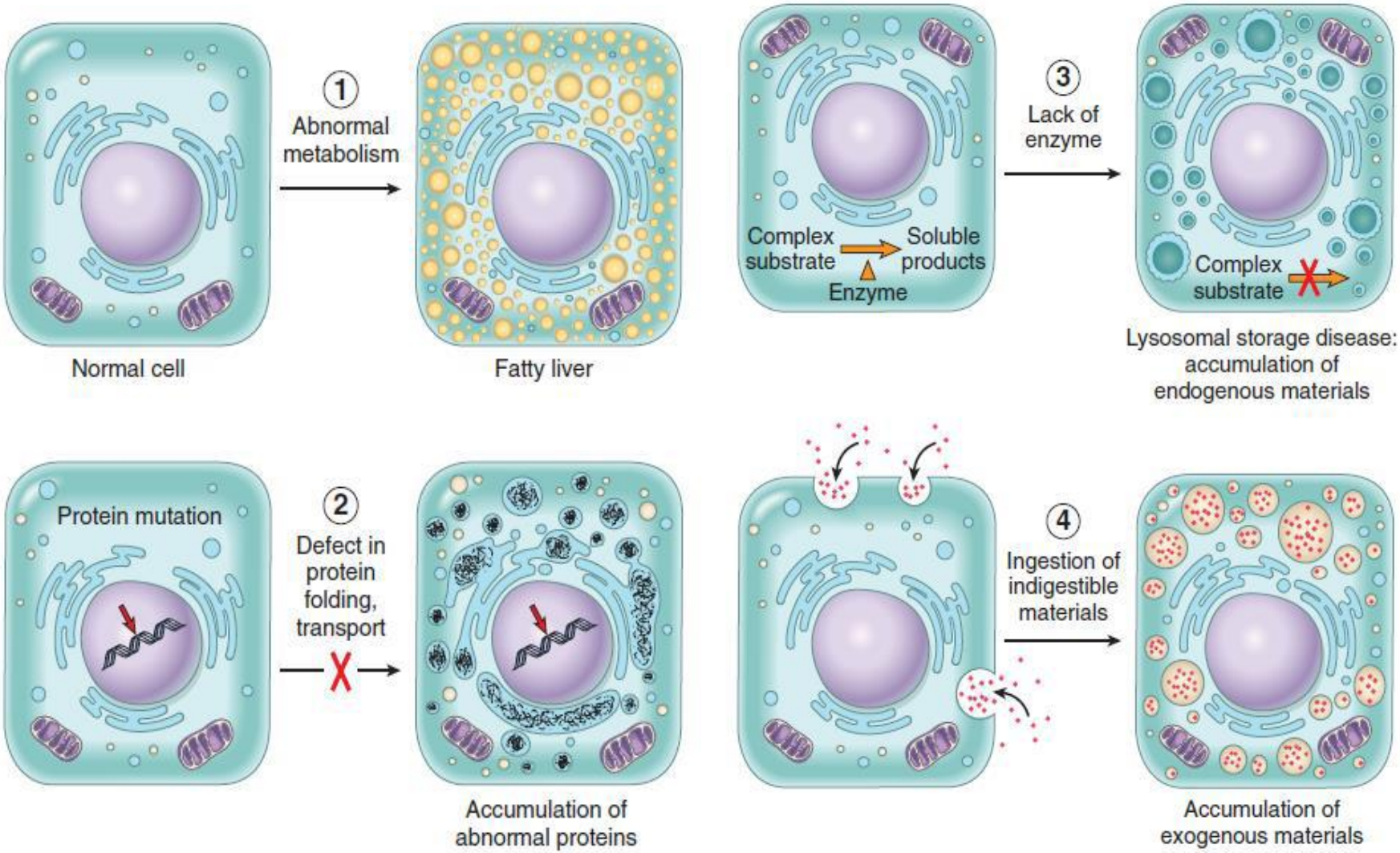
Intracellular accumulations and calcifications

