PATHOLOGY

بسم الله الرحمن الرحيم

# MID – Lecture #5
# Intracellular accumulations and calcifications

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا


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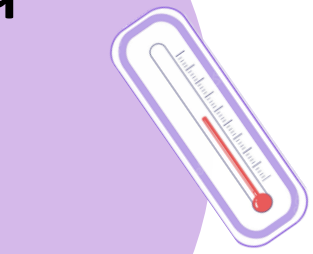


# Intracellular accumulations and calcifications

cell injury and adaptations

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# INTRACELLULAR ACCUMULATIONS

- Accumulation means the build up of a material inside the cell
This material could be endogenous or exogenous
- There are 4 mechanics by which this material is deposited :

- 1)Inadequate removal of a normal substance (fatty change in the liver)
Fats are normally stored in the hepatocytes
They will build up inside the liver cells upon inadequate removal
Example : fatty liver disease

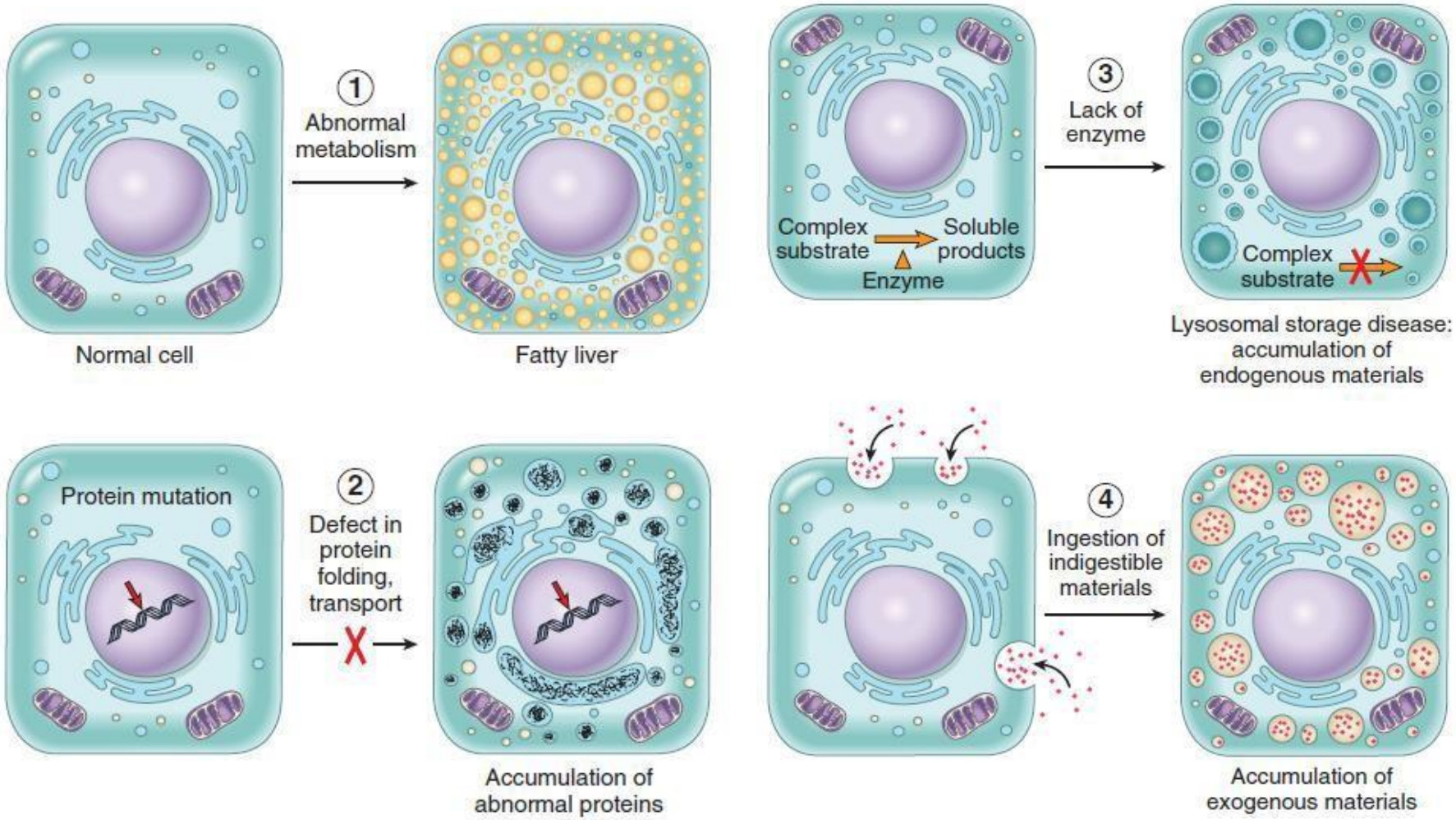
- 2)Accumulation of an abnormal endogenous proteins due to folding defect (α1-antitrypsin defficiency) When α1-antitrypsin enzyme is mutated and abnormal, it accumulates inside the cytoplasm

