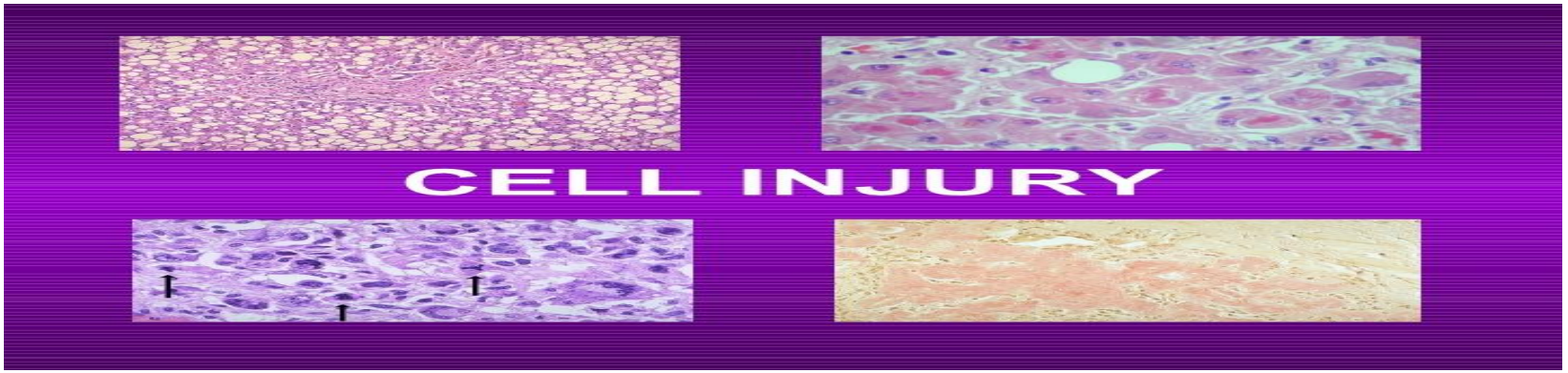
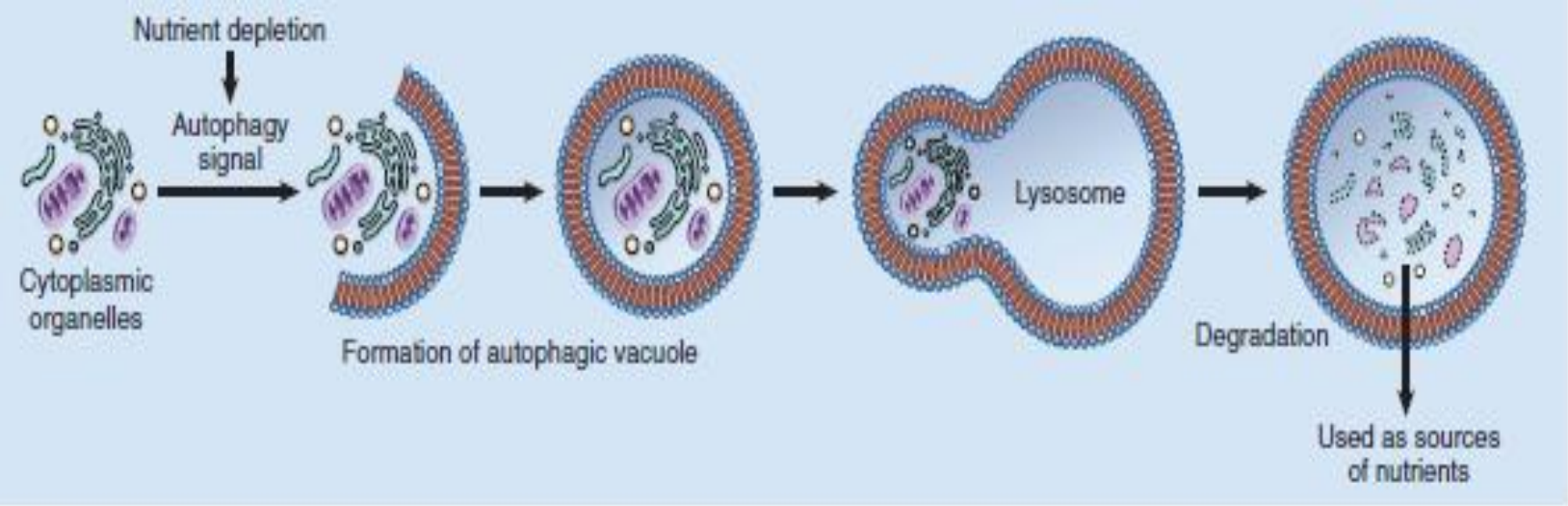


Autophagy and intracellular accumulations

Manar Hajeer, MD, FRCPath.

