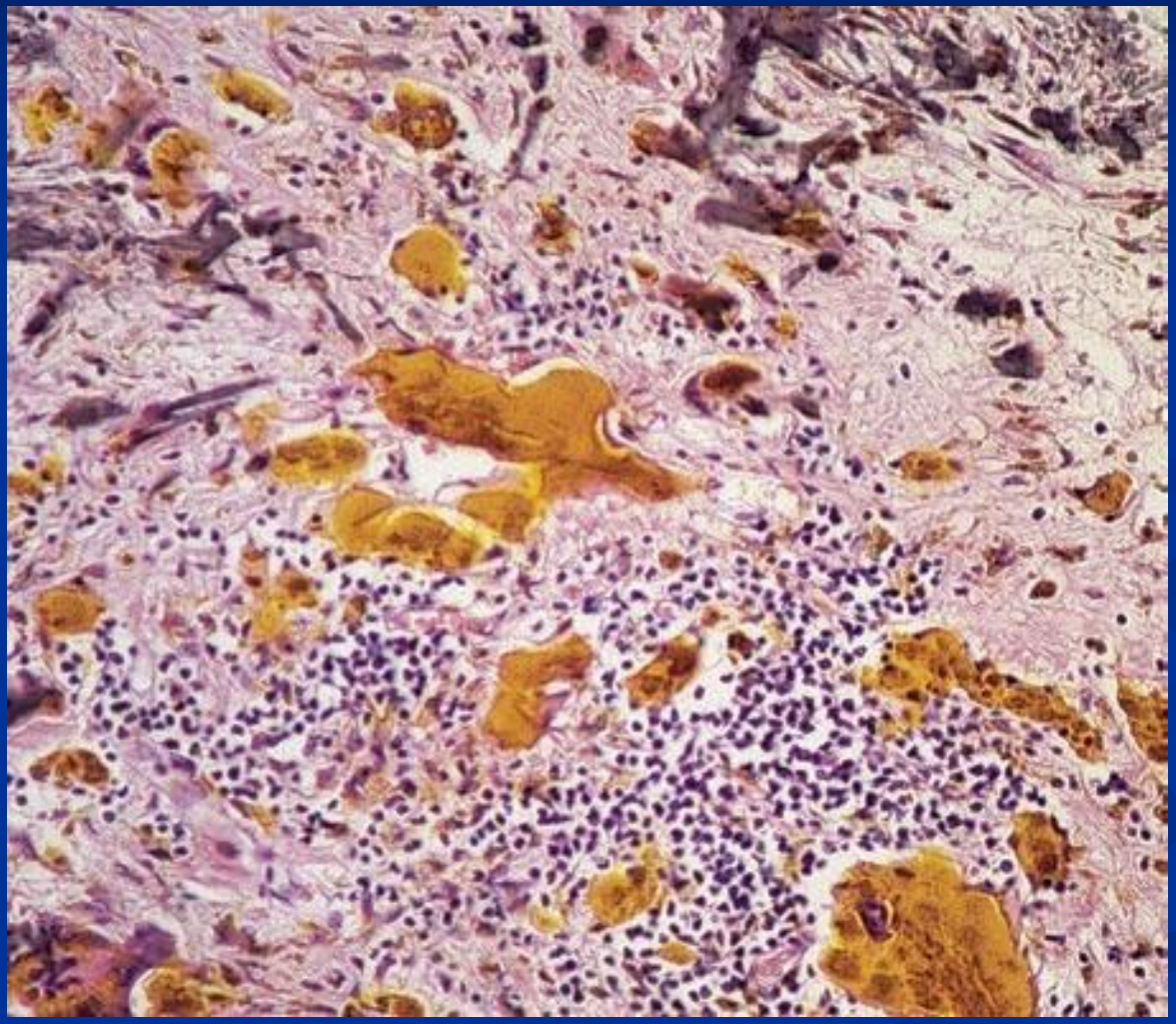
- Hemosiderosis of spleen. Perl's method. X 400.



Hematoidin

- Definition: Nonferrous, reddish brown pigment containing pyrrole (indirect bilirubin).
- Pathogenesis: Macrophages are unable to approach erythrocytes in the center of a hemorrhage. The resulting disintegration of hemoglobin results in the release of iron and crystallization of residual material containing pyrrole rings. The disorder takes three weeks to develop.

- **Hematoidin** (HE) x 150



Bilirubin

- Hyperbilirubinemia
- General definition: The cardinal symptom is jaundice with yellow discoloration of the skin, sclera, soft palate, and internal organs.

Jaundice

- Hemolytic jaundice
- Parenchymal jaundice
- Obstructive jaundice

Hepatic processing of bilirubin involves

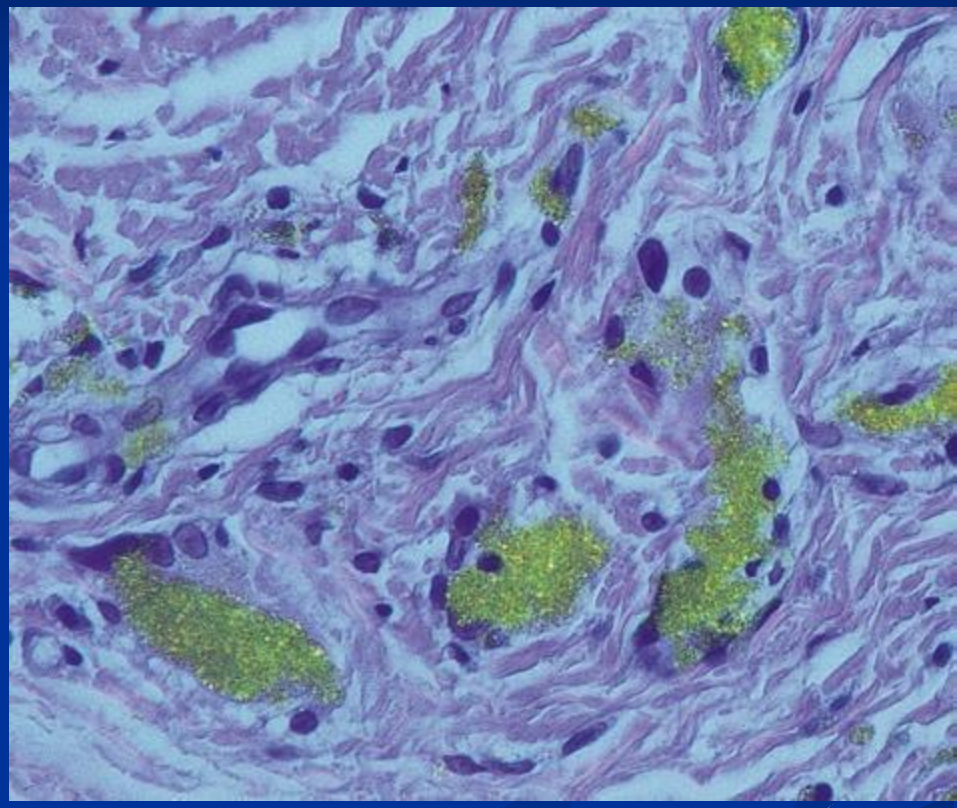
1) carrier-mediated uptake at the sinusoidal membrane;

- 2) intracellular binding, especially to ligandin;
- 3) delivery to endoplasmatic reticulum, possibly by rapid membrane-membrane transfer;
- 4) conjugation with one or two molecules of glucuronic acid by bilirubin glucuronosyltransferase;
- 5) excretion of the water-soluble, nontoxic bilirubin glucuronides into bile.

- Clinical jaundice appears when bilirubin is elevated in blood and is deposited in tissues.
- Normal blood levels of bilirubin are less than 1.2 mg/dl.
  Jaundice becomes evident when bilirubin levels rise above 2.0 to 2.5 mg/dl;
  levels as high as 30 to 40 mg/dl can occur in severe disease.

- **Skin jaundice**

- Bilirubin in the breakdown of a hematoma (HE) x 250



Excessive Bilirubin Production

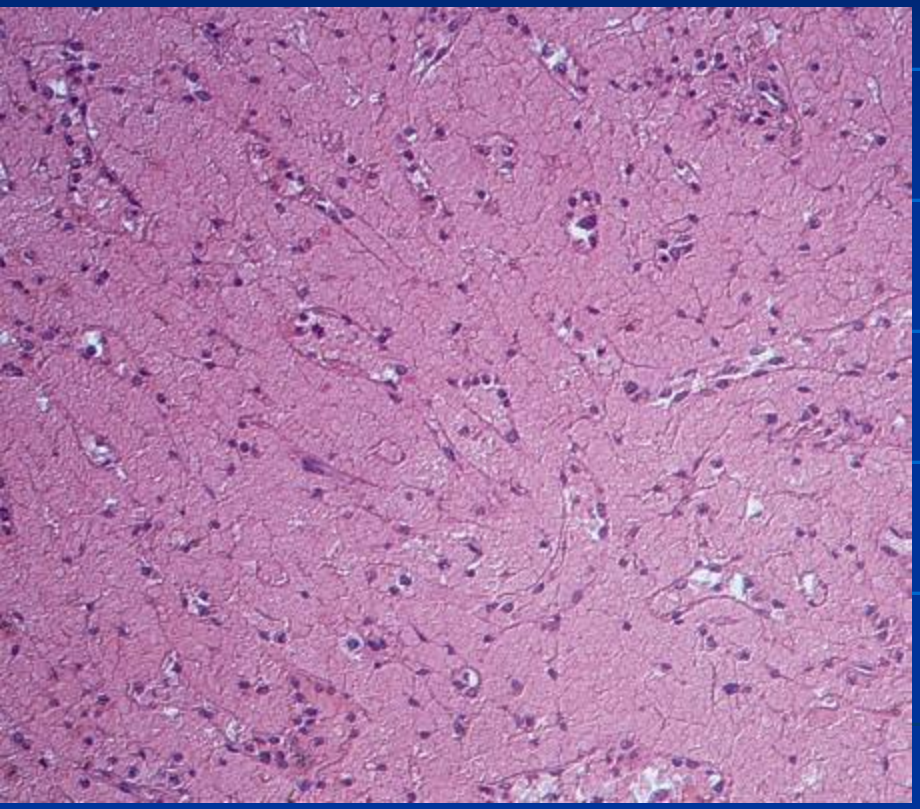
Hemolytic jaundice

Pathogenesis: Etiologic factors: — Hemolysis (erythrocyte disintegration) involves massive premature destruction of erythrocytes due to membrane, enzyme, or hemoglobin defects, or due to mechanical, toxic, immunologic, or microbial damage. The resulting increased breakdown of erythrocytes in the spleen causes spent erythrocytes to accumulate in the sinus; the sinus epithelia contain iron due to the phagocytosis of erythrocytes.