- 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) Like deposition of carbon in the lymph nodes in lungs

Deposition of a normal substance because of inadequate removal, like fatty liver disease

Substrate accumulation due to enzyme deficiency.
Like glycogen storage diseases

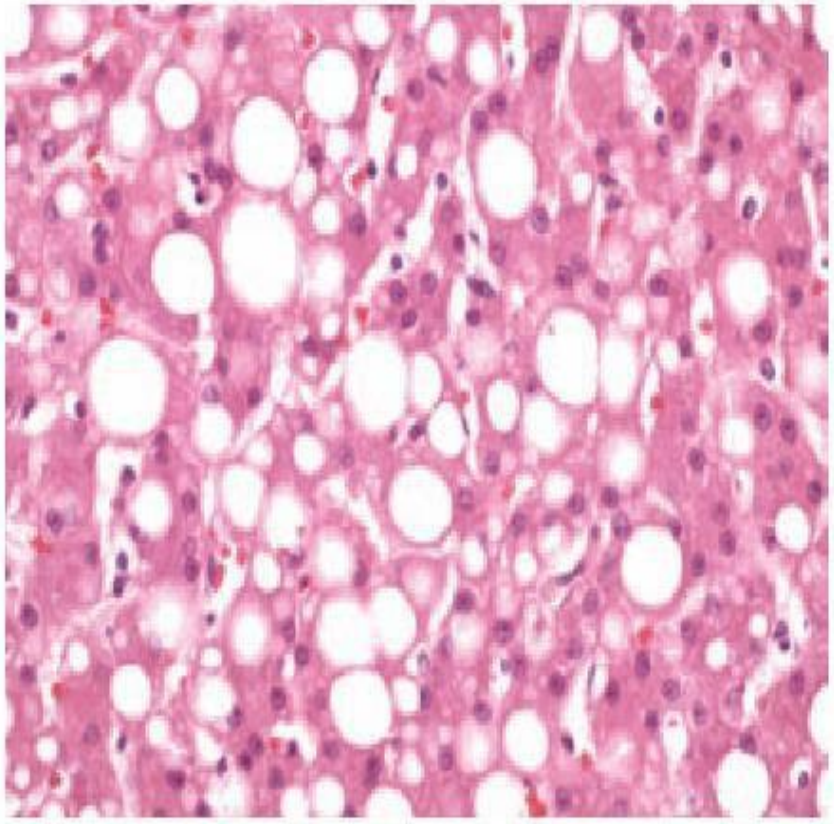



Deposition of an abnormal endogenous protein due to folding defect,
like in alpha-1 antitrypsin deficiency

Ingestion of an exogenous substance which is usually indigestible, such as carbon

