Intracellular Accumulations

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Fatty change

- Abnormal accumulation of lipids within cells

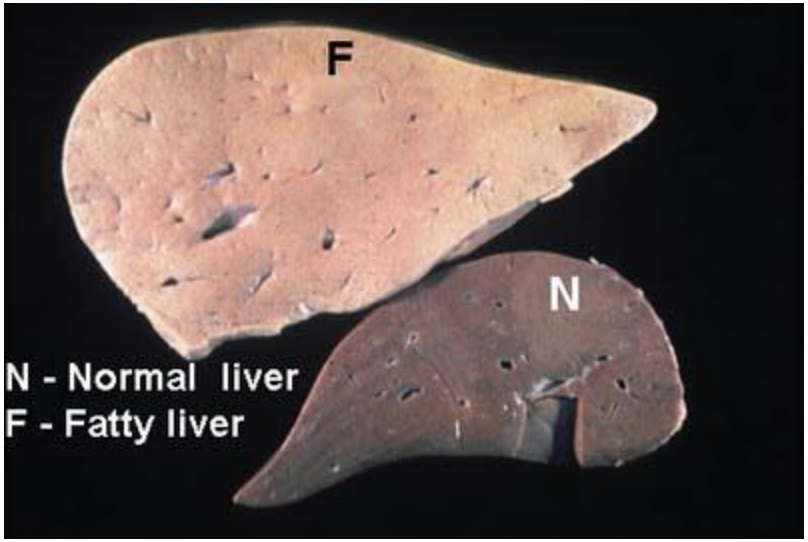
Foie gras

Fatty change cont.

- Most often seen in the liver. Why?
- Also occur in heart, skeletal muscle, Kidney
- Causes
  - DM
  - Obesity
  - Protein energy malnutrition
  - Toxins (phosphorus, drugs)
  - Anoxia

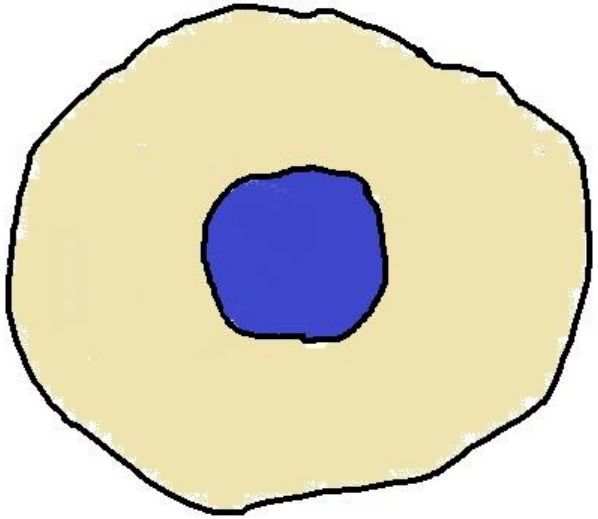
Morphology

- Macroscopy
  - Enlarged
  - Yellow in colour
  - Soft in consistency
  - Margins are rounded
  - The cut surface is greasy and bulges from the section

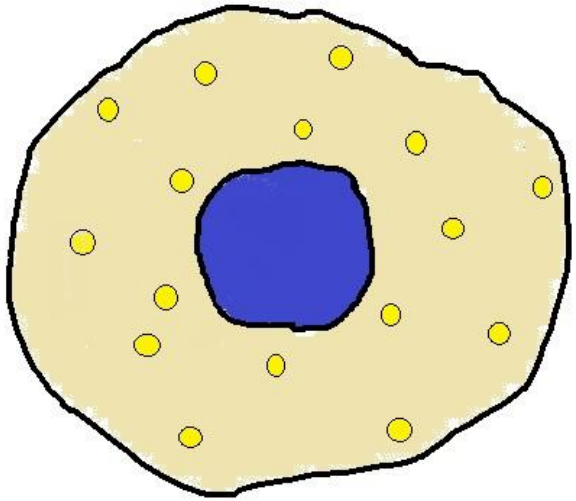


Microscopy

Normal cell



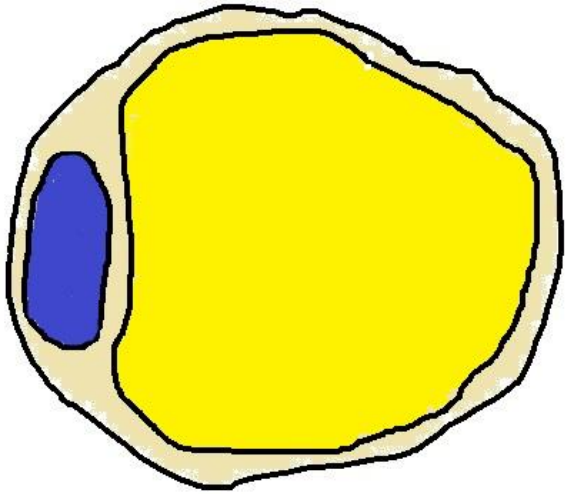
small fat vacuoles in the cytoplasm, first only around the nucleus