AUTOPHAGY
auto, self; phagy, eating

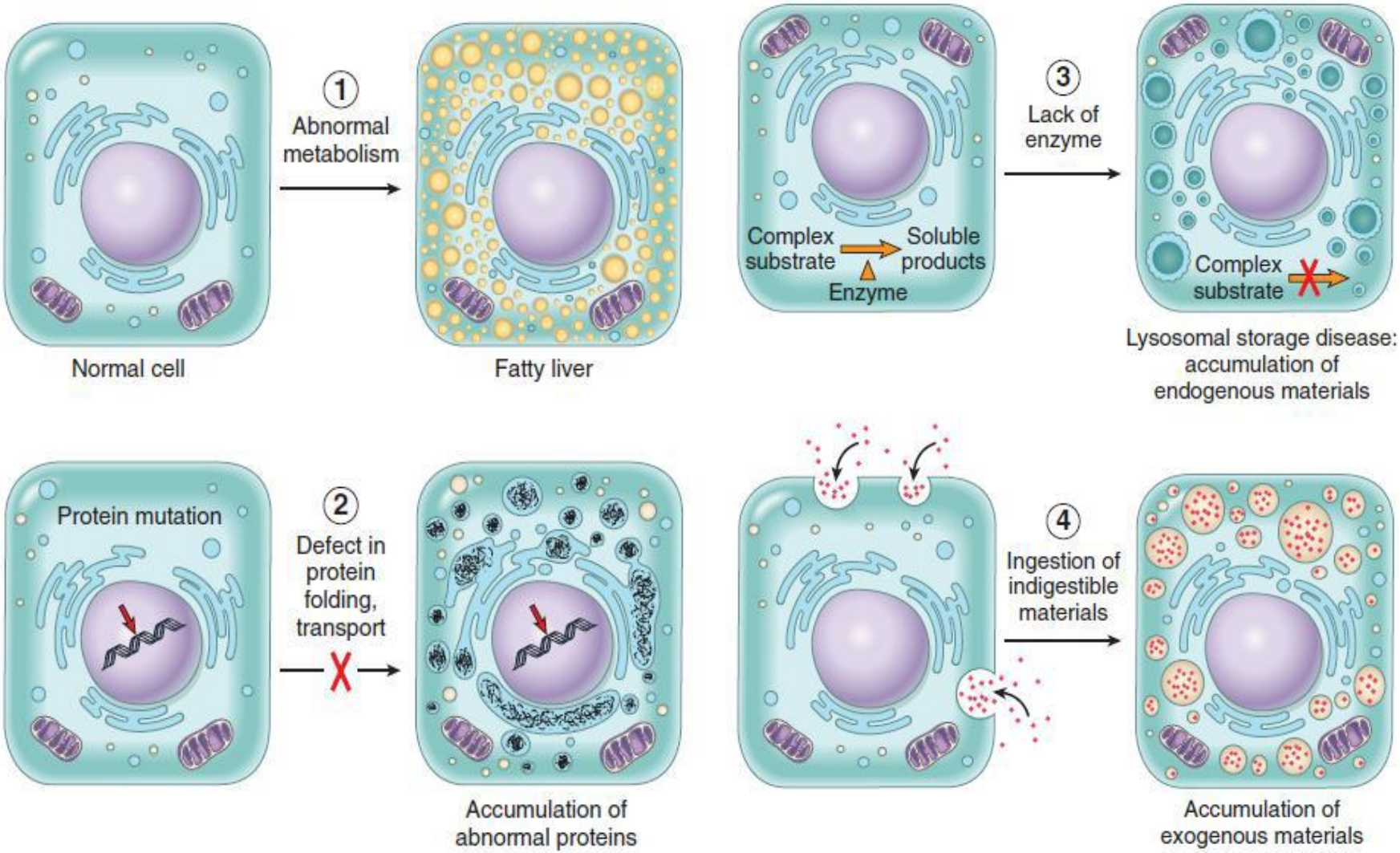


Roles of autophagy

- A survival mechanism in times of nutrient deprivation
- Atrophy (adaptive).
- Ischemia and myopathies
- With inflammatory bowel disease(unknown mechanism)
- Role in cancer…

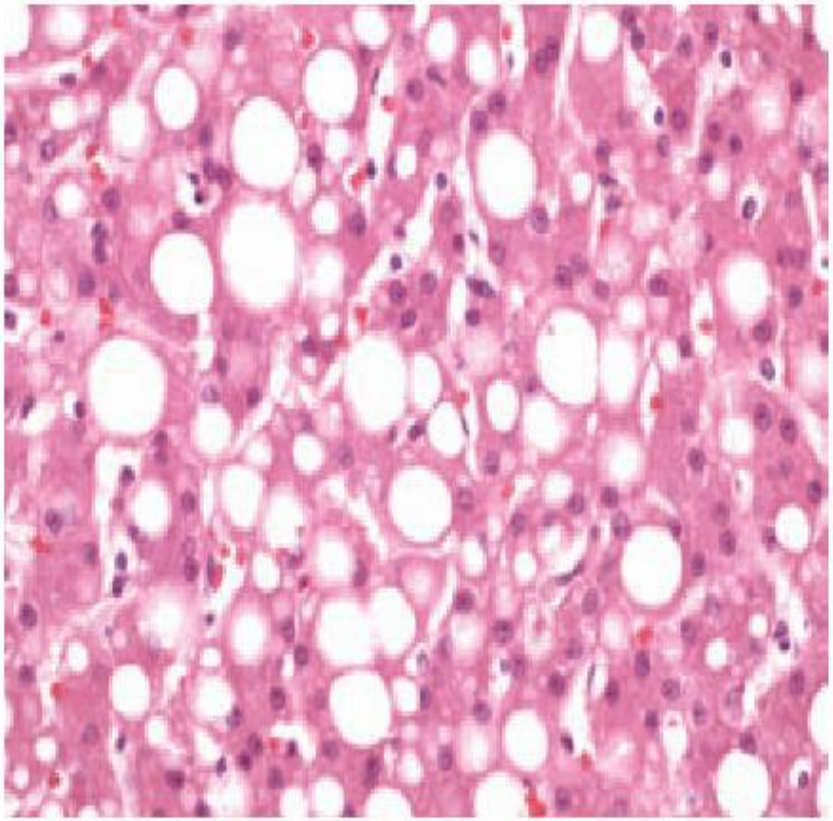
INTRACELLULAR ACCUMULATIONS

- 1)Inadequate removal of a normal substance (fatty change in the liver)
- 2)Accumulation of an abnormal endogenous substance (α1-antitrypsin)
- 3)Failure to degrade a metabolite due to inherited enzyme deficiencies (*storage diseases)*
- 4)Deposition and accumulation of an abnormal exogenous substance (carbon and selica)


1
Abnormal metabolism
Normal cell
Fatty liver
Complex substrate
Soluble products
Enzyme
3
Lack of enzyme
Complex substrate
Lysosomal storage disease: accumulation of endogenous materials
Protein mutation
2
Defect in protein folding, transport
Accumulation of abnormal proteins
4
Ingestion of indigestible materials
Accumulation of exogenous materials