cell injury and adaptations

Manar Hajeer, MD, FRCPath
University of Jordan , school of medicine

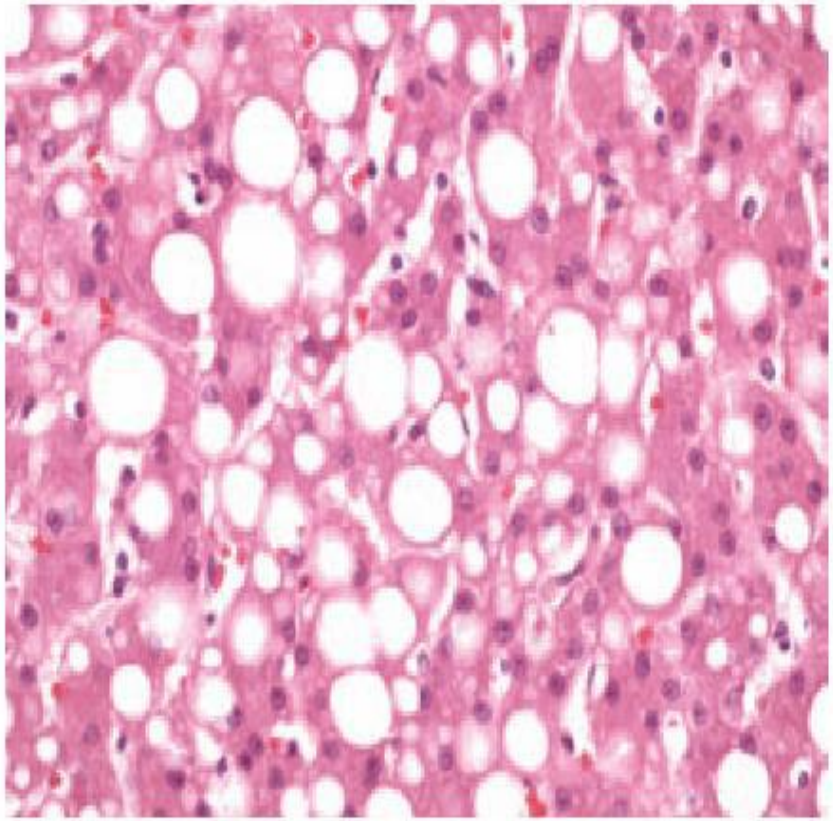
INTRACELLULAR ACCUMULATIONS

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


Normal cell
1
Abnormal metabolism
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

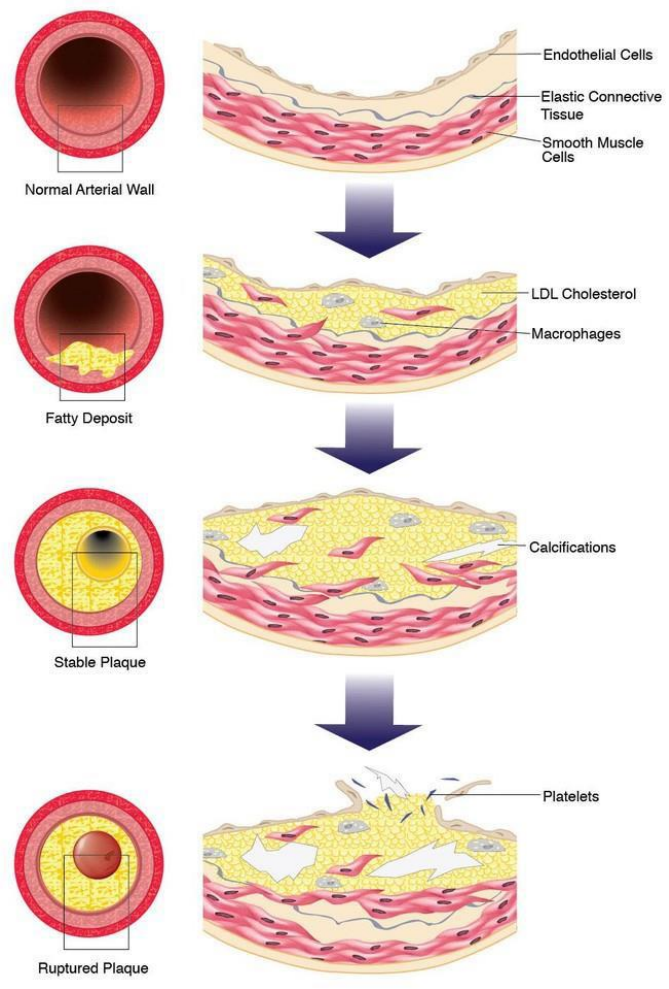
fatty change: steatosis

- Most common in liver
- Triglycerides
- 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