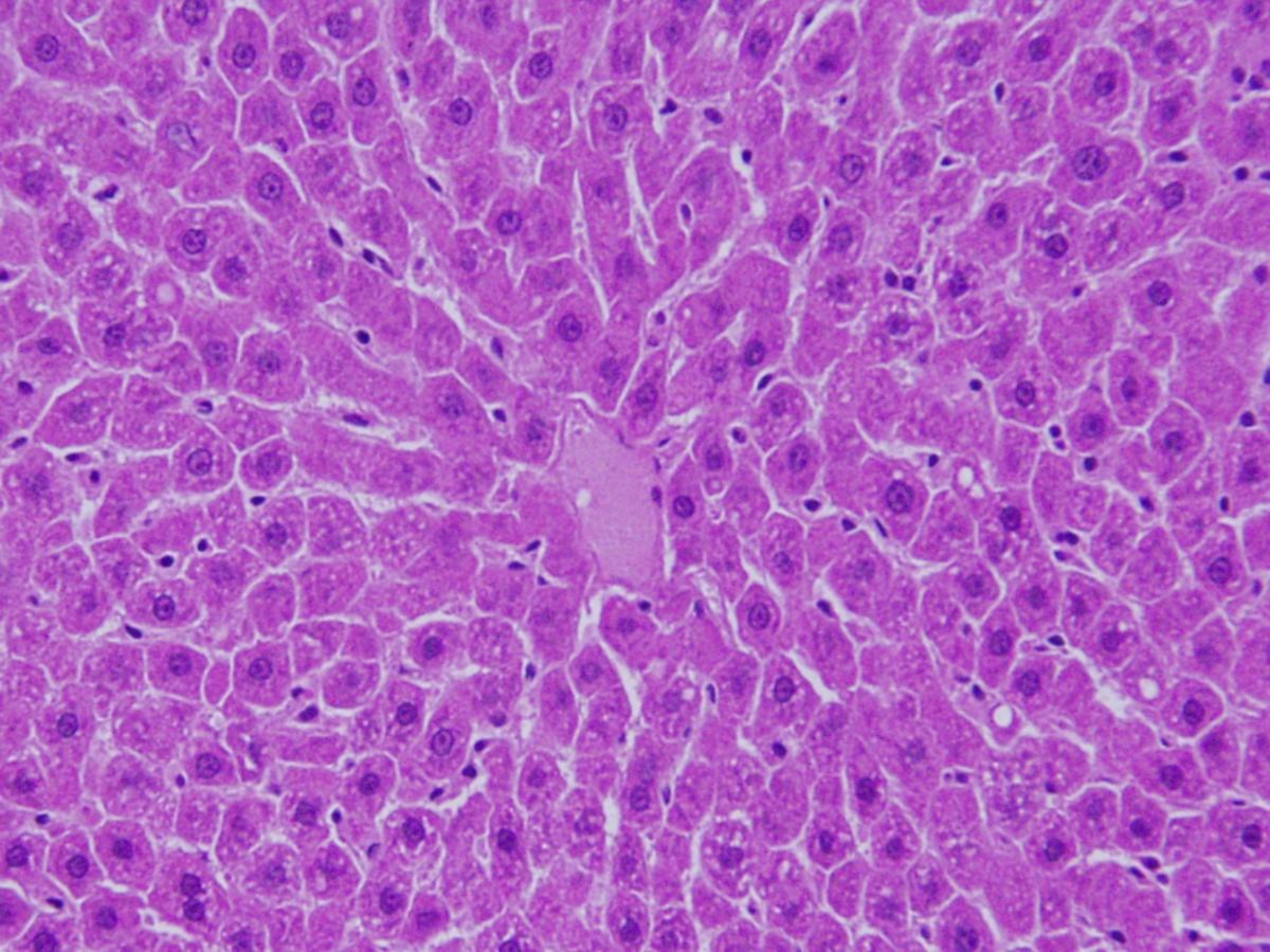


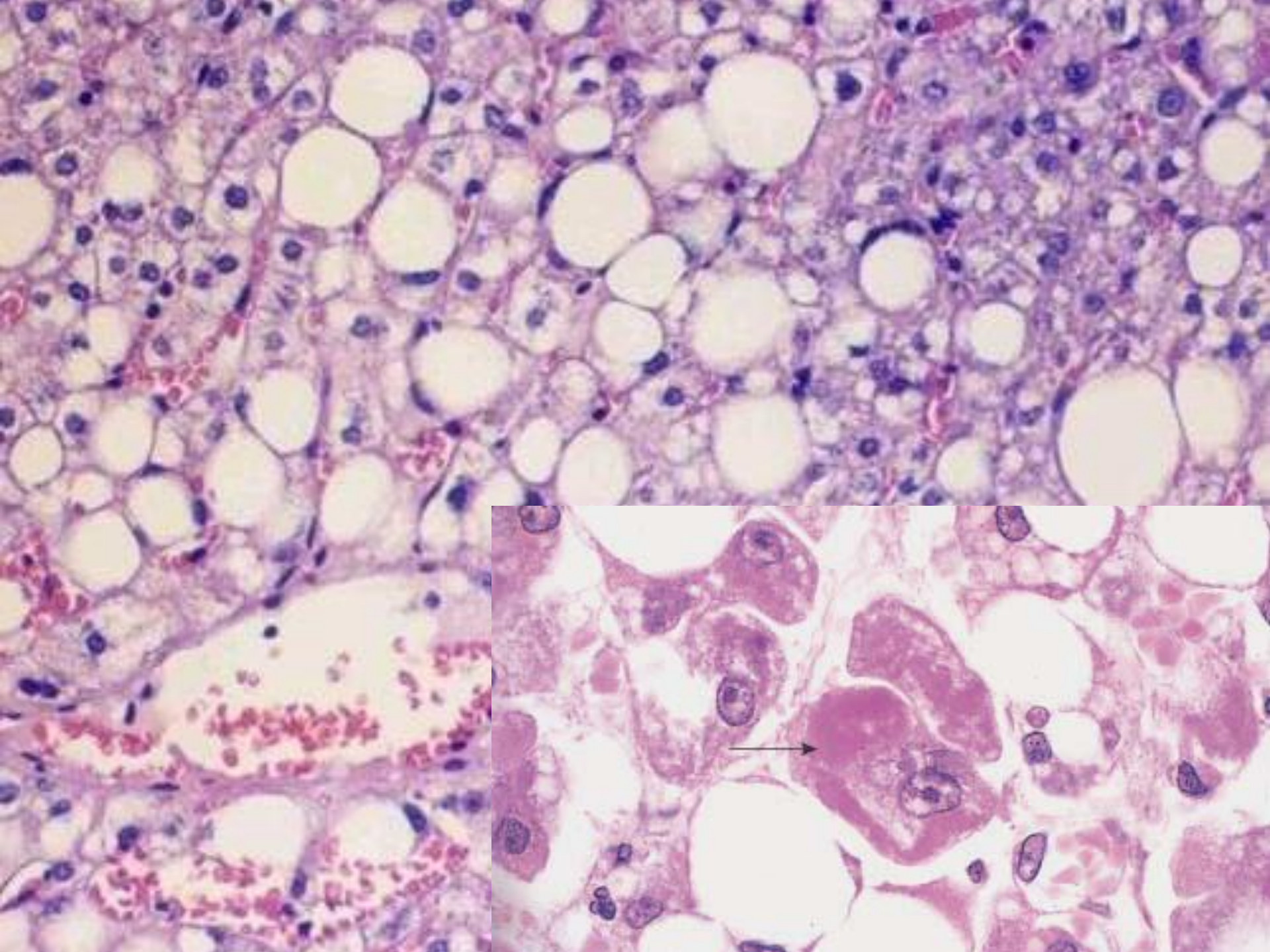
Microvesicular fatty change

later multiple vacuoles coalesce and may create large clear spaces - nuclei are displaced to the periphery of the cell

Macrovesicular fatty change

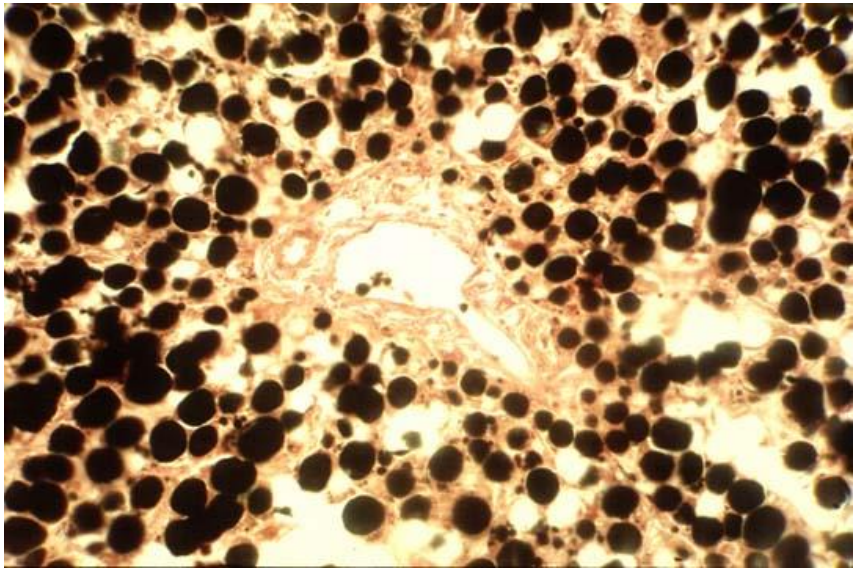




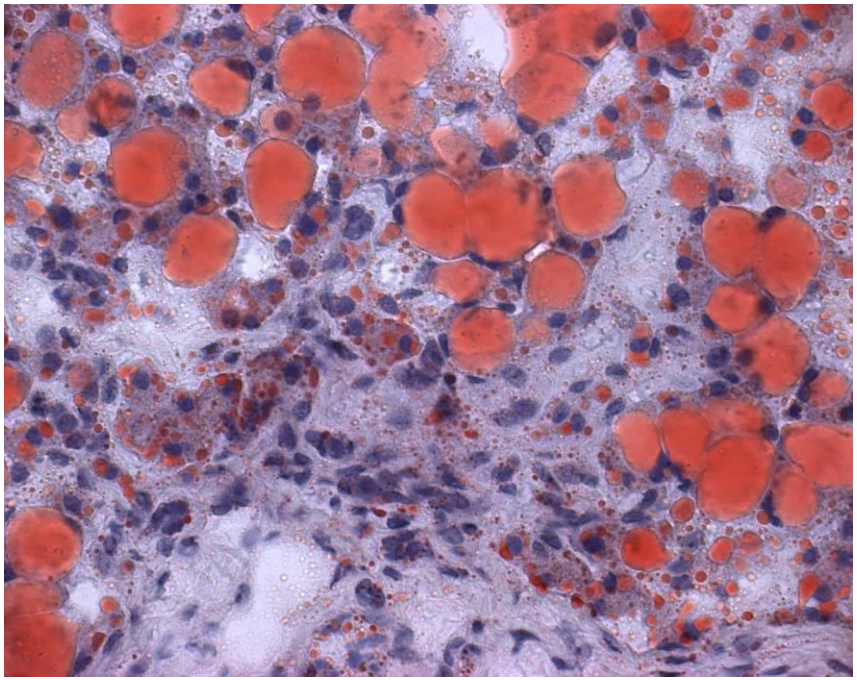


Special stains

Sudan IV



Oil red-O



Clinical significance

- Depends on the cause and severity of the accumulation.
  - **Mild** it may have no effect on cellular function.
  - **Severe** fatty change may transiently impair cellular function
  - In the severe form, fatty change may precede cell death, and may be an early lesion in a serious liver disease called nonalcoholic steatohepatitis