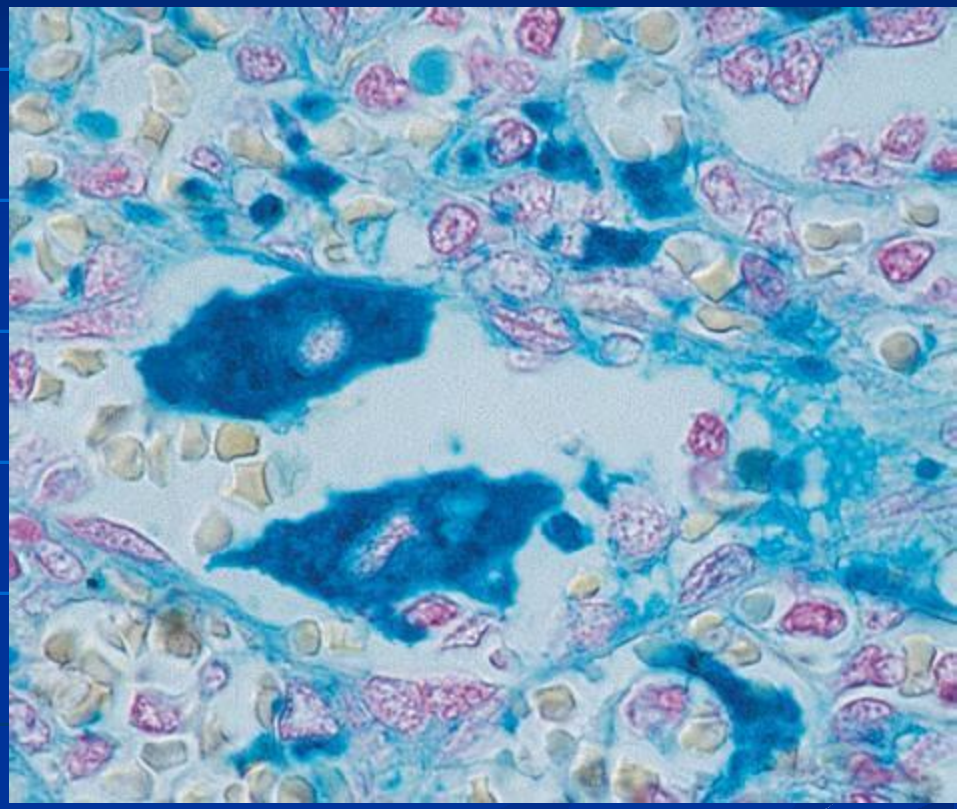
- **Normal liver**

- **Liver in jaundice**

- **Spleen: immune hemolysis**
- (HE) x 100



Spleen: immune hemolysis (iron stain) x 100



Neonatal Jaundice

Definition and pathogenesis:

Underdeveloped enzyme leads to a relative deficiency of bilirubin uridine diphosphate glucuronyl transferase due to transient hyperbilirubinemia on the second through fifth day after birth. The disorder is common.

Parenchymal jaundice

- Hepatic diseases:
- Acute and chronic hepatic failure (poisons)
- Hepatitis
- Liver cirrhosis

Obstructive jaundice

- The definition of cholestasis varies according to specialty:
- – Morphology: bile retention in the bile ducts.
- – Physiology: impaired bile drainage.

– Clinical presentation: retention of substances normally eliminated with the bile.

Intralobular Intrahepatic Cholestasis

- Pathogenesis: Defective hepatocellular excretion of bilirubin. Causes include:
- — Toxic cholestasis;
- — Hepatitic cholestasis;
- — Gestational cholestasis;
- — Postoperative cholestasis;
- — Cholestasis due to venostasis.

Extralobular Intrahepatic Cholestasis

- Pathogenesis: Destructive cholangitis or cirrhotic liver changes destroy the intrahepatic bile drainage routes. This in turn disrupts the intrahepatic passage of bile, resulting in intrahepatic obstructive jaundice.

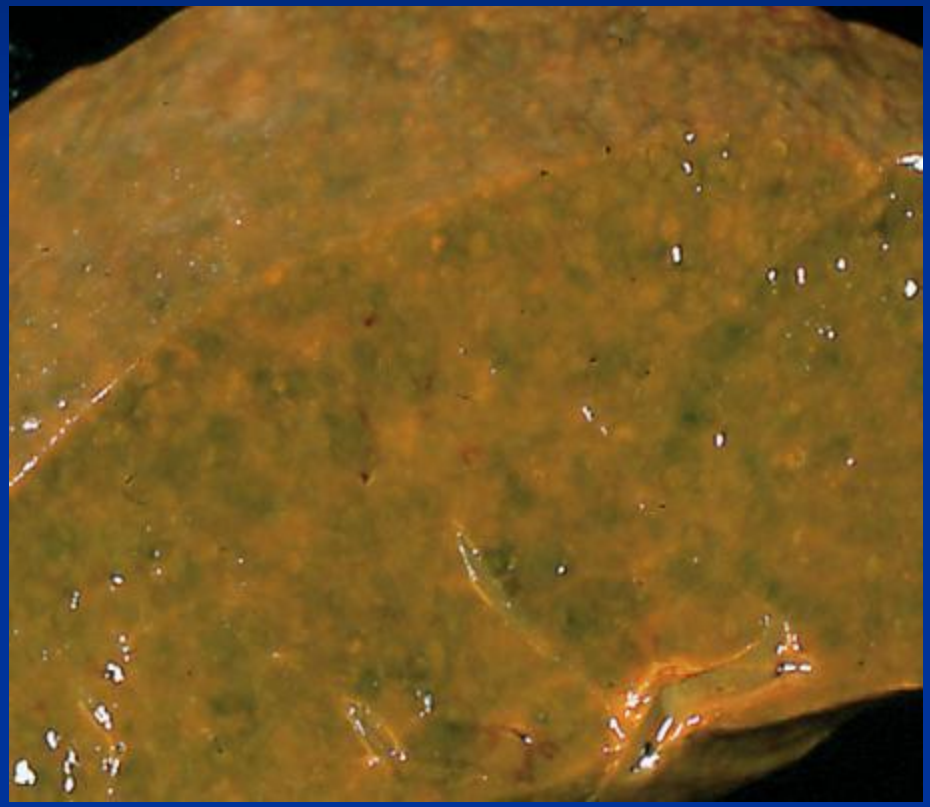
Extrahepatic Cholestasis

- Pathogenesis: Gallstones, tumors, inflammatory strictures, or biliary tract deformities result in the mechanical blockage of bile excretion, resulting in occlusive jaundice.
- Morphology: Greenish cylinders of bile (bile thrombi), occasionally resembling antlers, are observed in expanded intracellular canaliculi. This is accompanied by droplets of bile in the hepatic epithelia, progressing from the center to periphery of the lobes. Extrahepatic obstructive jaundice leads to accumulation of bile in the periphery of the lobes, with bile excretion from the ductuli.

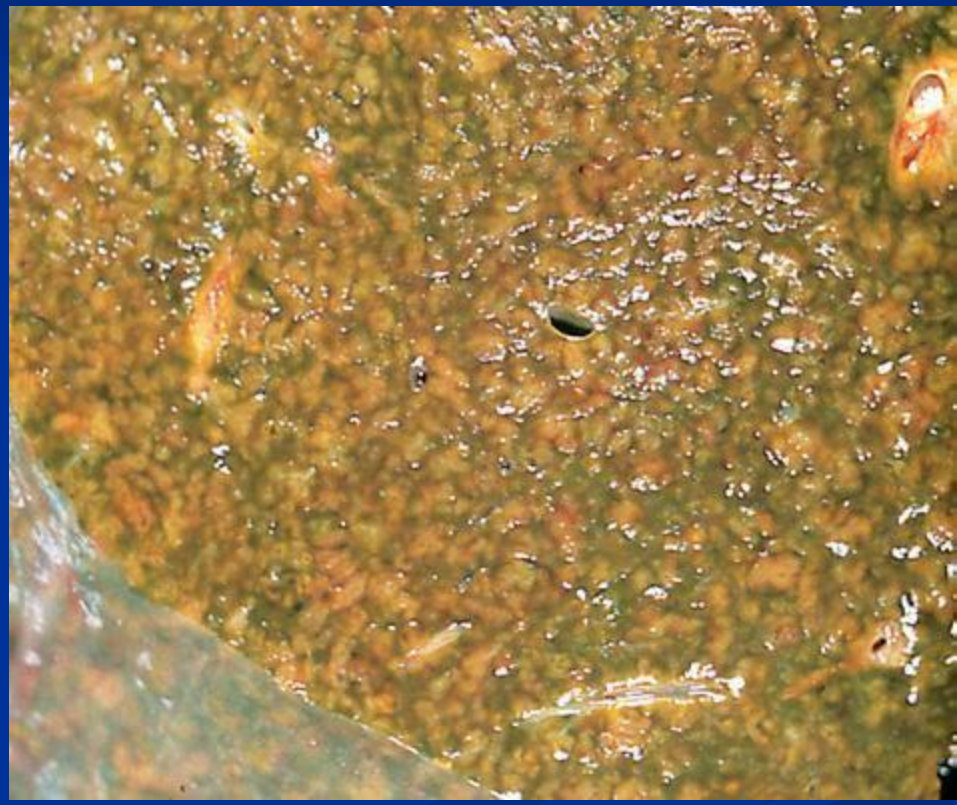
Accumulation of bile inthe periphery of lobes has several repercussions:

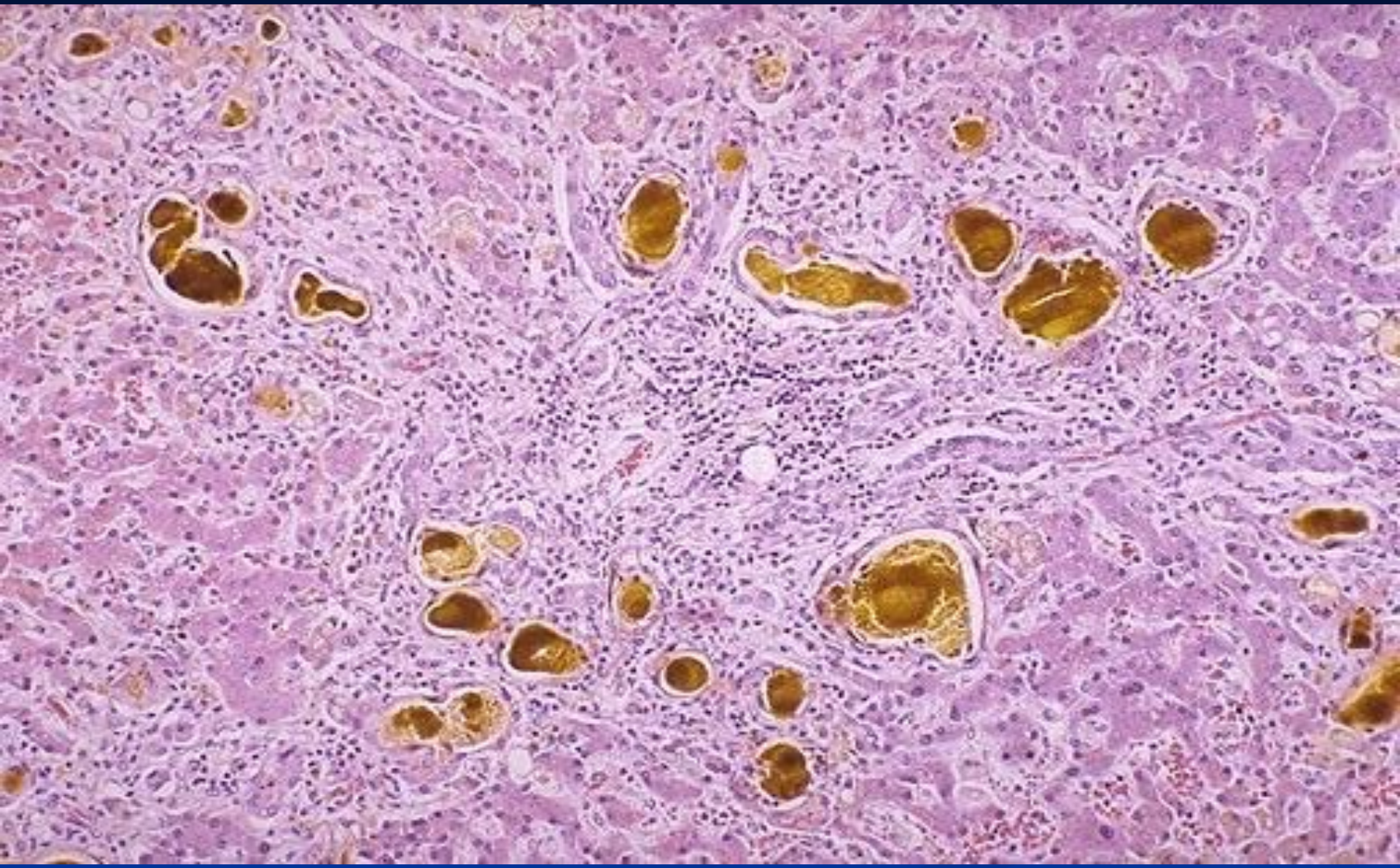
- Greenish discoloration of the liver parenchyma occurs.
- — Damage to the hepatic and biliary epithelia successively results in hepatocyte degeneration (ballooning), bile infarction and necrosis, phagocytosis of the excreted bile droplets by macrophages, infiltration of histiocytes into the portal regions, and elimination of the necrotic tissue.
- — Ductuli from interrupted biliary ducts proliferate into the portal regions.