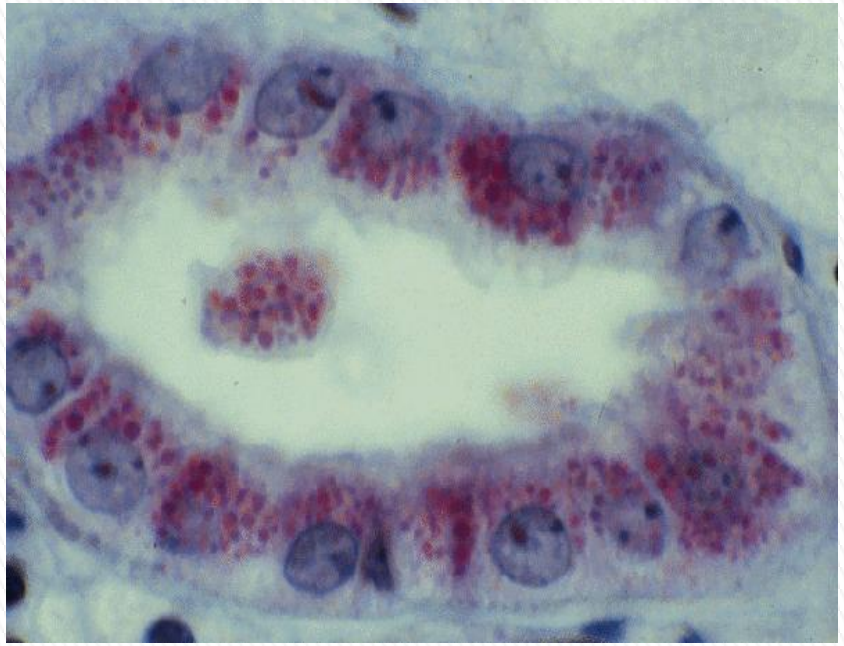
Cholesterol and Cholesteryl Esters

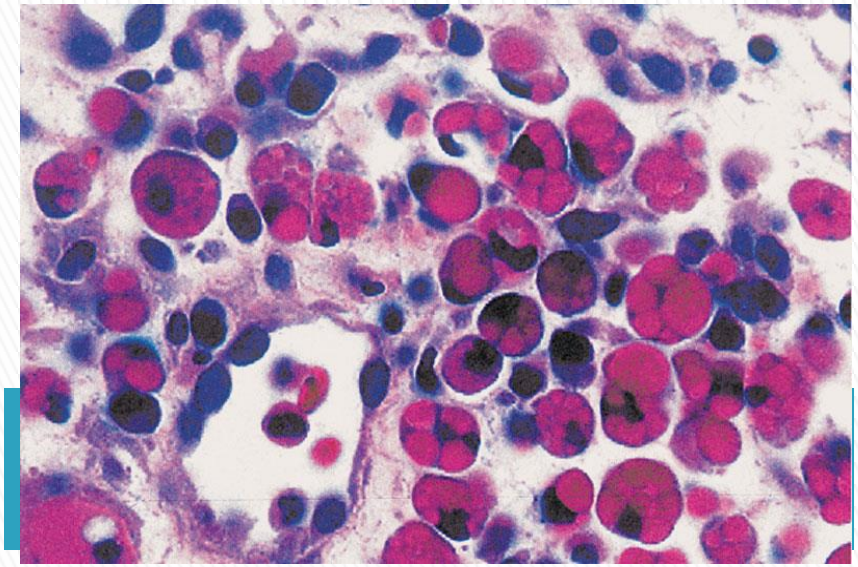
- Phagocytic cells become overloaded with lipid (triglycerides, cholesterol, and cholesteryl esters)
- Due to Increased intake or decreased catabolism
- Atherosclerosis