Pigments

- Pigment refers to a material that has color and can be seen without staining.
- Pigments play an important part in the diagnosis of diseases and conditions.
- It can be either normal or pathological.
- Endogenous/exogenous

Exogenous pigments

- Carbon
- Tattoo pigments

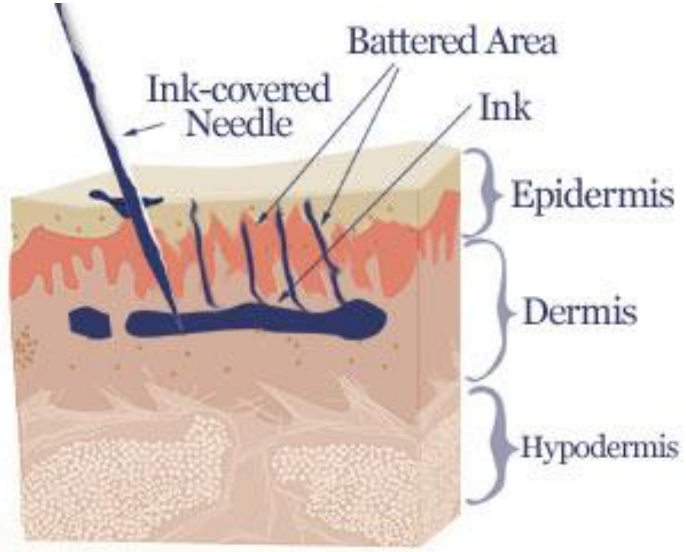
Carbon

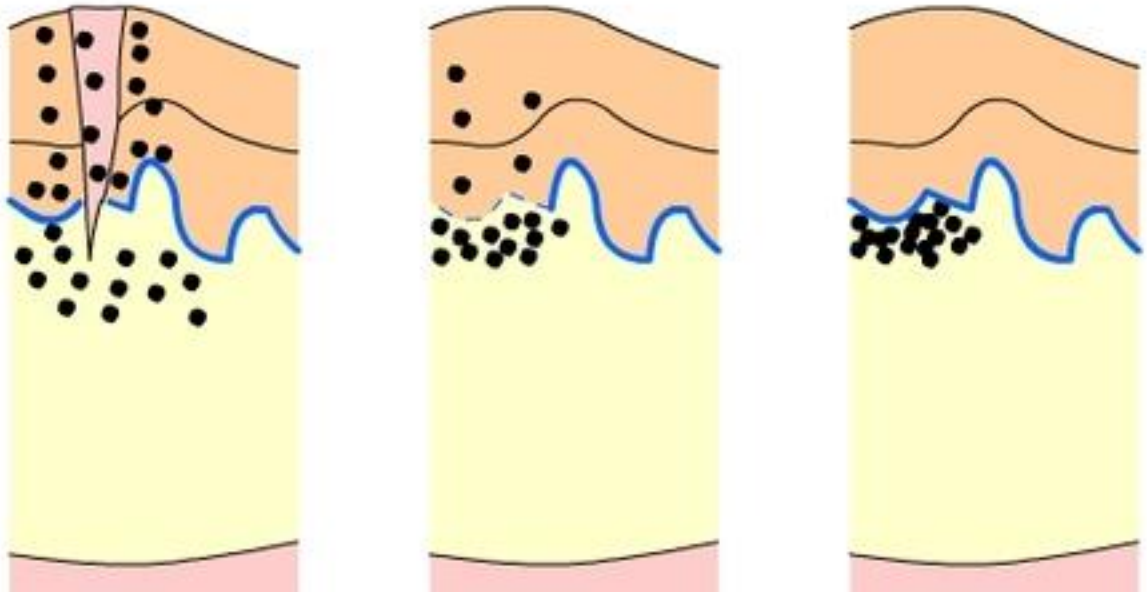
- Air pollutant in urban life-dirty air/smokers
- Inhaled→taken up by macrophages→ transported by lymphatics→ to regional LN
- Lungs (Anthracosis) & LN turns black
- Coal miners→carbon dust aggregation →fibroblastic reaction/emphesema→serius lung disease

→coal worker's pneumoconiosis

Tattoo

- Ink is placed at the top layer of the dermis.
- Phagocytosed by dermal macrophages
- Ink remains indefinitely inside macrophages





Endogenous pigments

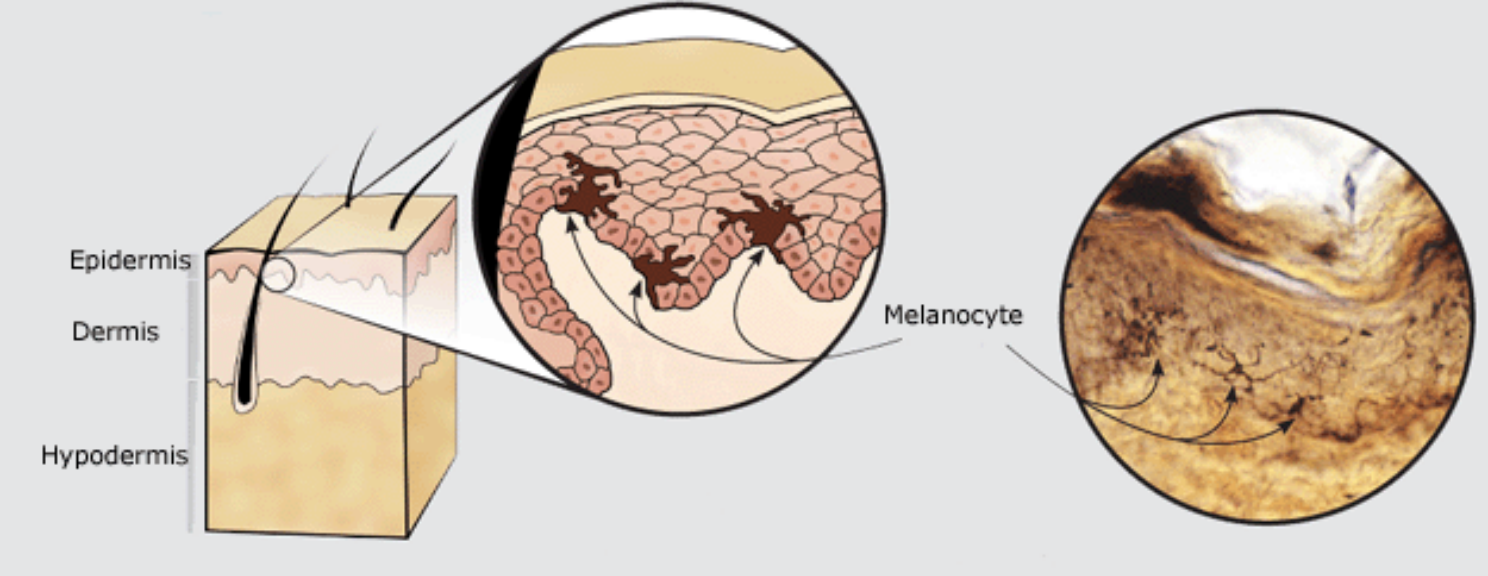
- Melanin
- Haemosiderin
- Lipofuscin
- Bile pigments