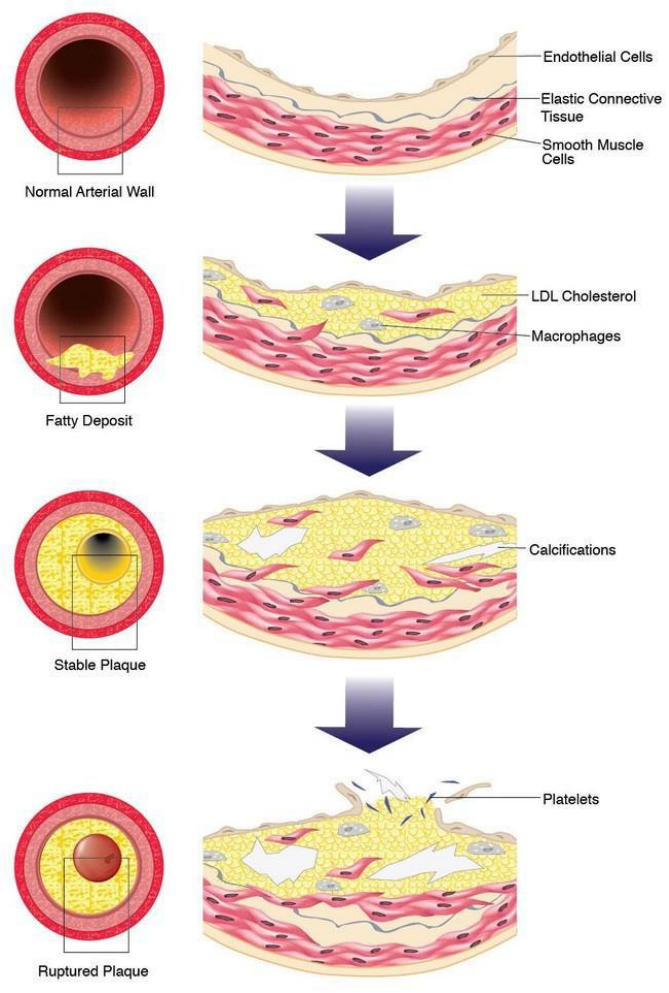
fatty change: steatosis

- Most common in liver
- Also in heart, kidney, muscle
- Causes: toxins, protein malnutrition, DM, obesity, anoxia
- *Alcohol abuse and DM+obesity are the most common causes of fatty liver*