Proteins

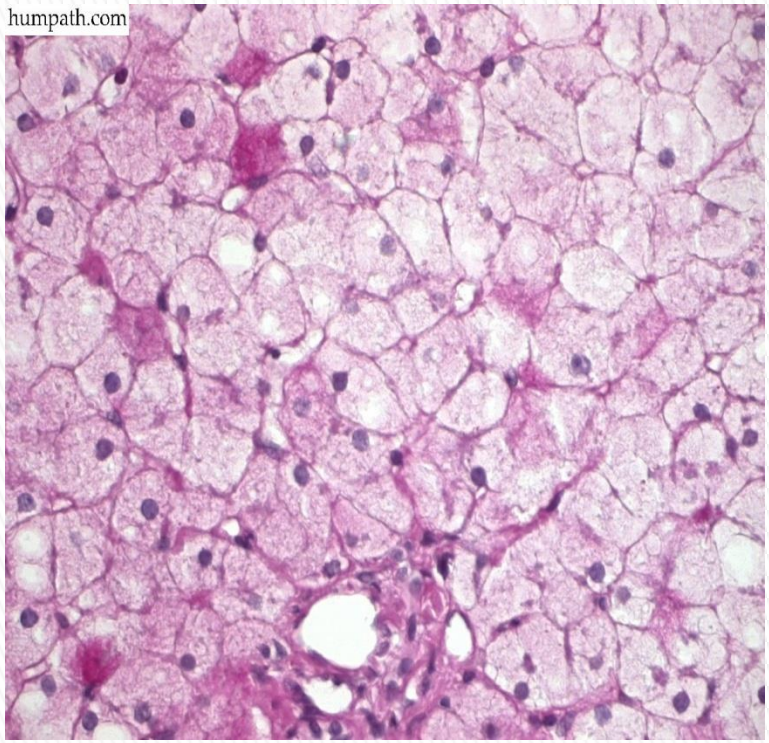
- Much less common than lipid accumulations
- Either excess external or internal synthesis
- Proximal renal tubules in nephrotic syndrome
- Russell bodies in plasma cells.
- Alcoholic hyaline in liver.
- Neurofibrillary tangles in neurons