# 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



Toxins like acetaminophen and CCl3

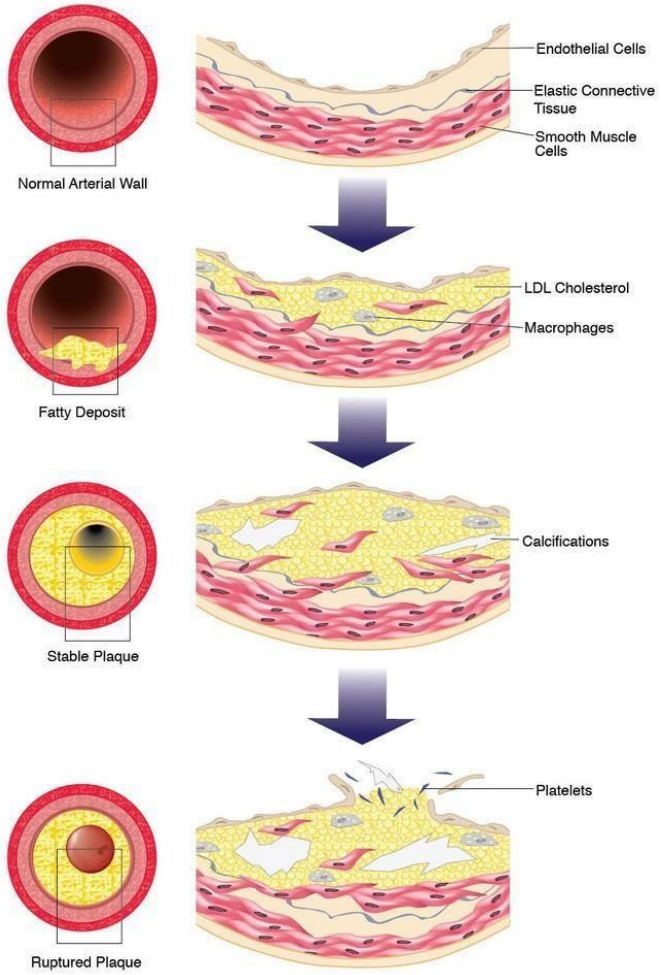
Anoxia : Loss of oxygen supply (not decreased but totally lost)

Lipids need apoproteins
If they are absent, lipids will accumulate in the liver

# Cholesterol and Cholesteryl Esters

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

Cholesterol is a normally found substance in the body; however, when present in high amounts, it could accumulate in the walls of blood vessels. This accumulation can lead to atherosclerosis, which narrows the artery lumen and may result in ischemia, myocardial infarction, and other cardiovascular issues.



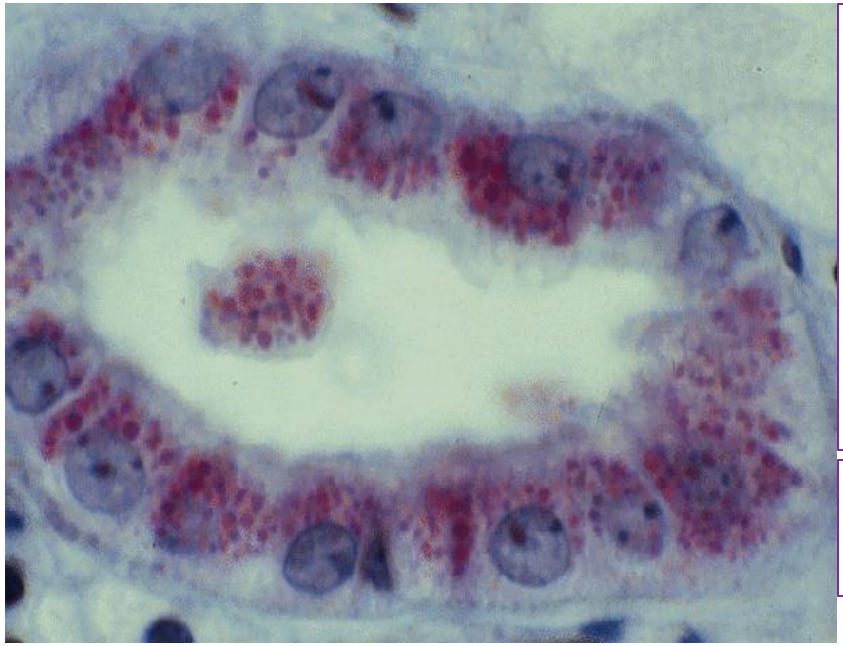
# Proteins

- 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.