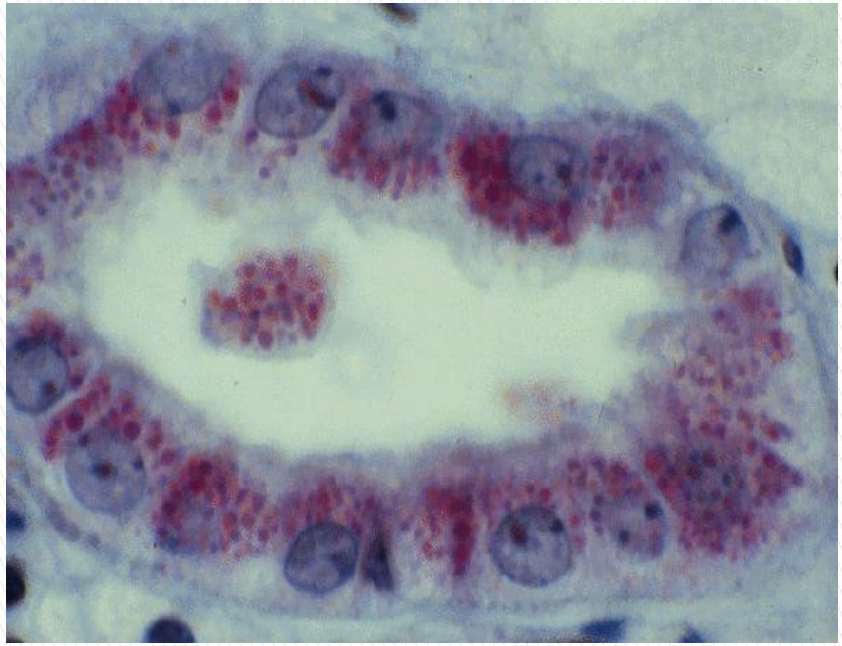
Cholesterol and Cholesteryl Esters

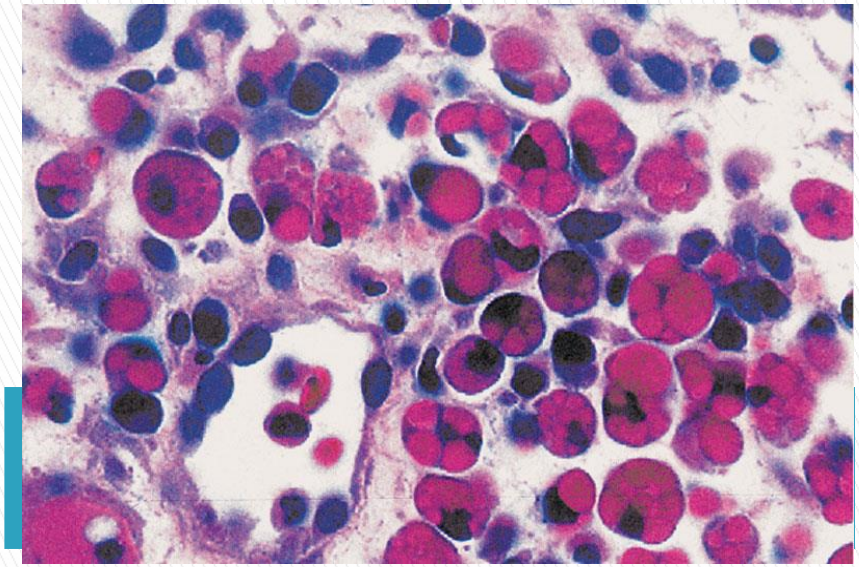
- Phagocytic cells become overloaded with lipid (triglycerides, cholesterol, and cholesteryl esters)
- atherosclerosis is the most important example.



Proteins

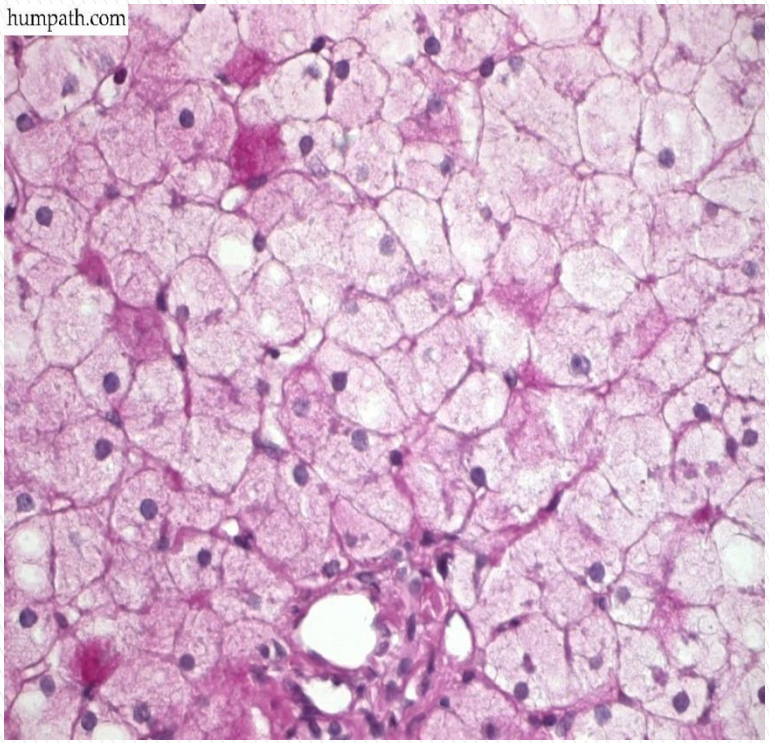
- Much less common than lipid accumulations
- Either excess external or internal synthesis
- Proximal renal tubules in nephrotic syndrome
- Russell bodies in plasma cells.
- Alcoholic hyaline in liver.
- Neurofibrillary tangles in neurons