Melanin

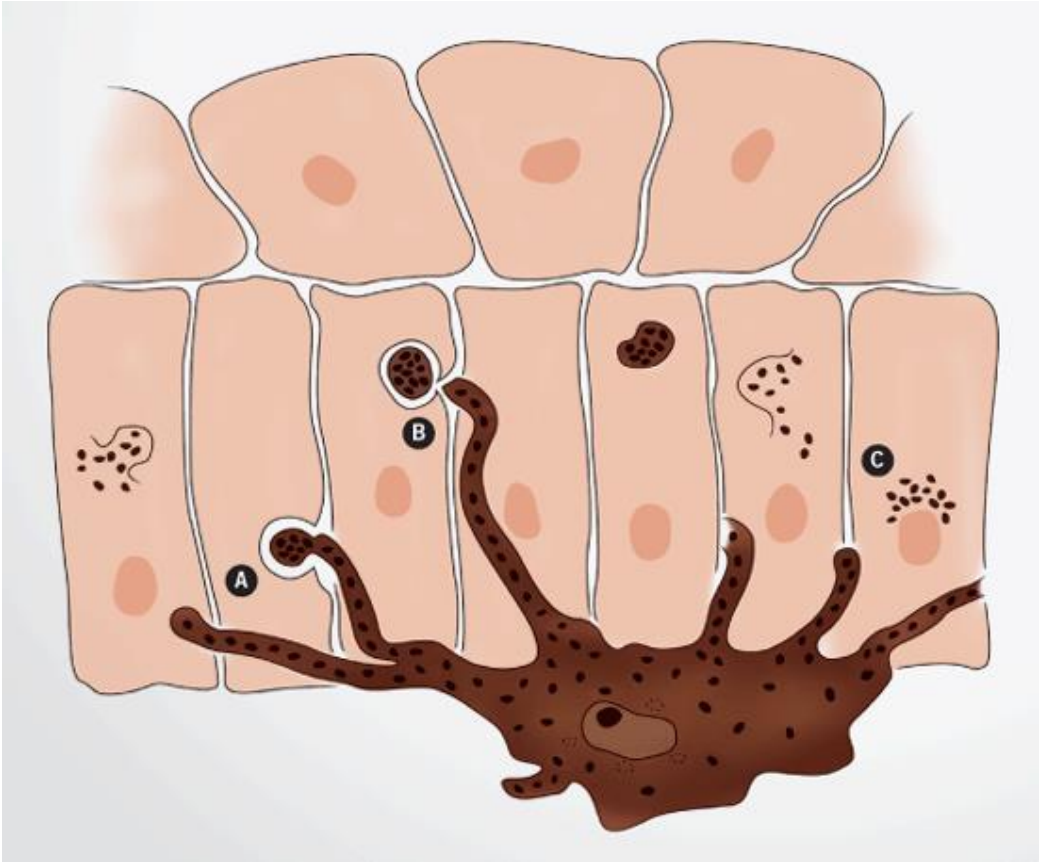
- Melanins are brown to black pigments formed from the amino acid tyrosine

  Tyrosine→→Melanin

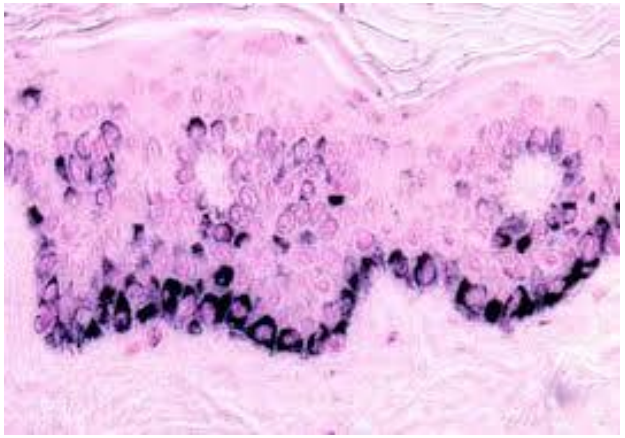
- In skin, melanocytes, branched cells at the junction of the epidermis with the dermis.

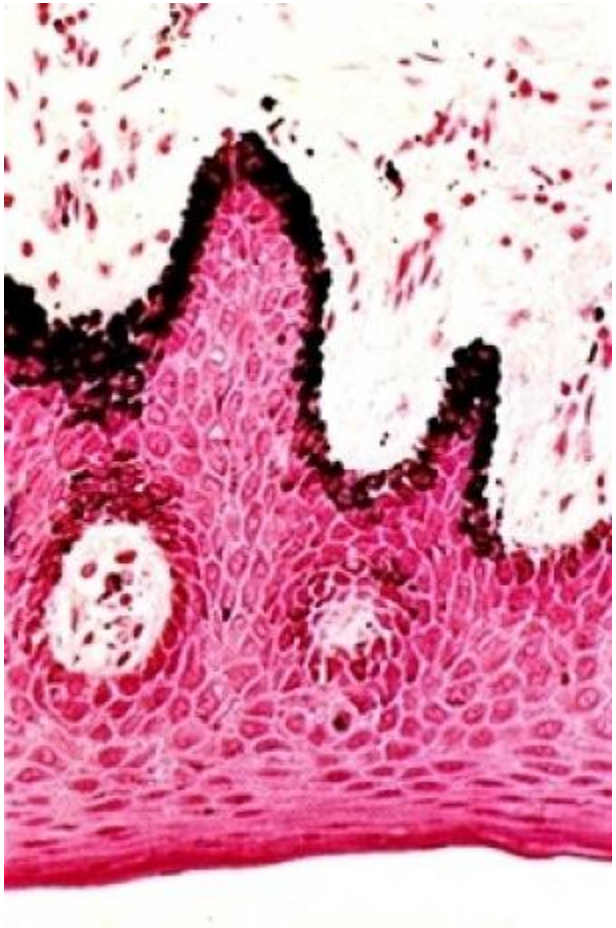


Melanocytes synthesize the pigment and package it into protein containing granules called melanosomes.