  Alcoholic hyaline pink material deposites in the hepatocytes
- Neurofibrillary tangles in neurons

  In Alzheimer's disease

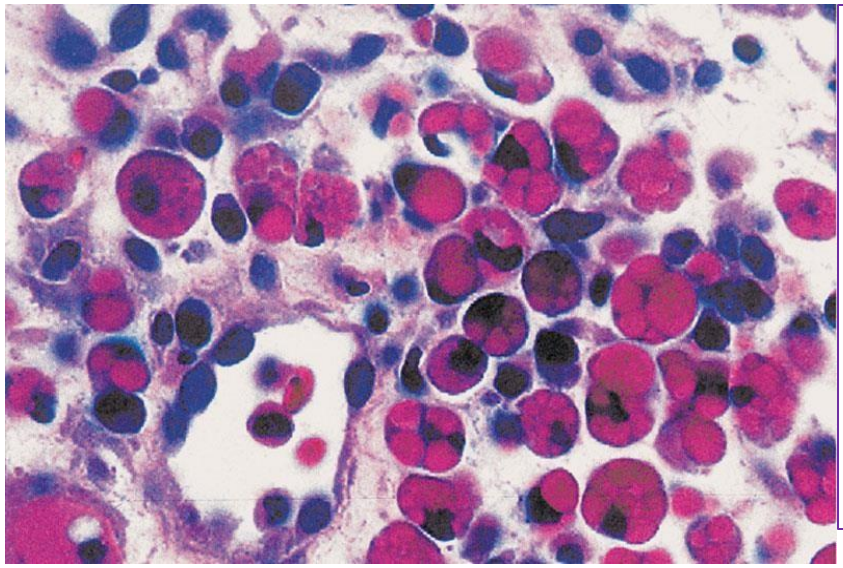
A general rule : ☺
Anywhere excessive plasma cells are existing , there must be a lot of antibodies



Renal tubule in nephrotic syndrome

Excess proteins leak out from the kidney
In nephrotic syndrome, the kidney tries to reabsorp them from the urine back to the renal tubules leading to their accumulation there

Pink dots around the nucleus are protein deposites



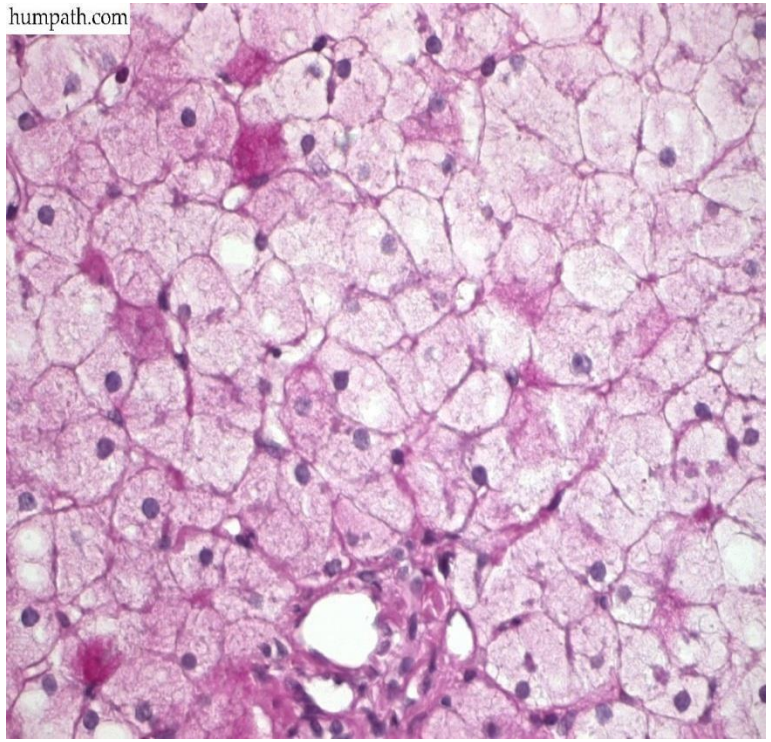
Russell bodies are immunoglobulins (normally existing substances) ,
when their amount get raised, they get accumulated in the cytoplasm of plasma cells.
They appear as pink deposites within the cytoplasm of plasma cells