- **Liver in cholestasis**

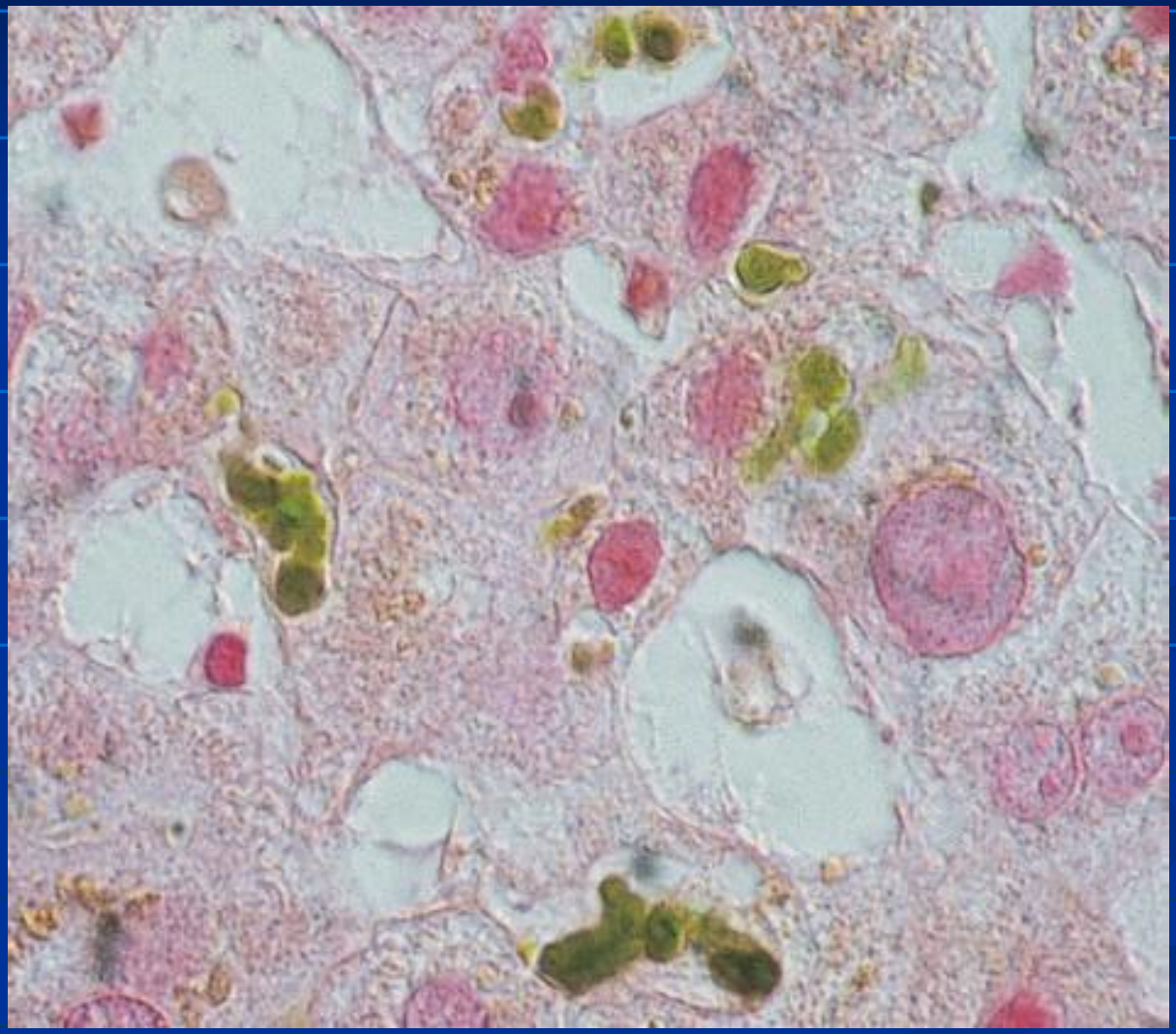


- **Cholestatic liver cirrhosis**





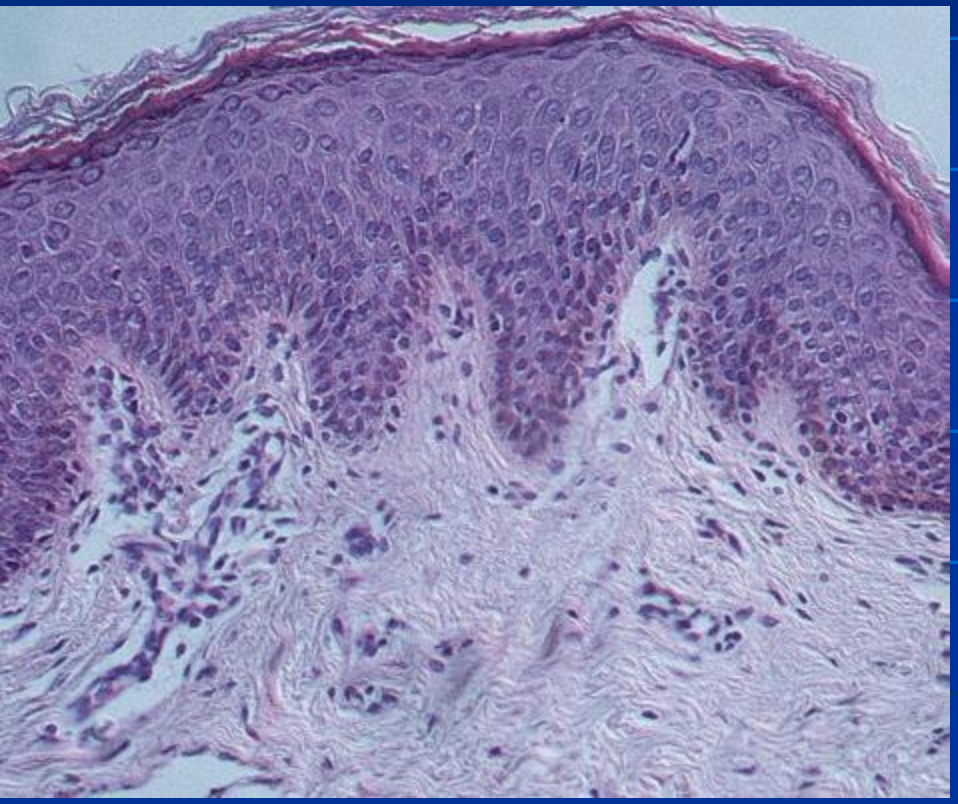
Cholestasis (nuclear-fast red) x 400



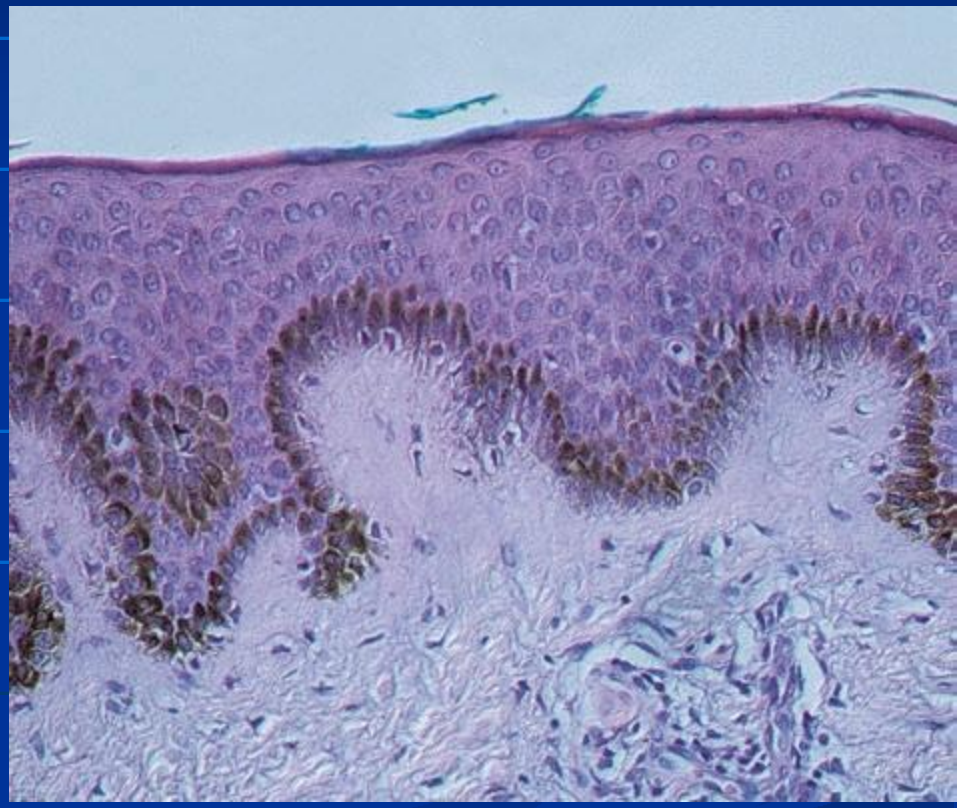
Tyrosine-Derivative Pigments

- Cutaneous Melanin
- Physiology: Melanin is a brownish-black pigment. It is generated in the form of small granules in normal melanocytes and in melanoma cells.
- Melanogenesis : Melanin formation begins in the melanoblasts of the neural crest. Beginning in the eighth week of pregnancy, they form families of cells that migrate in a mosaic-like pattern initially into the epidermis and later into the hair follicles.

Normal skin: (white)
(HE) x 100



Normal skin: (black)
(HE) x 100

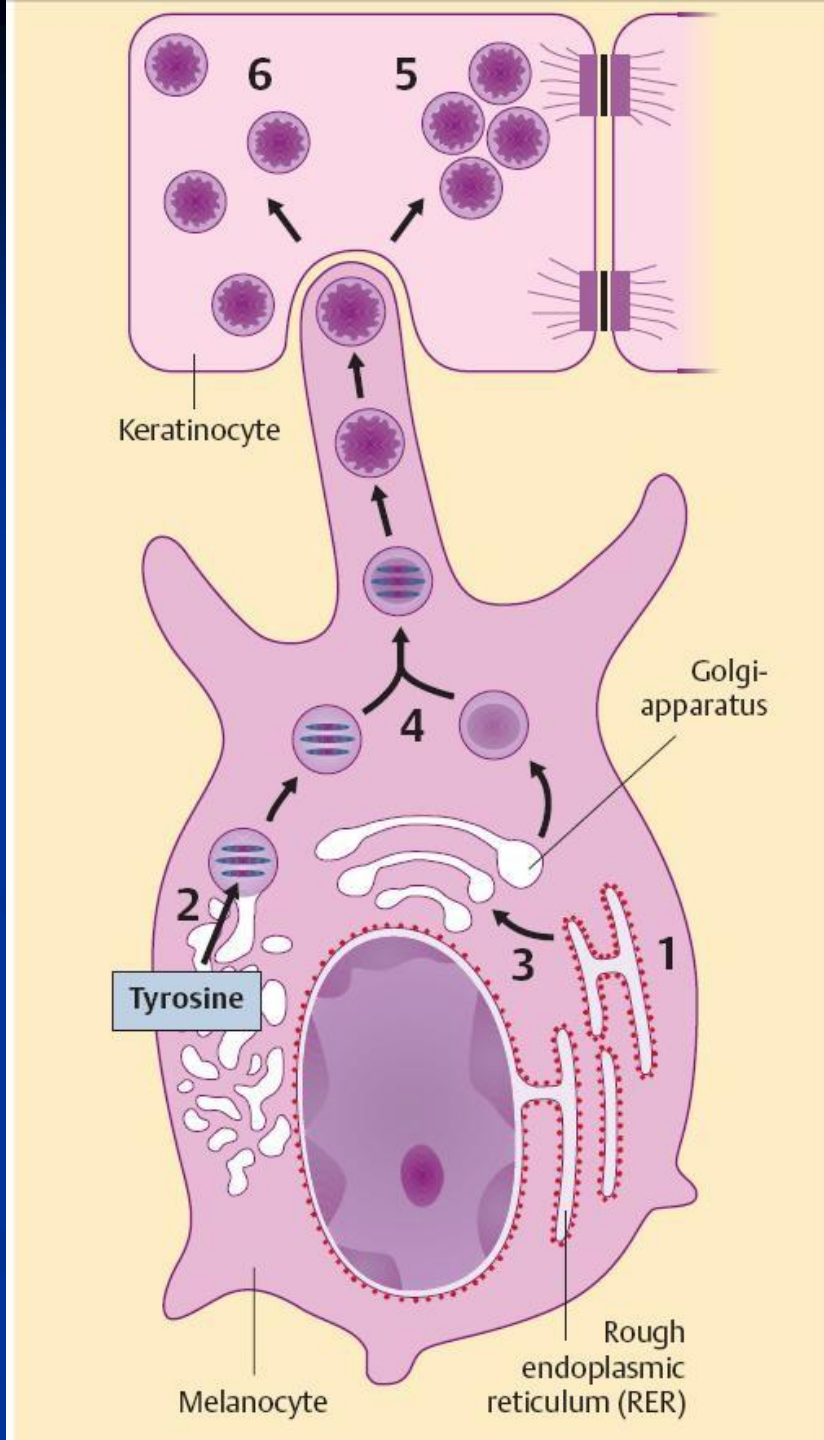


Melanogenesis:
Melanoblasts differentiate in the skin into melanocytes:

- Ribosomal synthesis of tyrosinase, which is controlled by a gene in the albino locus.
- Transport of tyrosinase into the cisterns of the rough ER.

Active membrane transport of tyrosine into the melanocytes.

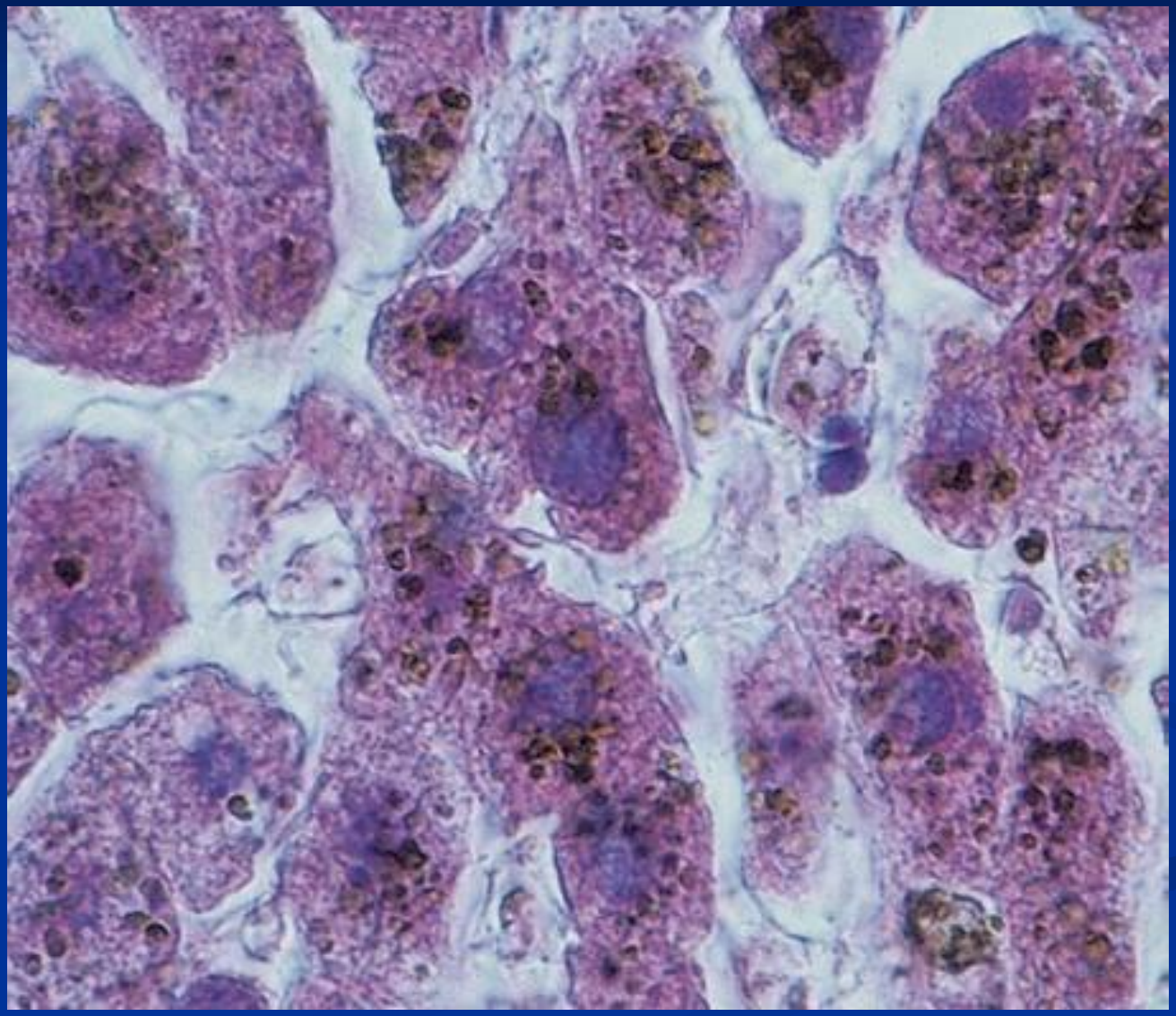
- The tyrosinase enters the Golgi apparatus and is packaged together with the tyrosine in melanosomes. There the melanin is synthesized. Synthesis is controlled by tyrosinase (phenol oxidase); the sequence is tyrosine to dopa to dopaquinone to ndole quinone to polymerization and protein binding.