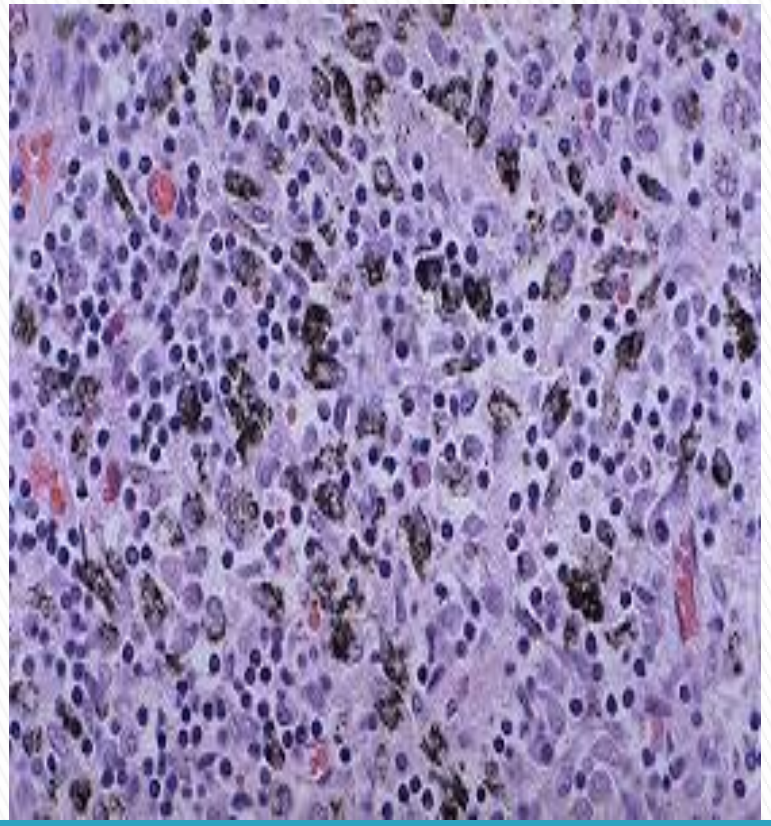
Glycogen

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



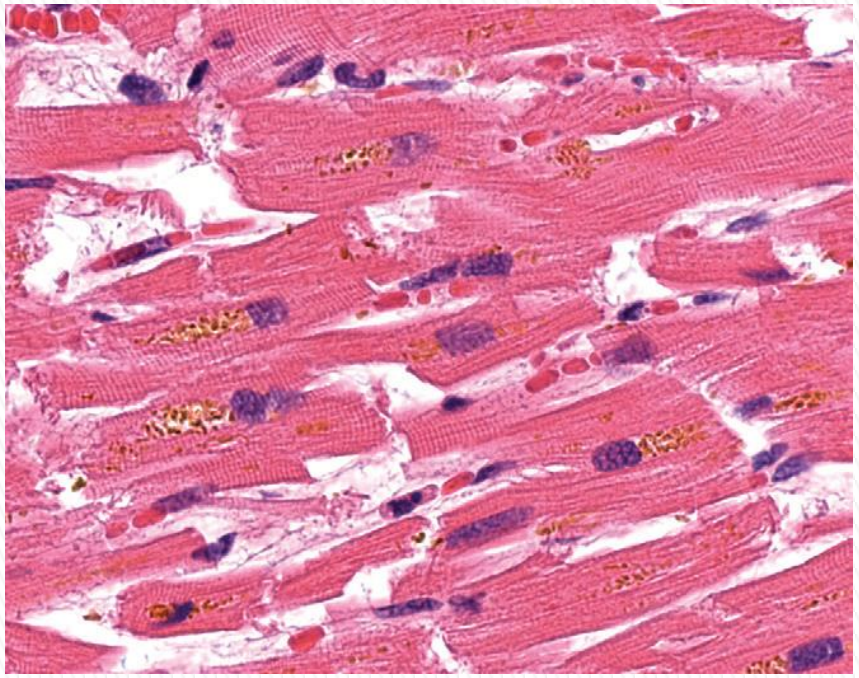
Pigments

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



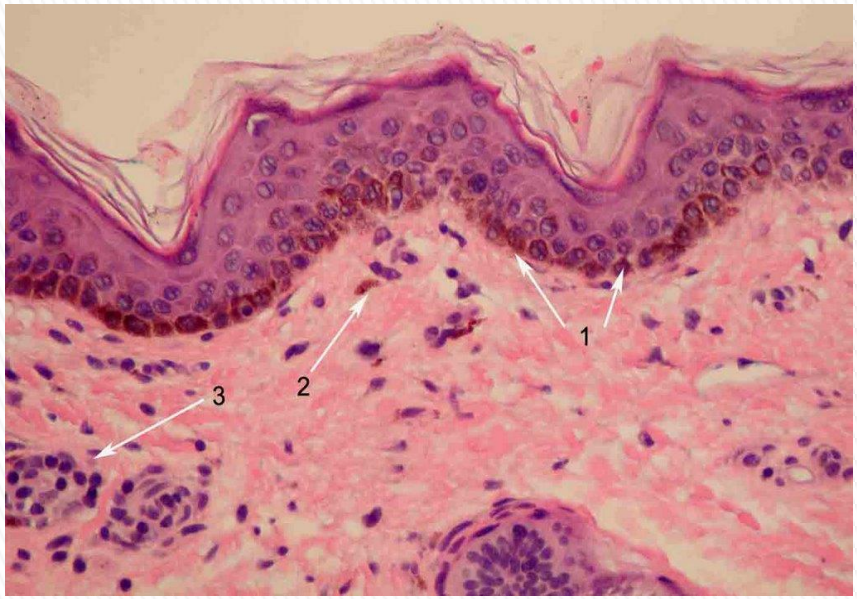
Pigments

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



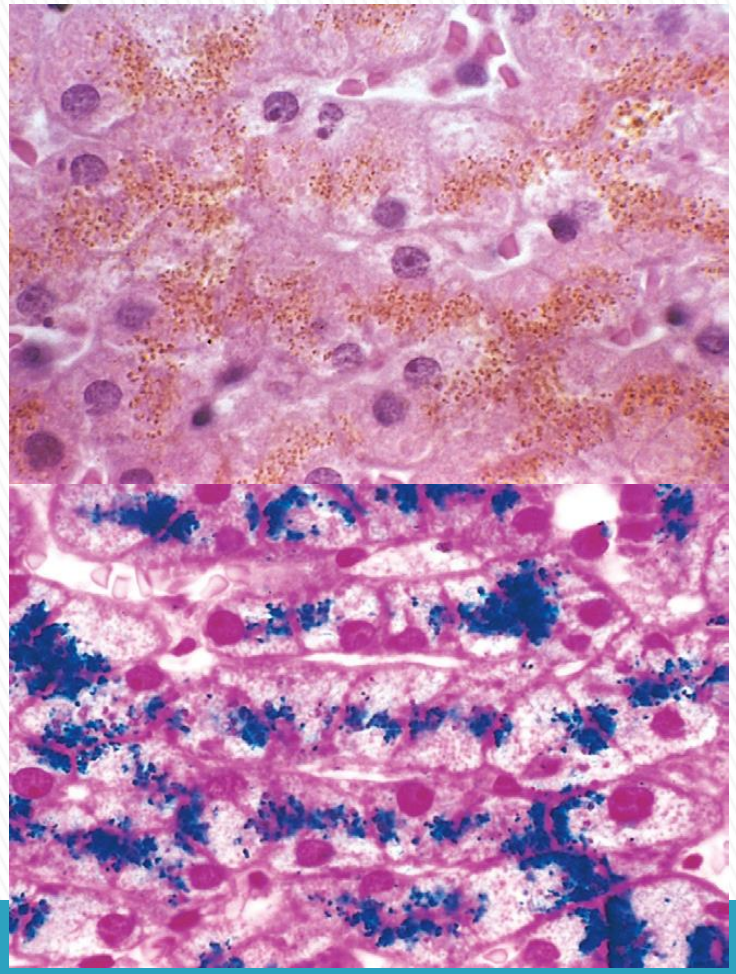
Pigments

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



pigments

- **Hemosiderin**