# Glycogen

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

Glycogen degrading enzymes are deficient, so glycogen will build up

People who have diabetes also suffer from glycogen accumulation and deficiency in glycogen metabolism




H &E stain

This picture is from the liver.
Normal hepatocytes cytoplasm appears with pink colour under a microscope ,but here (in this case) it appears like foam

# Pigments (Exogenous or Endogenous)

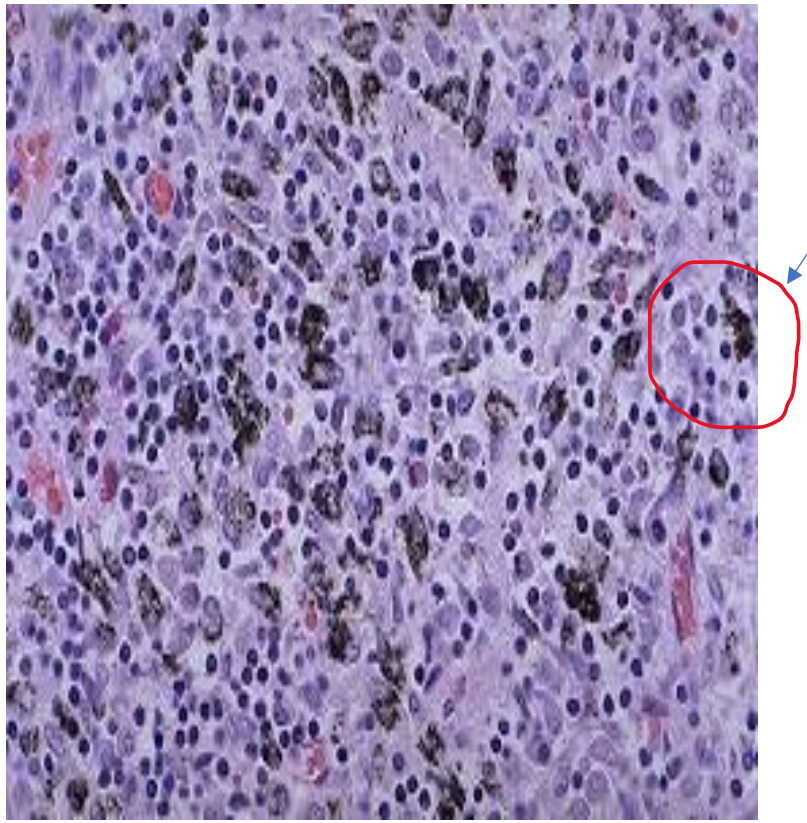
- **Exogenous**

- Most common exogenous, **carbon** (coal dust, air pollution) Also smoking
  It's a nondigestible material (especially smokers)

- Alveolar macrophages → lymphatic channels → tracheobronchial LN

- *Anthracosis* (Clinical name for the carbon pigment deposition)

Black color because of carbon



If we take a lung biopsy or lymph node (like bronchial lymph nodes), in laboratory it appears black (even if by the naked eye)

# Pigments

- **Endogenous**
- **Lipofuscin**
- “wear-and-tear pigment”