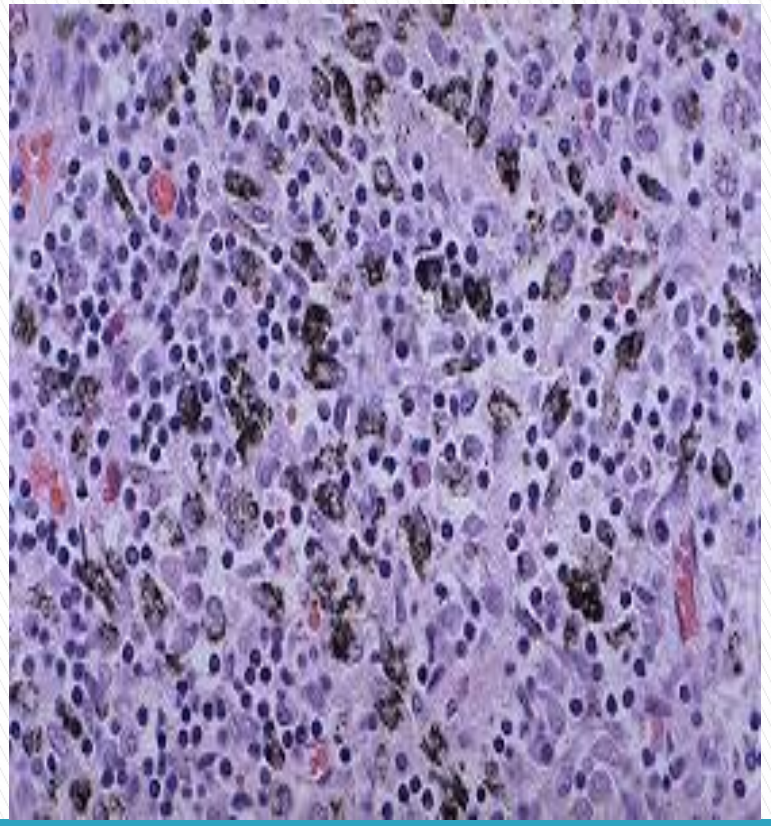
Glycogen

- Abnormality in glucose or glycogen metabolism
- **DM** (in renal tubules, heart, B cells of pancreas).
- **Glycogen storage diseases**



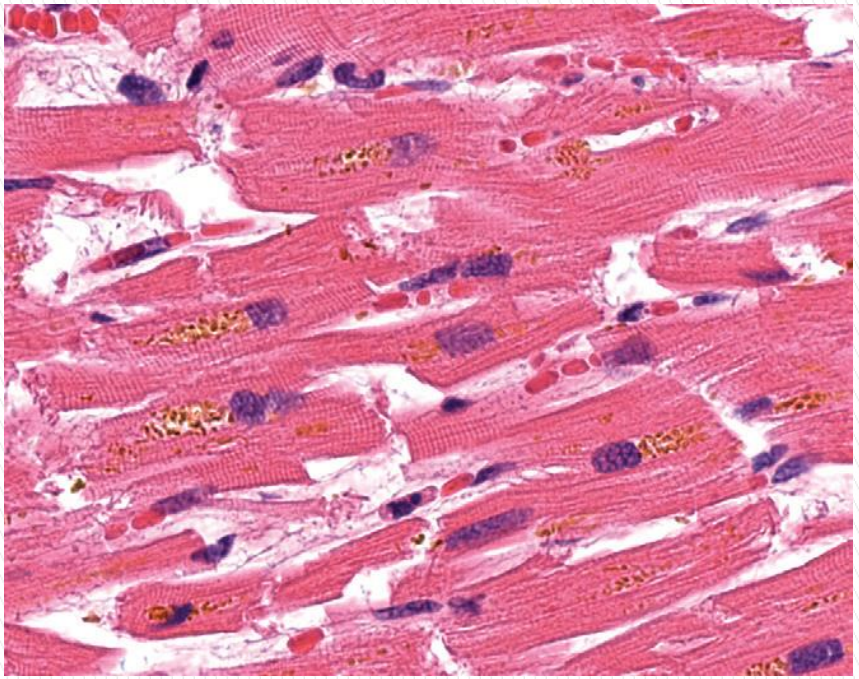
Pigments

- **Exogenous**
- Most common exogenous, **carbon** (coal dust, air pollution)
- Alveolar macrophages → lymphatic channels → tracheobronchial LN
- *Anthracosis*