- Stain-Masson Fontana





Abnormalities of Melanin

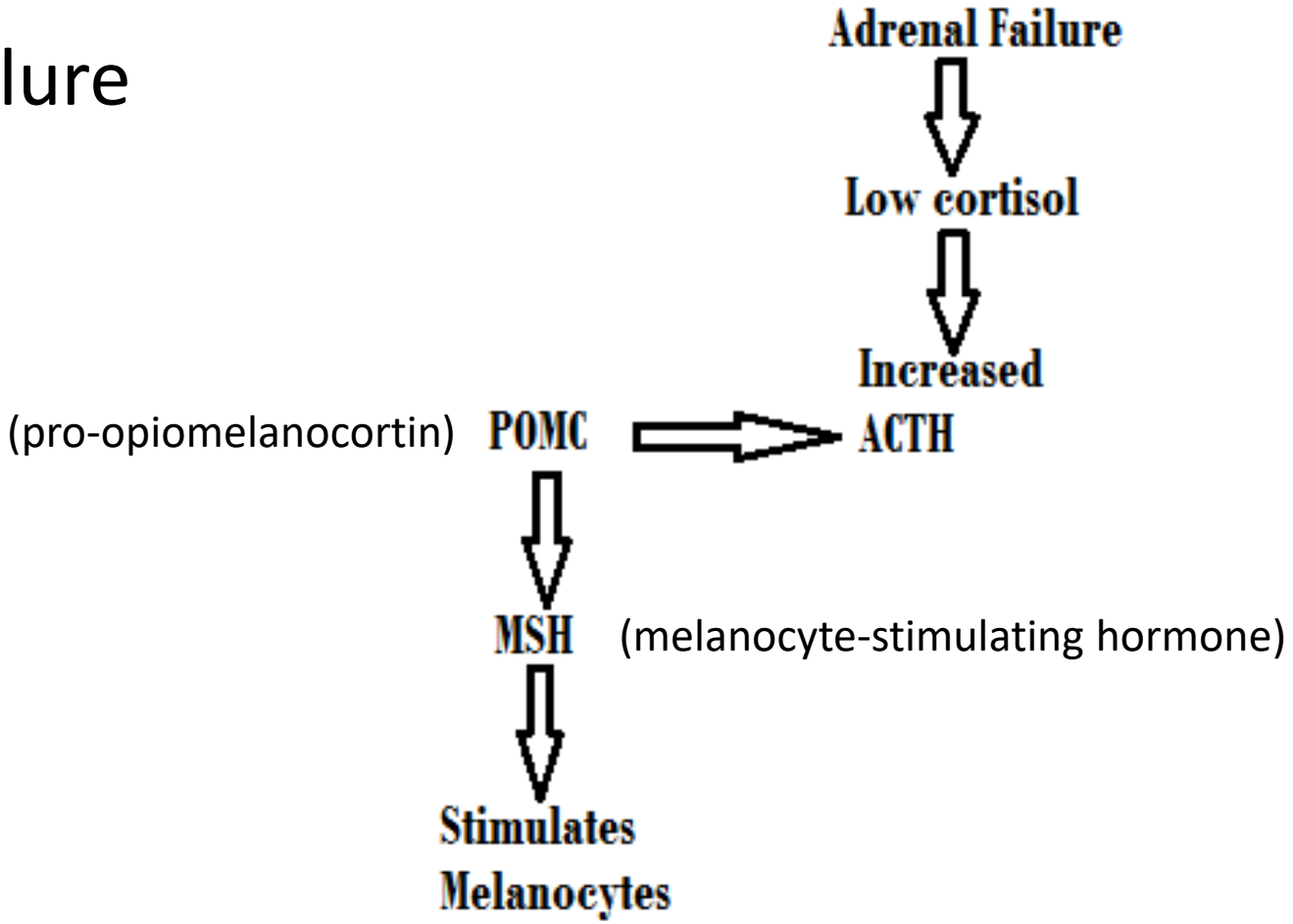
- If your body makes too much melanin, your skin gets darker.
  - Chloasma
  - Addison's disease
  - Café-au-lait spots
  - Sun exposure

Chloasma

- Seen on face, nipples & genitalia of pregnant women.
- Birth control pills and hormone replacement medicine also can trigger this.

Addison's disease

Adrenal failure



Addison's disease

- darkening of the skin, including areas not exposed to the sun; characteristic sites are
  - skin creases (e.g. of the hands),
  - nipple,
  - the inside of the cheek (buccal mucosa);
  - old scars may darken.

Café-au-lait spots

French coffee drink, coffee with milk

- Pigmented patches on skin
- Seen in
  - Neurofibromatosis
  - Albright's syndrome

Abnormalities of Melanin cont.

- If your body makes too little melanin, your skin gets lighter.
  - Vitiligo is a condition that causes patches of light skin.
  - Albinism is a genetic condition affecting a person's skin. A person with albinism may have no color, lighter than normal skin color, or patchy missing skin color.
  - Infections, blisters and burns can also cause lighter skin.

Vitiligo

- Auto-immune destruction of melanocytes

Albinism

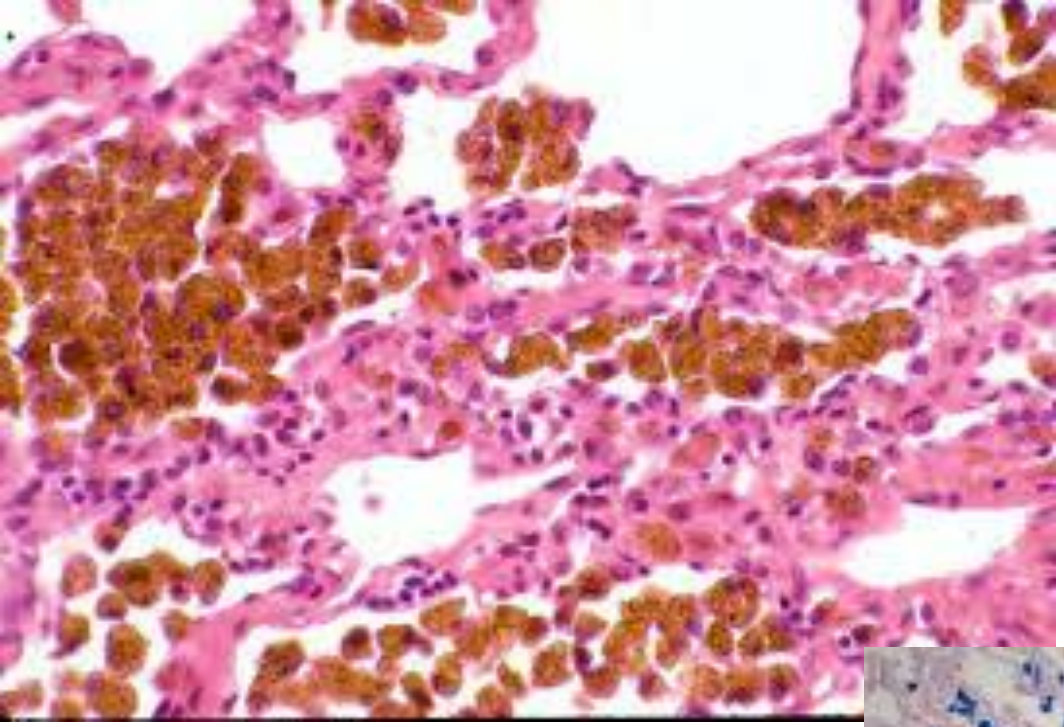
- Congenital disorder
- little or no production of melanin
- Albinism is caused by a mutation in one of several genes. Each of these genes provides instructions for making one of several proteins involved in the production of melanin

Moles & Melanomas

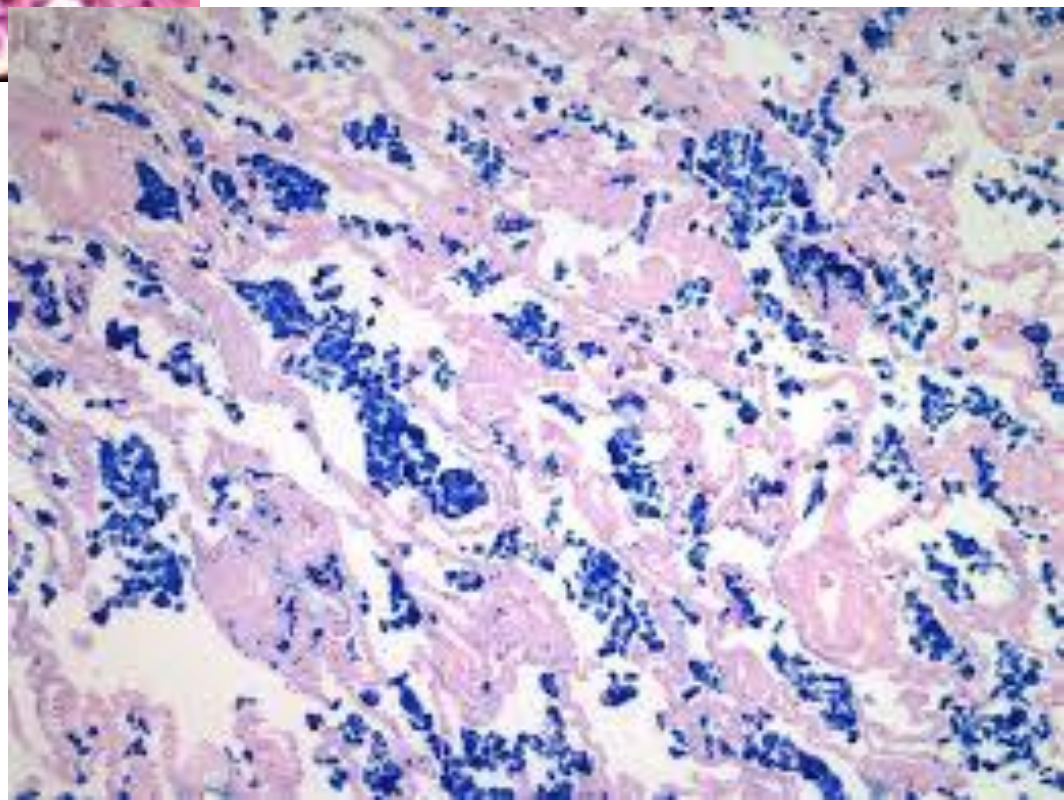
- A mole (nevus) is a benign skin tumor that develops from melanocytes. Almost everyone has some moles. Nearly all moles (nevi) are harmless
- Melanoma is a cancer that begins in the melanocytes. Because most melanoma cells still make melanin, melanoma tumors are usually brown or black. But some melanomas do not make melanin and can appear pink, tan, or even white.