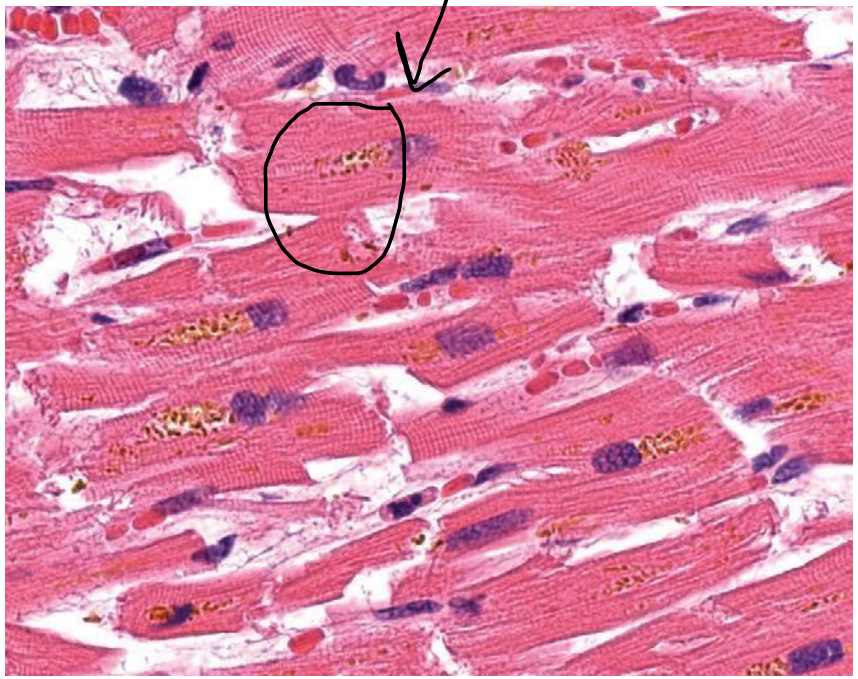
Caused by

- Age/atrophy (hypertrophy, on and off)

It can be in the

- Heart, liver, and brain
- Lipid and protein (Derived from damaged cell membrane)
- Marker of past free radical injury (Previous injury)
- *brown atrophy*