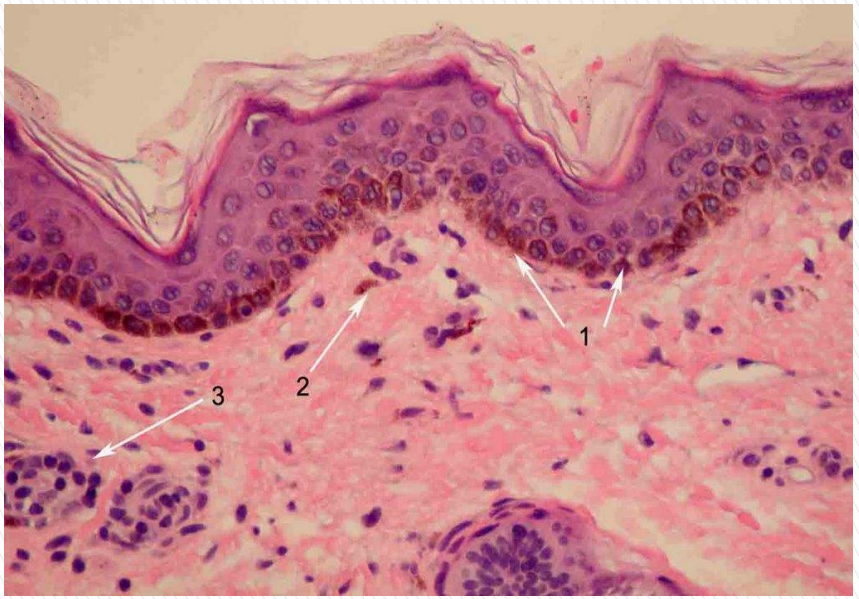
Pigments

- **Endogenous**
- **Lipofuscin**
- “wear-and-tear pigment”
- Age/atrophy
- Heart, liver, and brain
- Lipid and protein
- Marker of past free radical injury
- *brown atrophy*



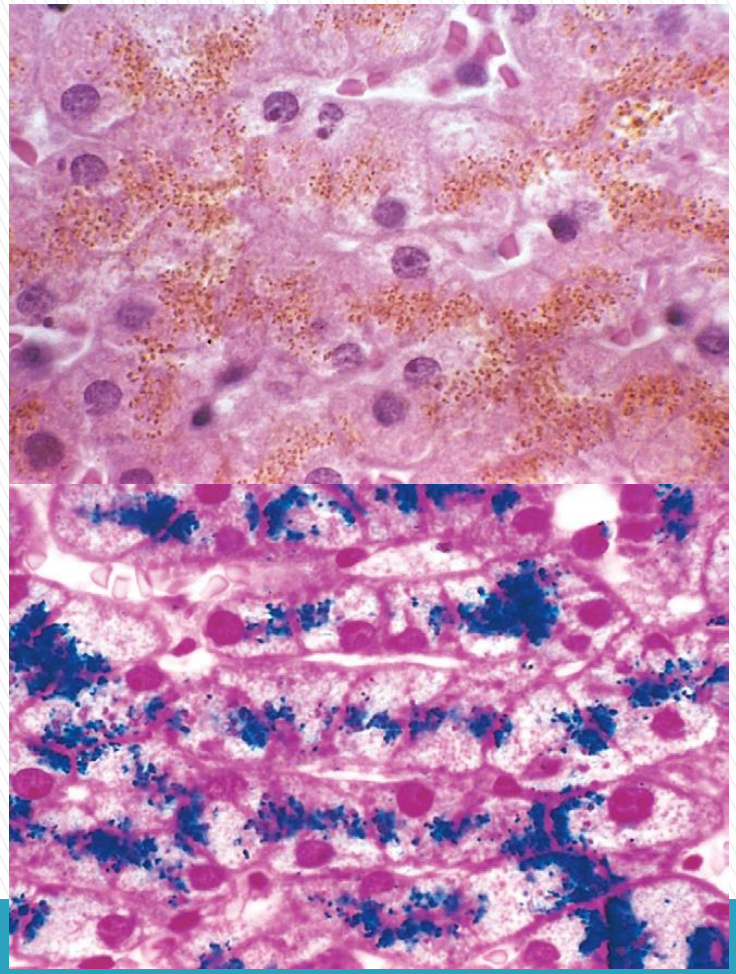
Pigments

- **Endogenous**
- **Melanin**
- Source: melanocytes
- UV protection
- Accumulates in dermal macrophages and adjacent keratinocytes
- Freckles