Melanogenesis

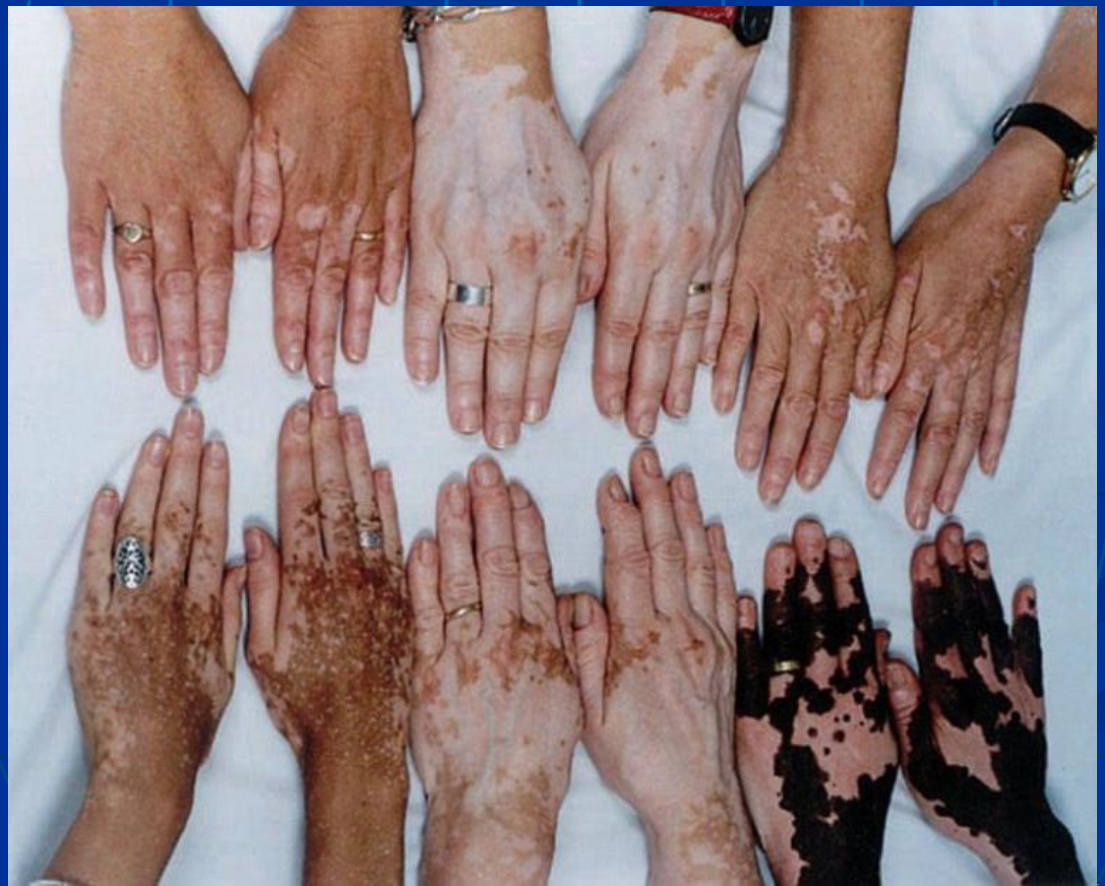
- Melanogenesis can be inhibited or stimulated according to the cell cycle. In the G1 phase, tyrosinase activation (ACTH and estrogens) results in increased melanin synthesis. In the G2 phase, melanotropin (MSH) stimulates melanin synthesis. Inhibitors of the tyrosinase system include melatonin (epiphyseal hormone), phenylalanine, and glutathione.

Malignant melanoma (HE) x 400



Vitiligo

- Definition: Rare, focal absence of skin pigmentation (zebra effect).
- Pathogenesis: The genetically determined death of certain melanoblasts leads to areas devoid of melanoblasts.



Albinism

- Clinical presentation: Extreme sensitivity to sunlight leads to skin tumors induced by ultraviolet radiation, impaired vision, and photophobia.
- Prenatal diagnosis is made by amniocentesis.

Hemochromatosis

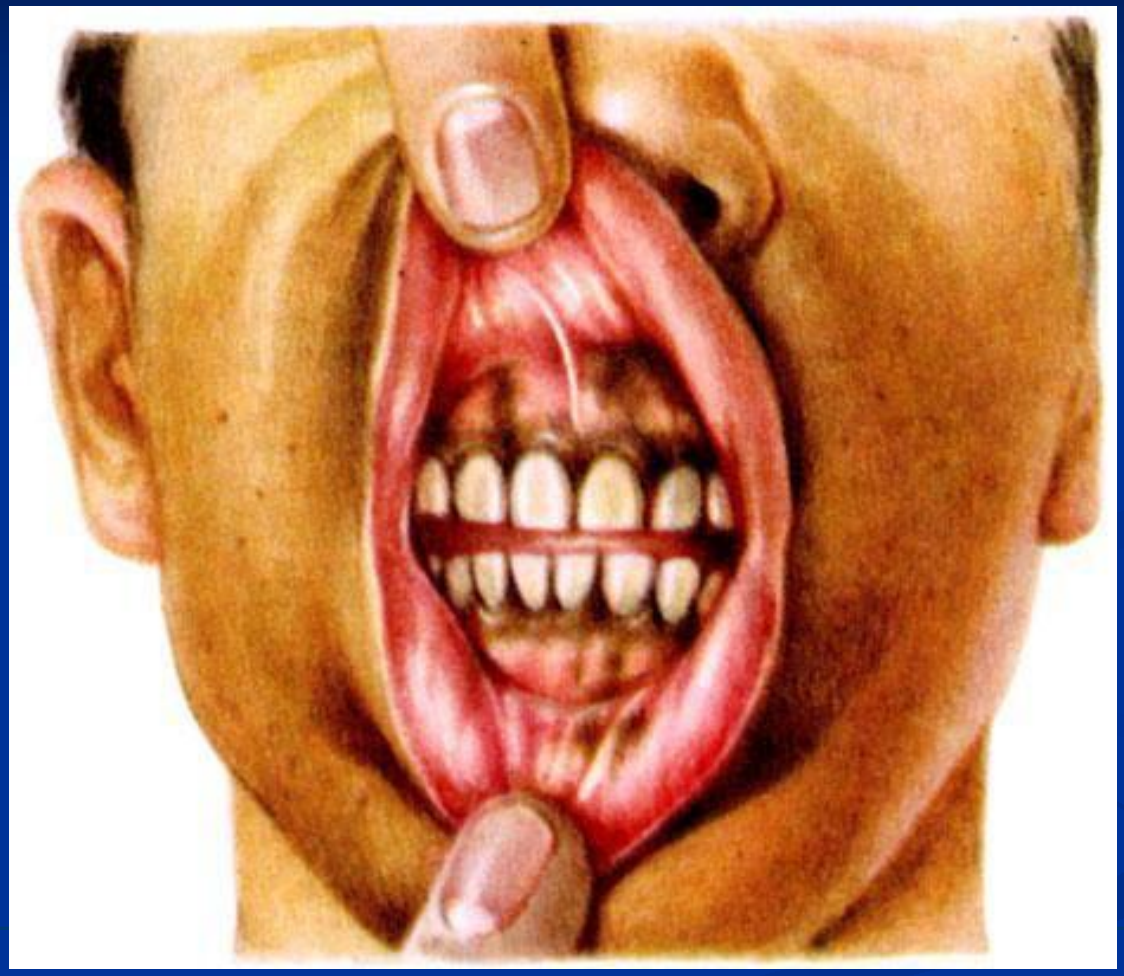
- Inactivation of glutathione by non-proteinbound iron leads to disinhibition of the tyrosinase system and increased melanin synthesis.
- The result is brown skin.

Addison's Disease

- Definition: This common disorder involves an adrenal cortex insufficiency syndrome with glucocorticoid deficiency (hypocorticism).
- Etiologic forms of Addison's disease:
- — Primary or adrenal forms involve hereditary (metabolic disorder or deformity), inflammatory (autoimmune or tuberculous), neoplastic, circulatory, or necrotic damage to the adrenal cortex.
- — Secondary or hypophyseal forms involve hereditary (brain deformity), necrotic, or neoplastic hypophyseal damage.

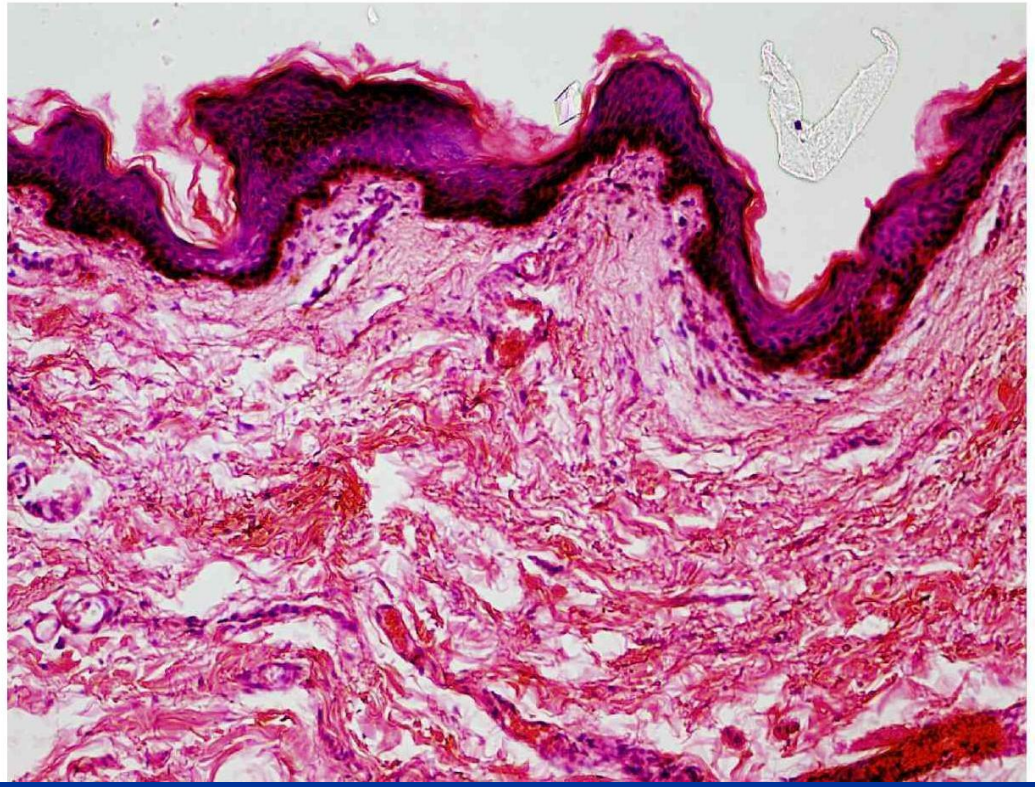
- Primary forms:
- Damage to the adrenal cortex lowers the level of
- glucocorticoids, androgens, and aldosterone, resulting in reactive overproduction of ACTH and MSH. This stimulates the melanocytes, which increase melanin synthesis.
- Secondary forms: Hypophyseal damage lowers the level of ACTH and MSH. This depresses the level of glucocorticoids but not the level of aldosterone, which is regulated by the renin-angiotensin system. The resulting MSH deficiency means that melanocytes are not stimulated, blocking melanin synthesis.