Haemosiderin

- Two forms of storage iron
  - Ferritin
  - Haemosiderin
- Hemosiderin is a golden- yellow, granular pigment which occurs in localized or systemic accumulations.



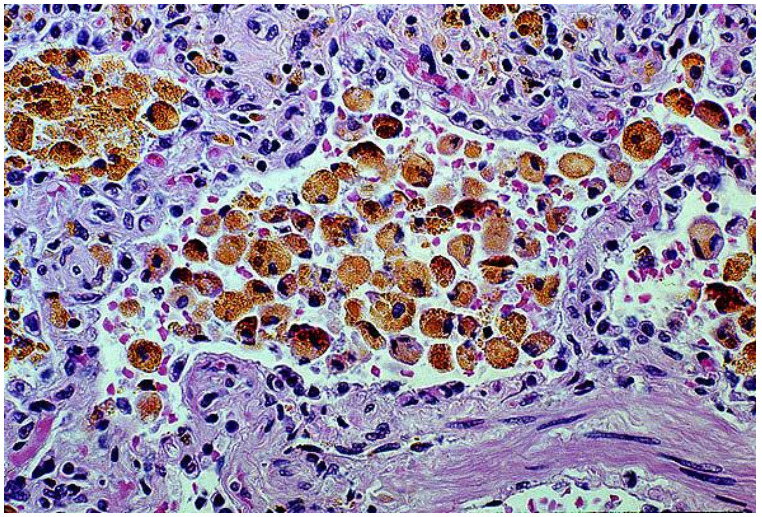
Prussian blue stain



localized haemosiderosis

- This occurs in local injuries, haemorrhages, bruises, hematomas etc.
- Grossly the bruise goes through different changes indicating formation of different pigments as below:
  - 1-Red blue – Hb
  - 2. Greenish blue (biliverdin green)
  - 3. Pinkish blue (bile pigment)
  - 4. Golden yellow – hemosiderin, observed in scars

Localized Haemosiderosis



Pulmonary congestion

↓

Alveolar microhaemorrhages

↓

Phagocytosis by macrophages

↓

Haemosidein laden macrophages

(Heart failure cells)

Longstanding →

Fibrosis & alveolar thickening

↓

Lungs become brown & firm

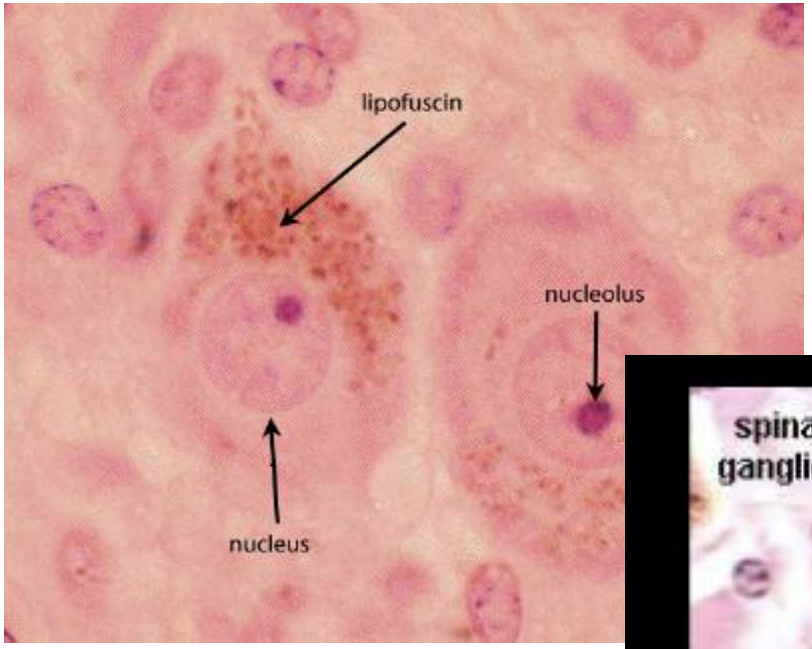
Brown Induration of lung

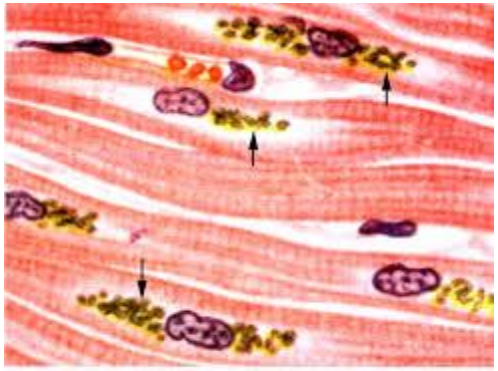
Systemic hemosiderosis

- hemosiderin is deposited in many organs and tissues, especially in the liver, spleen, lymph node, bone marrow etc.
- It is caused by increased dietary iron, impaired utilization, hemolytic anemia and transfusion