Granules of brown material in the cytoplasm

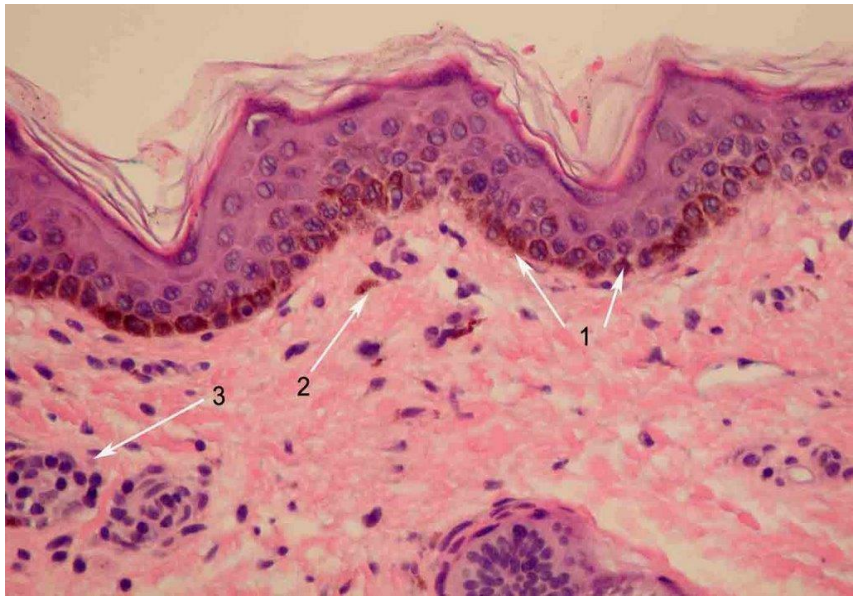


Cardiac muscle

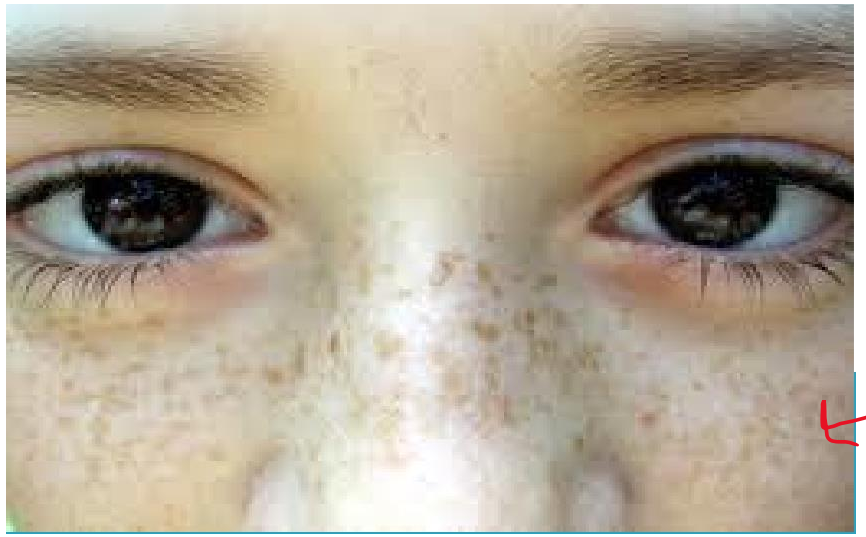
# Pigments

- **Endogenous**
- **Melanin**
- Source: melanocytes (Normally in the skin, but if there is an accumulation it will be an abnormality)

- UV protection
- Accumulates in dermal macrophages and adjacent keratinocytes
- Freckles



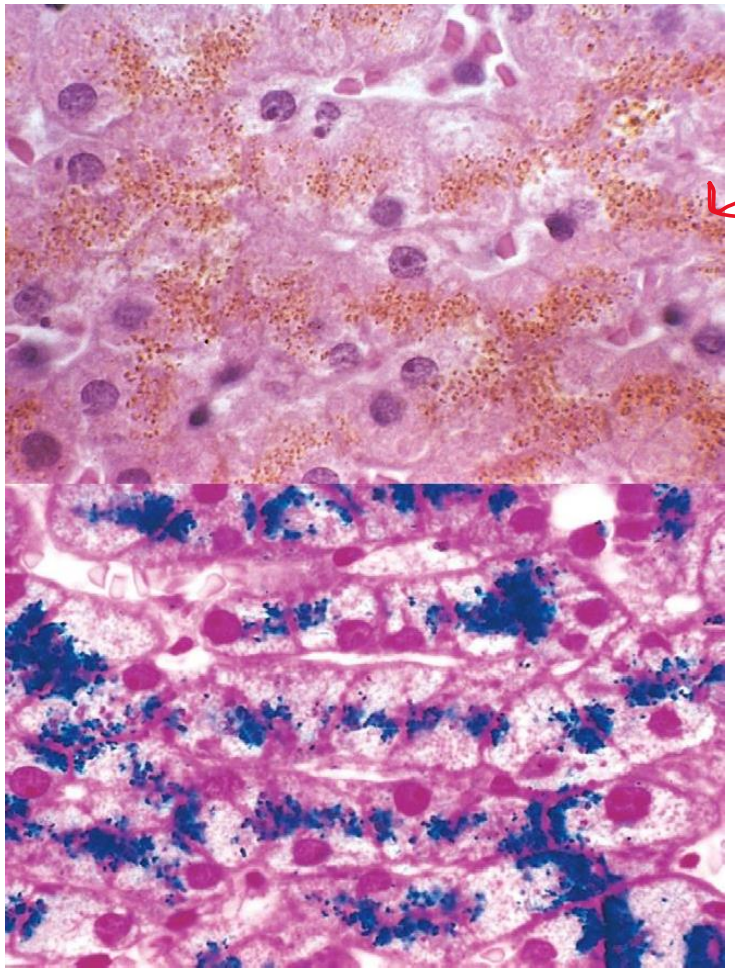

Increase of the brown pigment at the base of the basal keratinocytes



freckles

# pigments

- **Hemosiderin** (Iron-based pigment)
  - 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)



brown

To distinguish this case from another we can use (Prussian stain) which stains iron with blue color