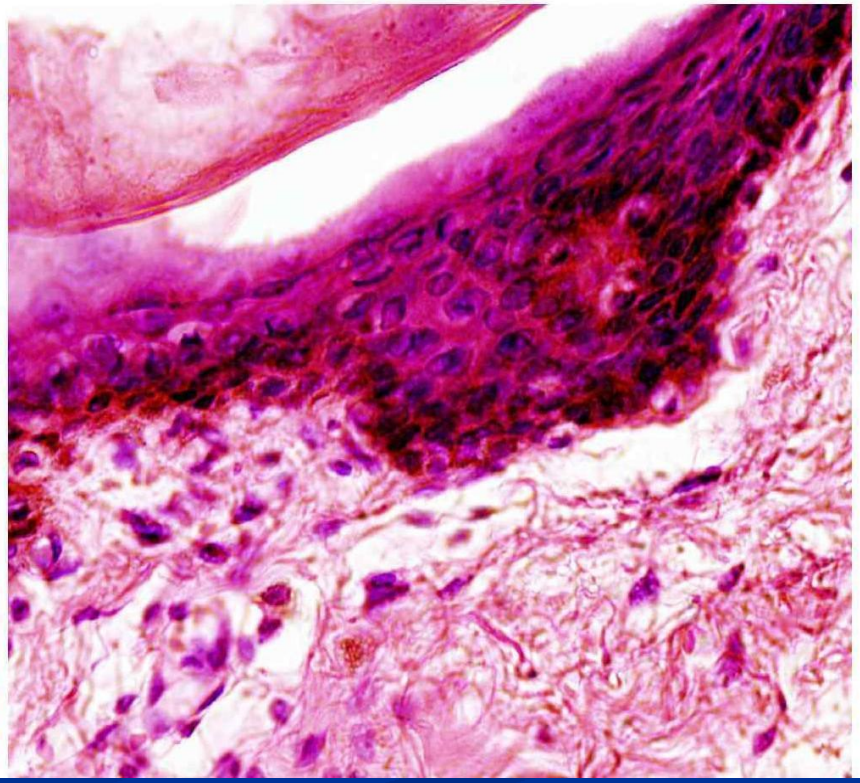
Skin in Addison's disease.



Pigmentation of the oral mucosa and hypermelanosis.

Micropreparation. Skin in Addison's disease.





- **Normal substantia nigra**
- **Parkinson disease**

Disorders of the metabolism of lipidogenic pigments

- Lipofuscin is a small granular golden brown pigment formed from phospholipids and proteins. It accumulates in the cytoplasm as a result of damage to the membranes of cytoplasmic organelles. This is due to a lack of cellular antioxidants, which normally prevent lipid peroxidation of organelle membranes.

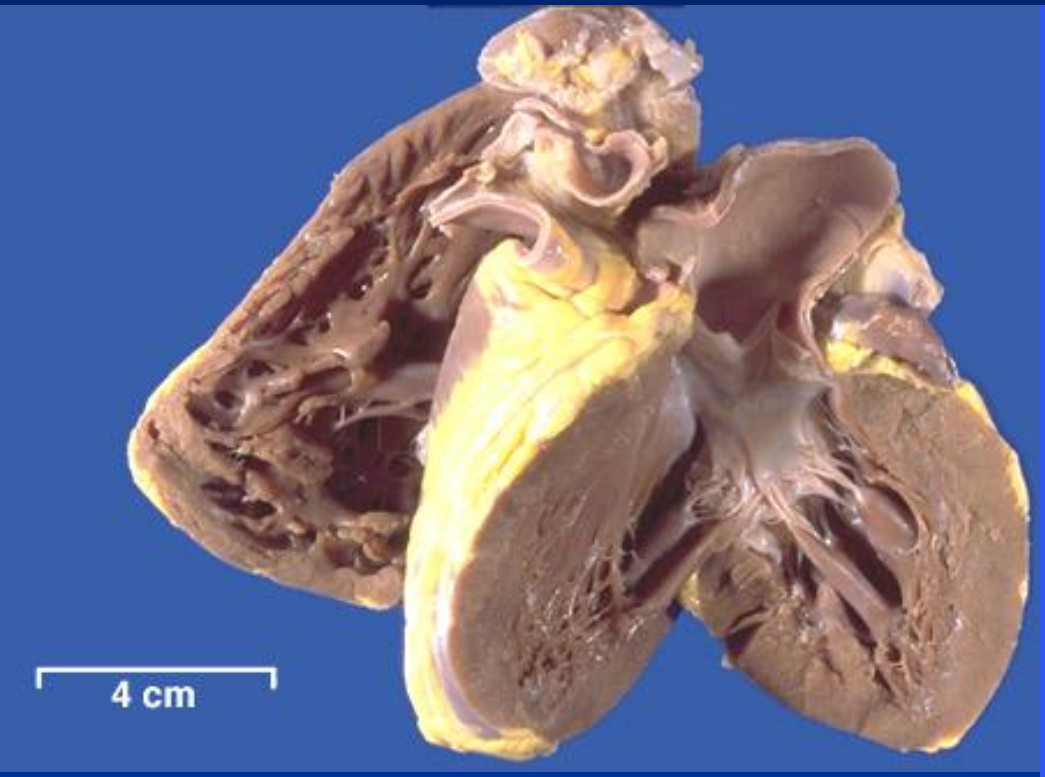
Lipofuscinosis

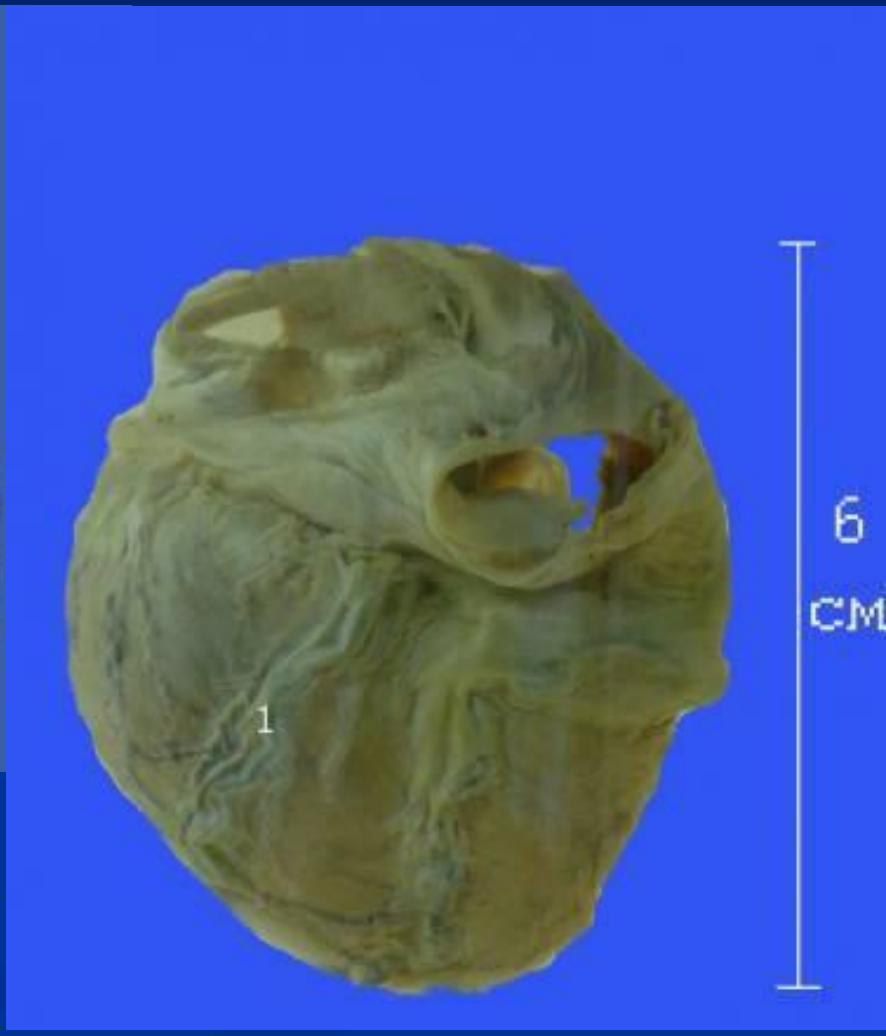
- Primary (hereditary) lipofuscinosis is characterized by the selective accumulation of lipofuscin in the cells of a particular organ.
- Examples of primary lipofuscinosis:
- - hereditary hepatosis (Dabin-Johnson syndrome) with selective accumulation of lipofuscin in hepatocytes, accompanied by benign hyperbilirubinemia.
- - neuronal lipofuscinosis (Spielmeier-Sjogren syndrome) is characterized by the accumulation of pigment in nerve cells, which is accompanied by a decrease in intelligence, seizures, and visual impairment.