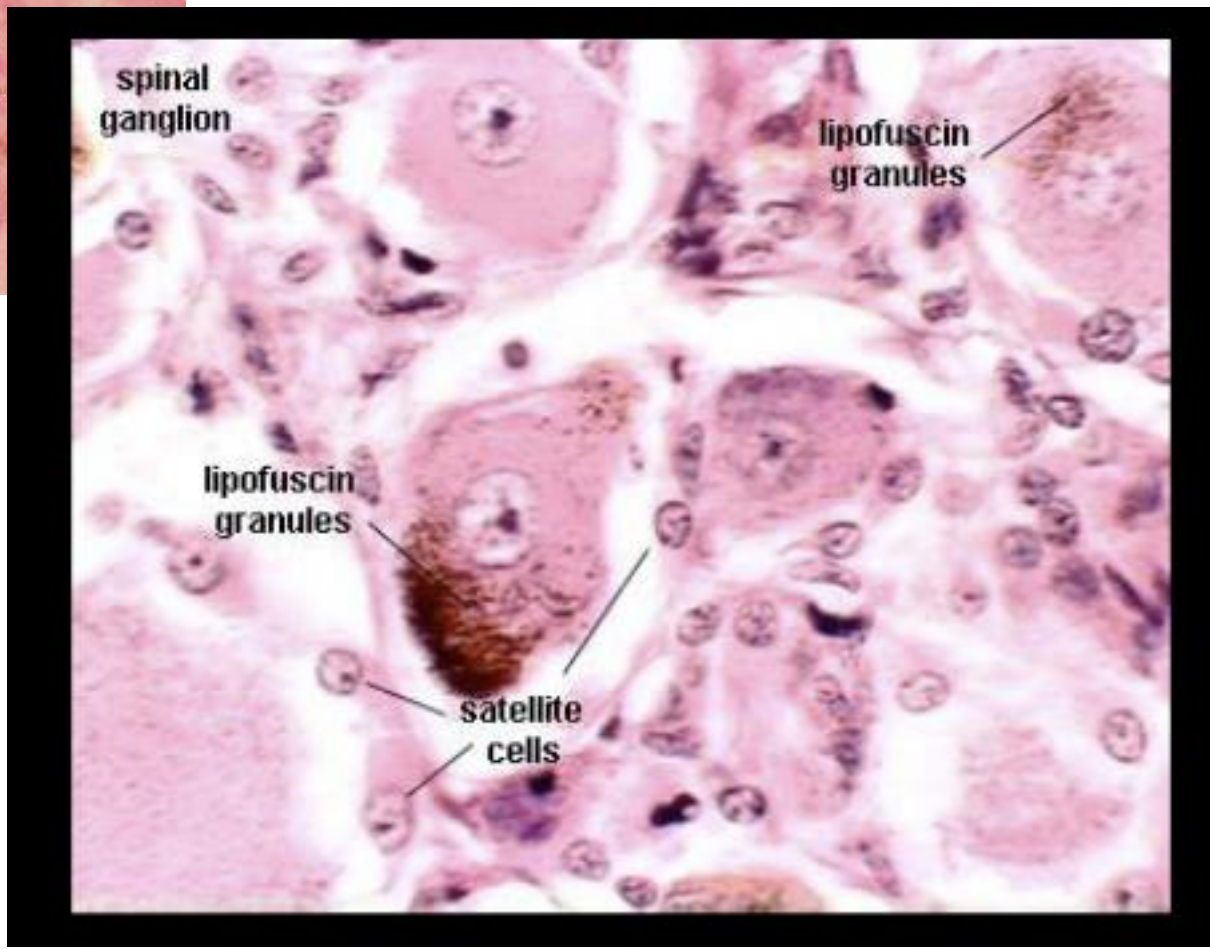
Lipofuscin

- An insoluble brownish yellow pigment, wear and tear pigment or ageing pigment.
- It contains complexes of lipid and protein derived from peroxidation of lipids by free radicals.
- It represents indigestible residues of autophagic vacuoles.
- It gives brown discolorations to tissues but is not injurious to the cell.
- Perinuclear



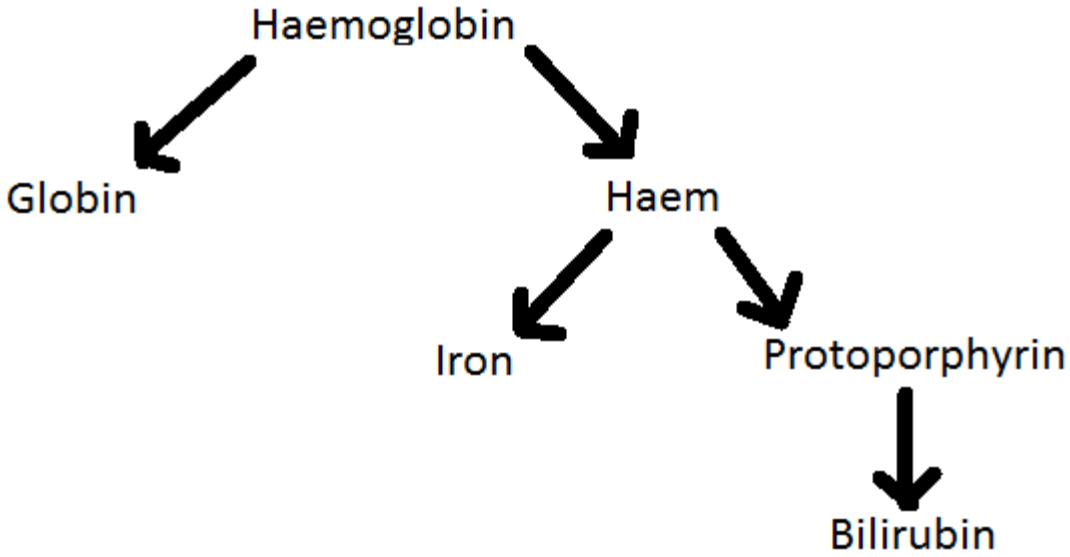


lipofuscin in cardiac cells



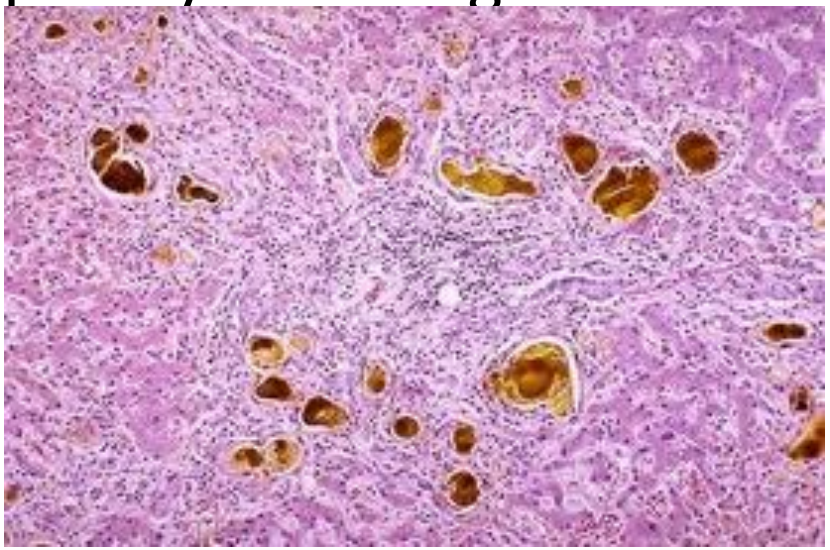
Bilirubin

- Breakdown product of haemoglobin
- Contains no iron



Bilirubin cont.

- Cholestasis
  - Hepatocytes→large bile-laden lysosomes
  - Canaliculi→dilated
  - Ruptured bile canaliculi→Bile leaks out→Bile is toxic to hepatocytes→Hepatocytic damage→ bile lakes



Pathologic calcification

- Implies the abnormal deposition of calcium salts in tissues.

- is a common process in a wide variety of disease states

There are two types of calcification

Dystrophic calcification

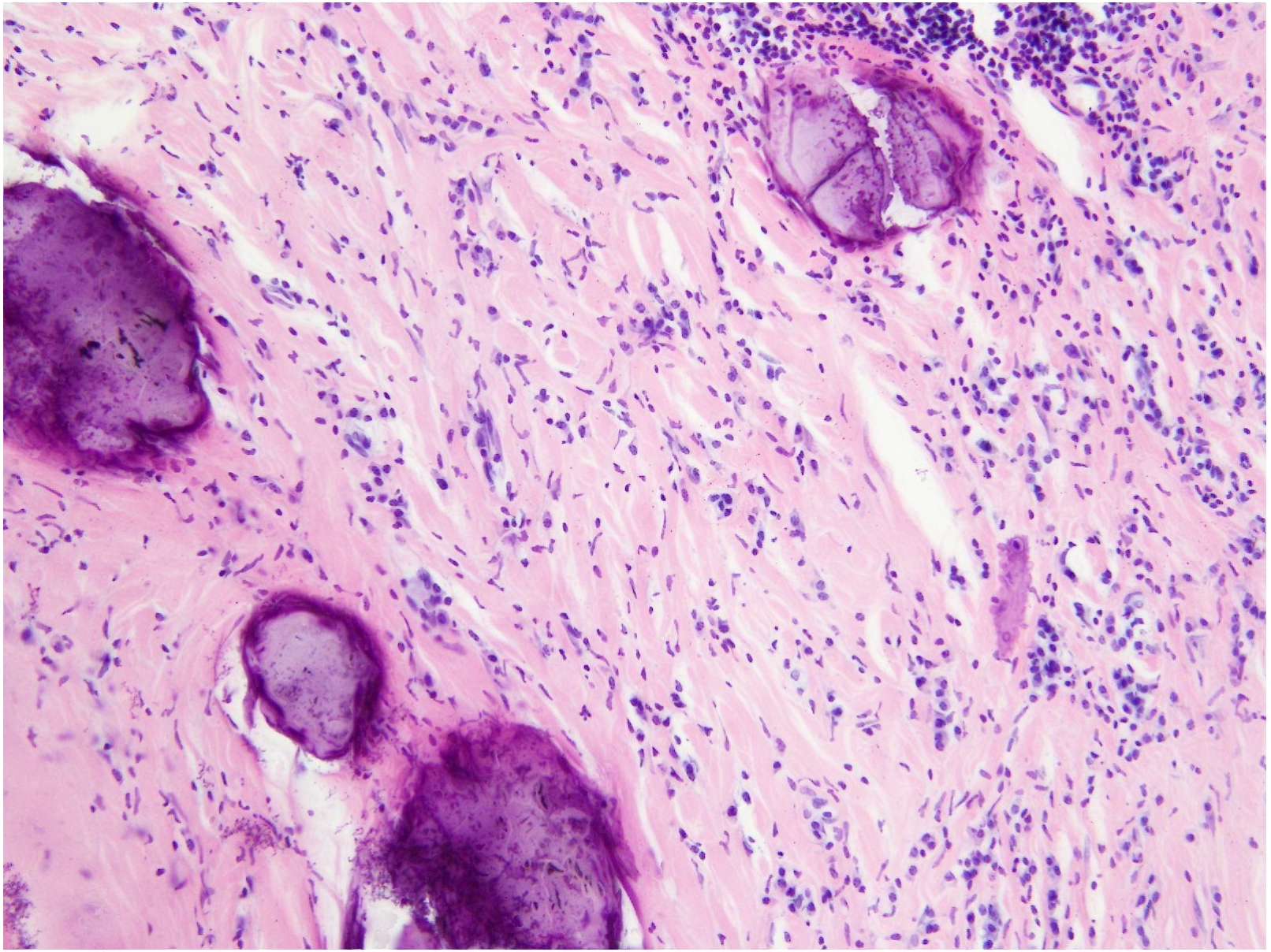
- When the deposition occurs in dead or dying tissues
- it occurs with normal serum levels of calcium