pigments

- **Hemosiderin**
- Hb-derived granular pigment
- Excess iron
- Iron +apoferritin==ferritin micelles
- Physiologic in the mononuclear phagocytes of the BM, spleen, and liver, from RBC turnover
- Bruise: local pathologic deposition from hemorrhage
- Hemosiderosis: systemic pathologic deposition of hemosiderin (hemochromatosis, hemolytic anemias, repeated blood transfusions)



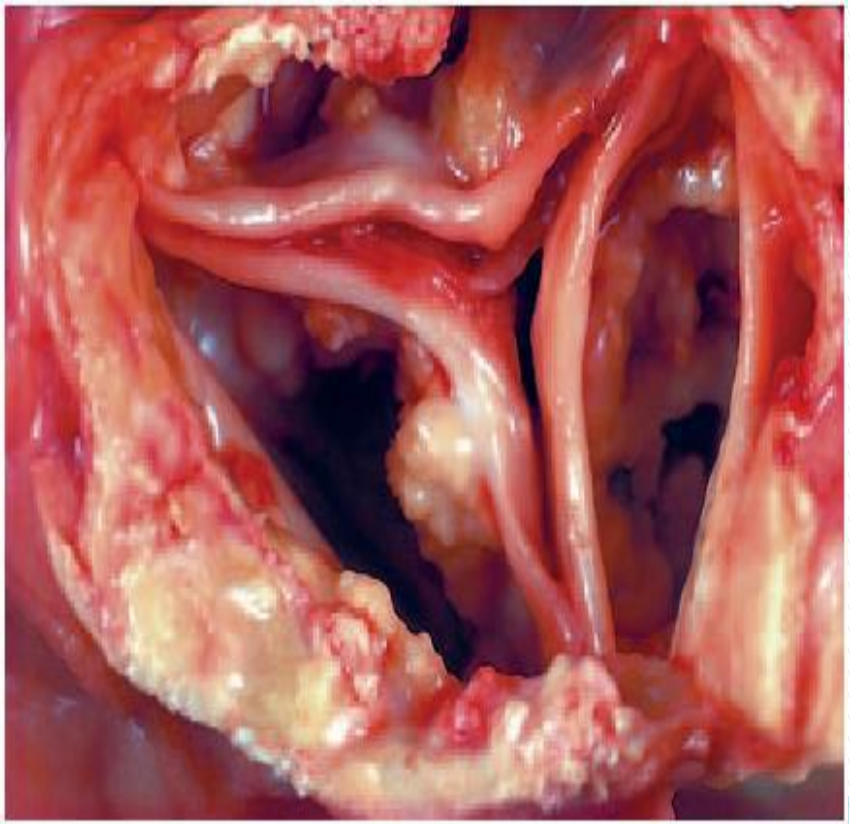
PATHOLOGIC CALCIFICATION

- Abnormal deposition of calcium salts, together with smaller amounts of iron, magnesium, and other mineral

- **Dystrophic Calcification**
- Deposition in dead/dying tissues
- Normal Ca2+ metabolism
- Exacerbated by Hypercalcemia

- **Metastatic Calcification**
- Deposition in normal tissues
- Almost always abnormal Ca2+ metabolism (hypercalcemia)

Dystrophic calcification



- **Incidental finding indicating insignificant past cell injury**
- **May be a cause of organ dysfunction.**
- **Necrosis of any type (e.g. atheromas, aging or damaged heart valves (aortic stenosis), tuberculosis)**

- **Initiation → propagation**
- **Extracellular /Intracellular**
- **Calcium phosphate crystals**

Metastatic Calcification

- Hyperparathyroidism (primary and parathyroid hormone related protein)
- Bone destruction (metastasis, MM, leukemia, Pagets, immobilization)
- Vit-D intoxication, Sarcoidosis.
- Renal failure with 2ry hyperparathyroidism.
- **VESSELS, LUNG, KIDNEY**
- **No clinical dysfunction except if severe.**