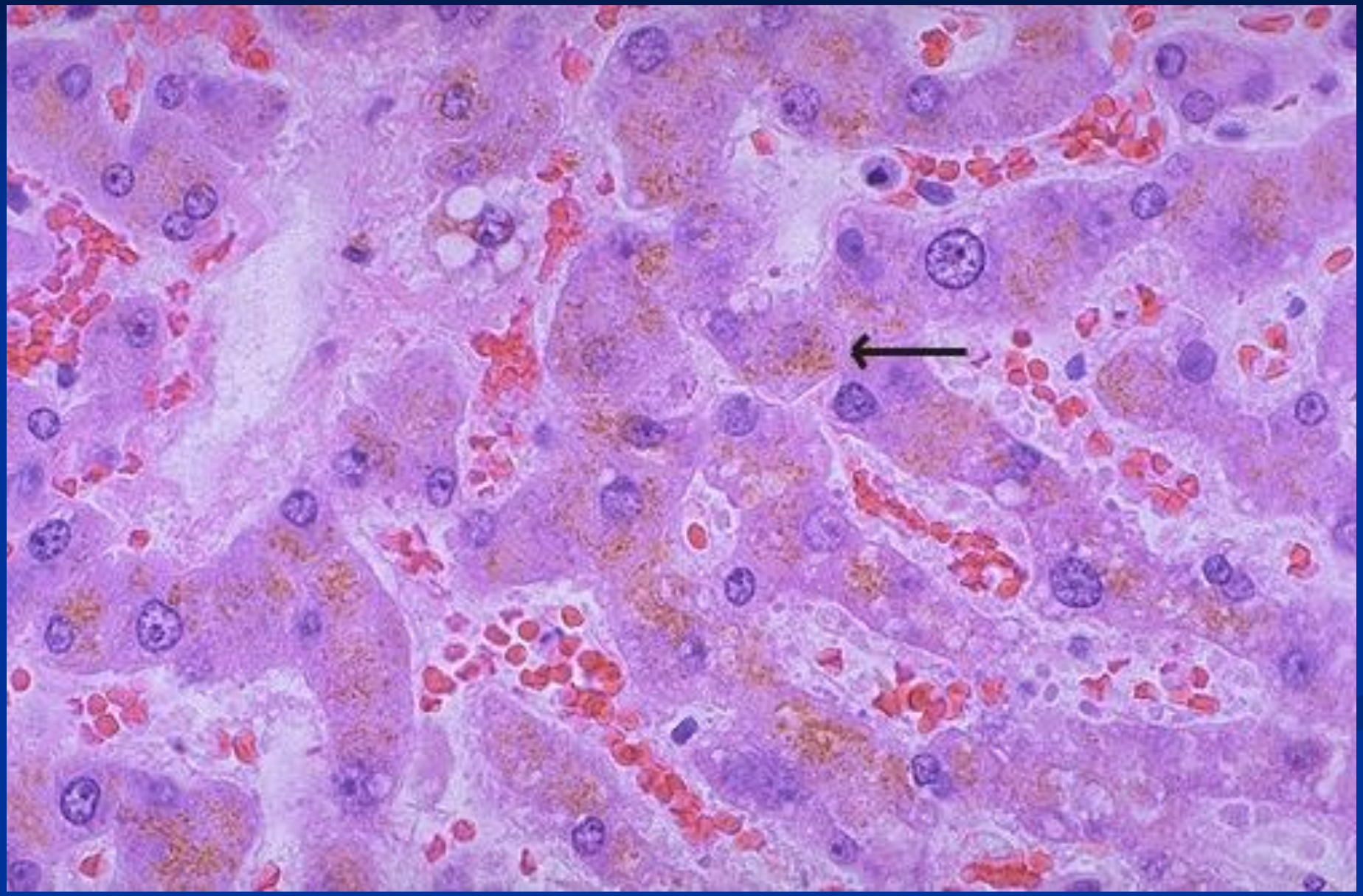
Secondary lipofuscinosis

- occurs more often in older people with severe malnutrition (cachexia) and in the presence of chronic diseases (brown myocardial atrophy, liver). Lipofuscin is also called the "wear" pigment. Most often, it accumulates in cardiomyocytes, hepatocytes and neurons. The reasons for its accumulation can be drug intoxication (analgesics), vitamin E deficiency. Sometimes it appears in cells with increased functional load (myocardial lipofuscinosis in heart disease). Lipofuscin does not cause any cell dysfunction.

Lipofuscinosis.
Brown myocardial atrophy







Hypocalcemia

- Definition: A decrease in the level of serum calcium below 2.2 mmol/l.
- Etiologic factors include:
- — Idiopathic, postoperative hypoparathyroidism;
- — Pseudohypoparathyroidism;
- — Malabsorption syndrome;
- — Vitamin D3 deficiency due to renal insufficiency.

  Morphology: The morphologic picture of hypocalcemia varies according to the specific etiology:

- Ineffectiveness of parathormone results in decreased osteoclastic and osteoblastic activity, which reduces bone turnover. This results in low-turnover osteoporosis
- Vitamin D3 deficiency: a malabsorption syndrome due to renal insufficiency; causes compensatory activation of the parathyroid glands results in increased release of parathormone (secondary hyperparathyroidism).
- This causes excessively high bone turnover with intensive bone resorption in which osteoclasts drill tunnels in the trabeculae (dissecting bone resorption), producing resorption cysts. Production of uncalcified osteoid material is simultaneously increased, and broad osteoid halos containing osteoblasts form. These fibrous osteoid formations trigger reactive fibrosis around the trabeculae (endosteal fibrosis).

Hypercalcemia

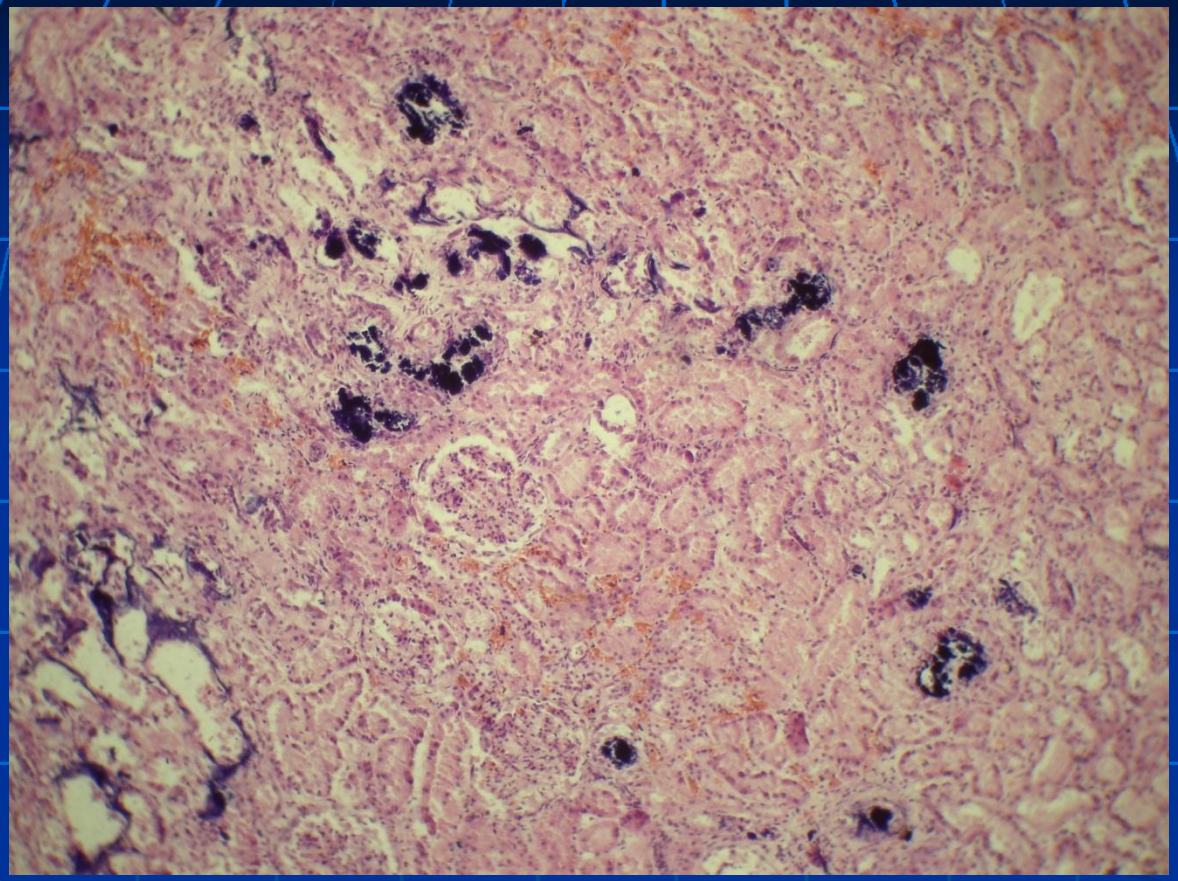
- Definition: An increase in the level of serum calcium above 2.8 mmol/l.
- Etiologic factors include:
- — Osteolytic bone metastases;
- — Parathormone-like substances excreted by tumor;
- — Primary hyperparathyroidism.

- Morphology: Endocrine-induced hypercalcemia leads to the following tissue changes:
- — Osteopenia (decreased bone density): An excessive quantity of parathormone results in proliferation of osteoclasts that gnaw away at bone trabeculae in dissecting bone resorption. At the same time osteoblasts with uncalcified fibrous osteoid proliferate, causing fibrosis adjacent to the trabeculae. The result is an increase in the level of serum calcium.

- — Kidney calcifications include kidney stones (nephrolithiasis) and metastatic calcification of the kidneys (nephrocalcinosis).
- — Gallstones (cholelithiasis) lead to cholecystitis.
- — Pancreatic stones in excretory ducts of the pancreas lead to pancreatolithiasis and inflammation.
- — Salivary stones in excretory ducts of the salivary glands lead to sialolithiasis and inflammation.
- — Gastric or duodenal ulcer results from increased gastrin secretion induced by calcium or parathormone.
- — Corneal calcification in the form of calcific band keratopathy.

Petrification in the lung

Depositions of calcium salts in the kidney.
H&E. X 100.