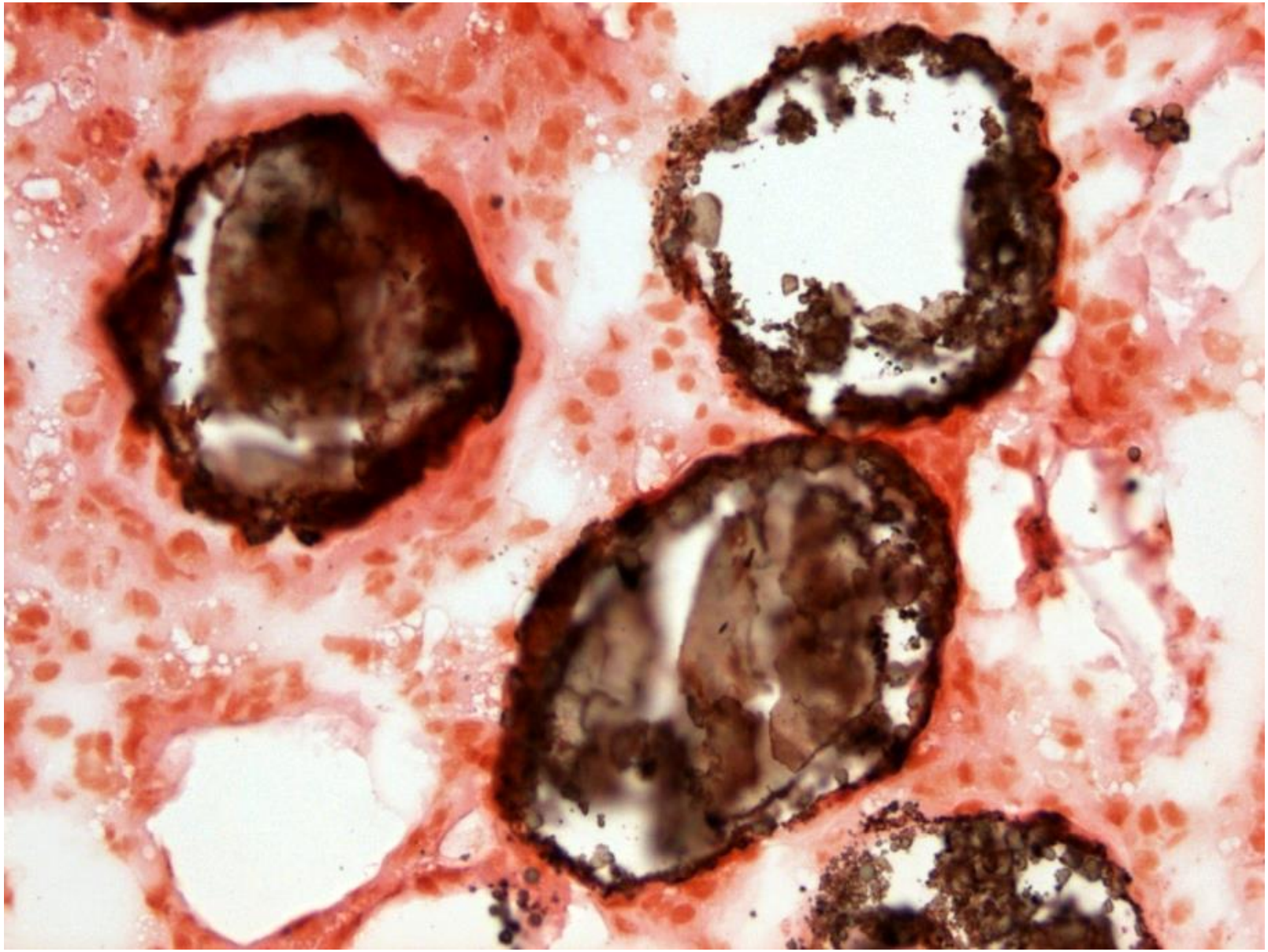
Metastatic calcification

- The deposition of calcium salts in normal tissues
- It almost always reflects some derangement in calcium metabolism (hypercalcemia)

Regardless of cause, calcium salts stain dark blue on H&E.

If there is any doubt, special stains like the Von Kossa of Alizarin red demonstrate it is calcium.





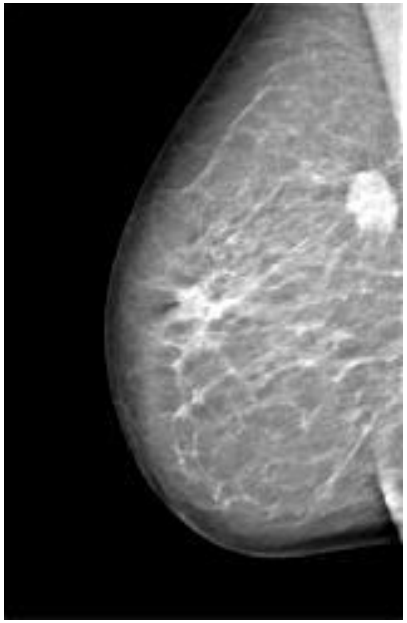
Dystrophic calcification

- Advanced atherosclerotic plaques undergo calcification.
- Malformed or damaged cardiac valves tend to calcify
- Caseous granulomas
- Scars (surgical, myocardial)
- Certain tumors contain "psammoma bodies", little spherules of basement membrane that calcify

Metastatic Calcification

- Metastatic calcification can occur in normal tissues whenever there is hypercalcemia.
- Causes:
  - increased secretion of parathyroid hormone
  - destruction of bone due to the effects of accelerated turnover (e.g., Paget disease), immobilization, or tumors (multiple myeloma, leukemia, or diffuse skeletal metastases)
  - vitamin D-related disorders including vitamin D intoxication and sarcoidosis
  - renal failure, in which phosphate retention leads to secondary hyperparathyroidism.

Breast Carcinoma



- A percentage of breast malignancies present as microcalcifications before they present as a mass.
- The ability to diagnose a malignancy early implies that the disease is potentially curable with less chance of metastatic disease and with potentially less invasive surgery.

Psammoma bodies

- Psammoma bodies are concentric lamellated calcified structures
- observed most commonly in
  - papillary thyroid carcinoma,
  - meningioma