  - Hb-derived granular pigment
  - 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)



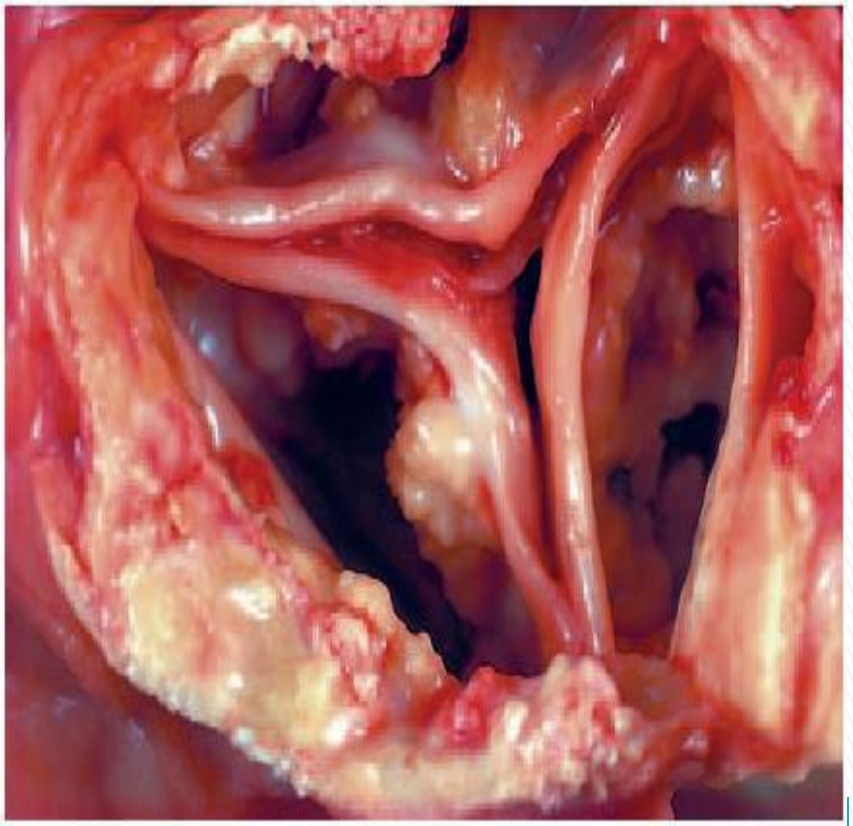
PATHOLOGIC CALCIFICATION

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

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

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

Dystrophic calcification



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

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**