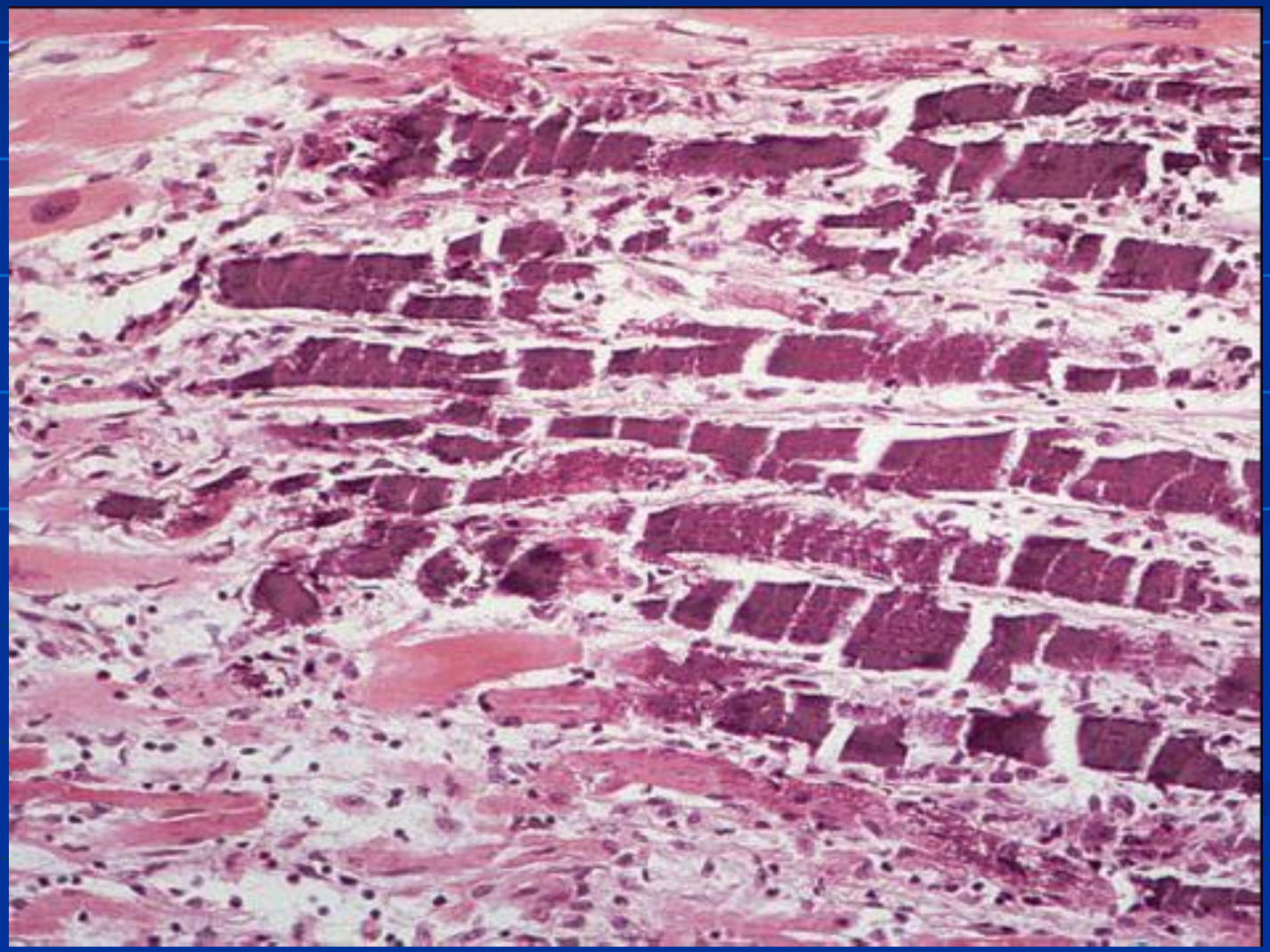


- Metastatic calcification
- Dystrophic calcification

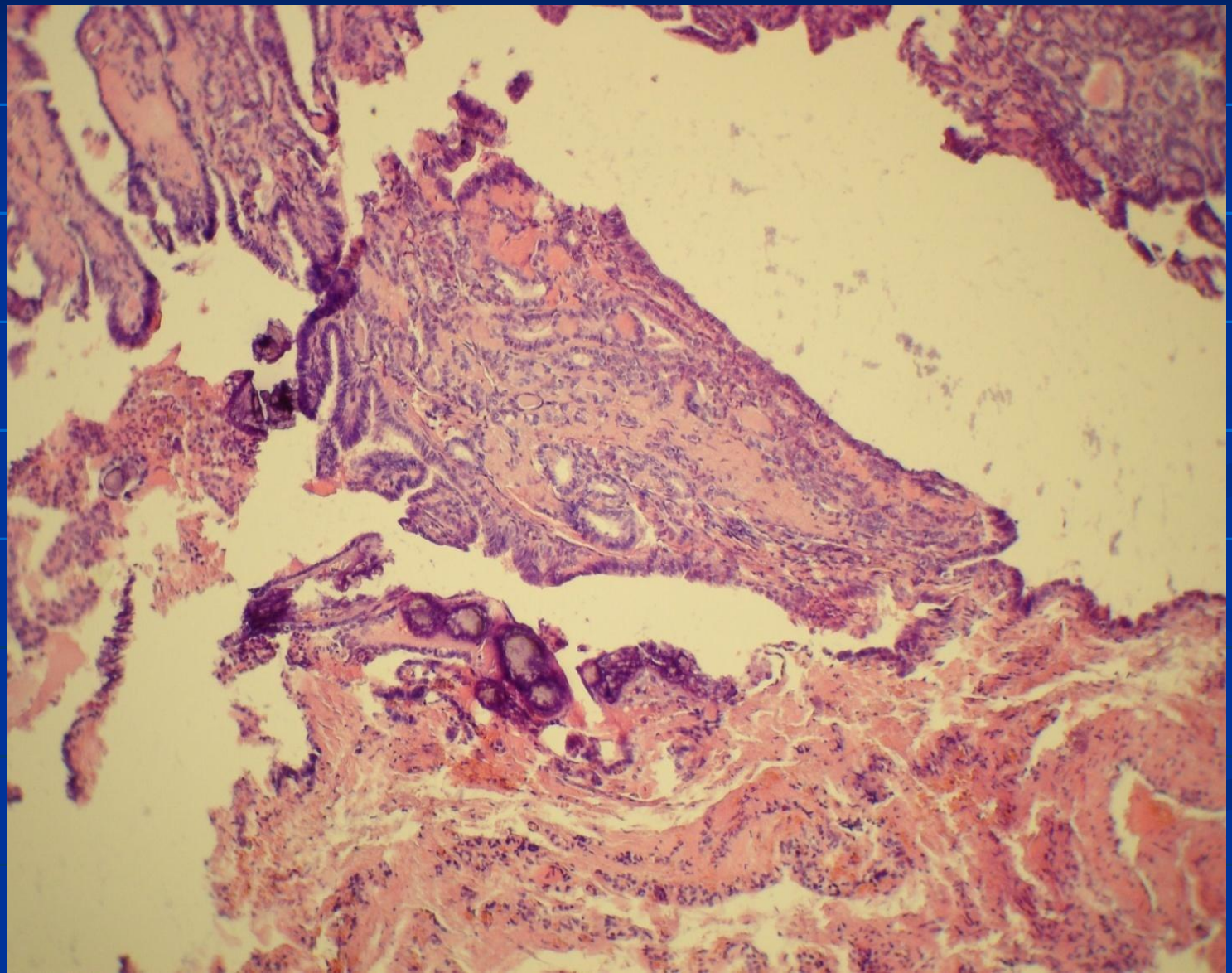
Metastatic calcification appears to begin also in mitochondria except in kidney tubules, where it develops in the basement membranes, probably in relation to extracellular vesicles budding from the epithelial cells.

Myocardial calcinosis

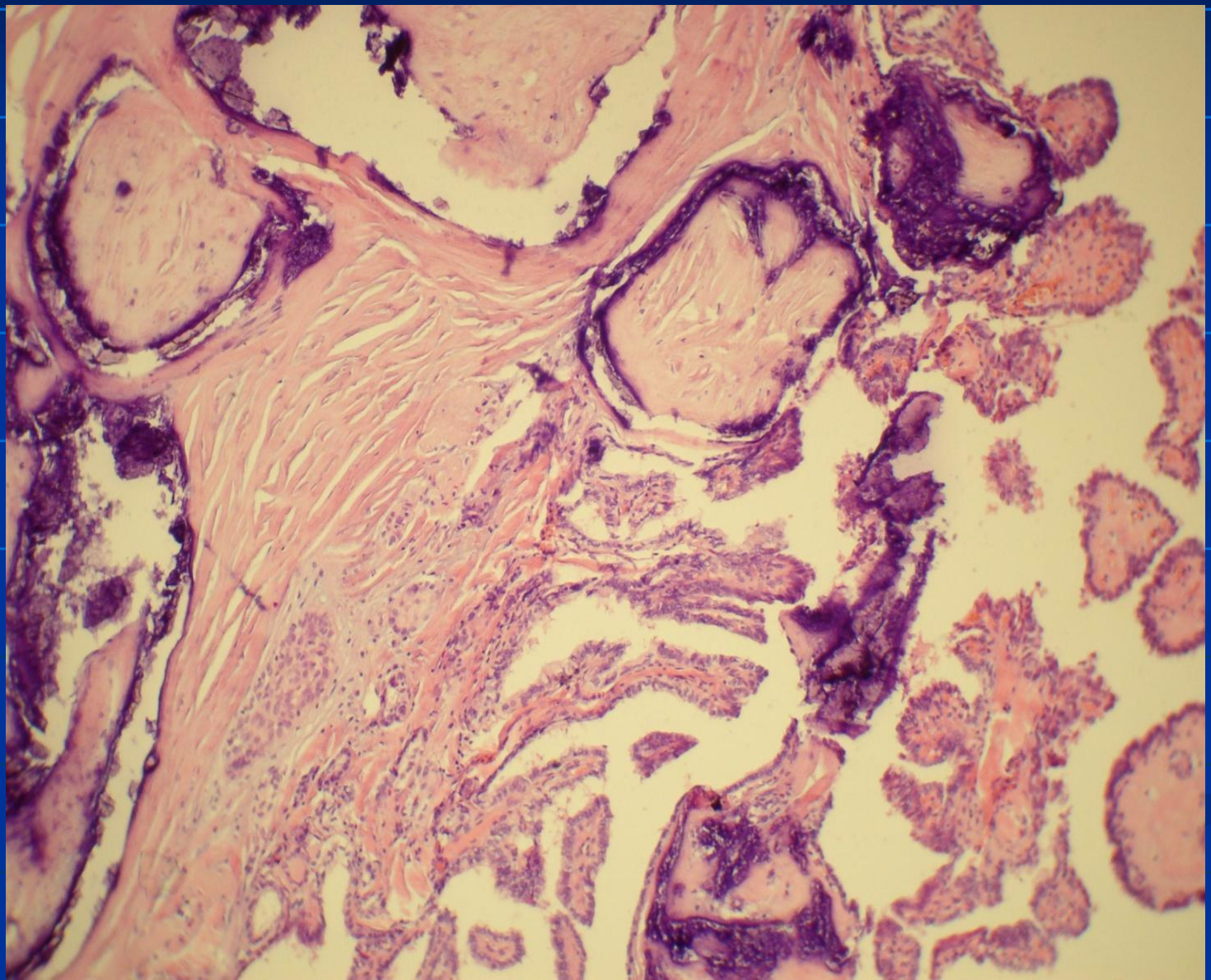
(HE) x 50



Depositions of calcium salts in the tyroid gland.
Papillary adenocarcinoma. H&E. X 100.



Depositions of calcium salts in the tyroid gland.
Papillary adenocarcinoma. H&E. X 100.



Thank you!