(Genetic inherited disease leads to accumulation iron in different areas of the body)

Macrophages will come to the area to clean or engulf the iron to degrade it
And use it again for introduction of RBC

# PATHOLOGIC CALCIFICATION

Also considered as an intracelluler accumulation but its related to calcium

(The main)

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

2 types:

- **Dystrophic Calcification**
- Deposition in dead/injured tissues
- Normal Ca2+ metabolism — If we check the calcium level in the blood , it will be normal
- Exacerbated by Hypercalcemia ← (here it isn't the main reason)

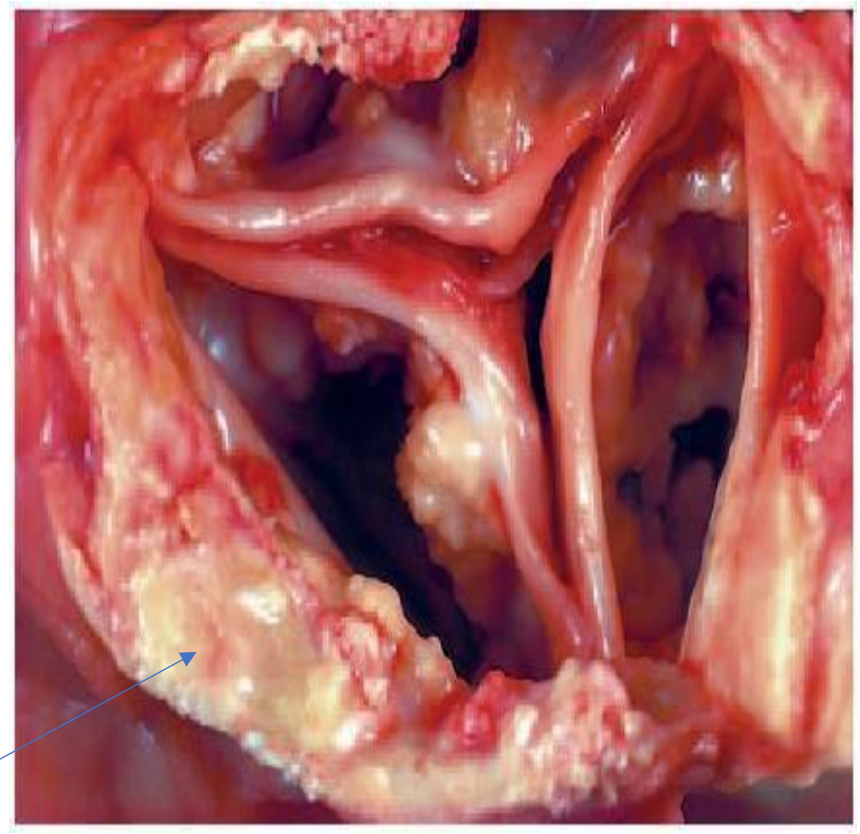
Calcium by the naked eye appears whitish, But under the microscope appears with a purple colour because we used the H&E stain

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

(The main cause)

Metastasis refers to cancer but here they call it metastatic because it's in everywhere of the body

# Dystrophic calcification



#white
#more rigid

Causes:

- **Necrosis of any type** Or inflammation of any type
- **Atherosclerosis, aging or damaged heart valves, aortic stenosis, tuberculosis)**

  Deposition in atherosclerotic blood vessels also make the vessel wall more rigid
- **Incidental finding indicating insignificant past cell injury**
- **Or May be a cause of organ dysfunction.** According to the amount of deposition

# Metastatic Calcification

## #Causes of Hypercalcemia:

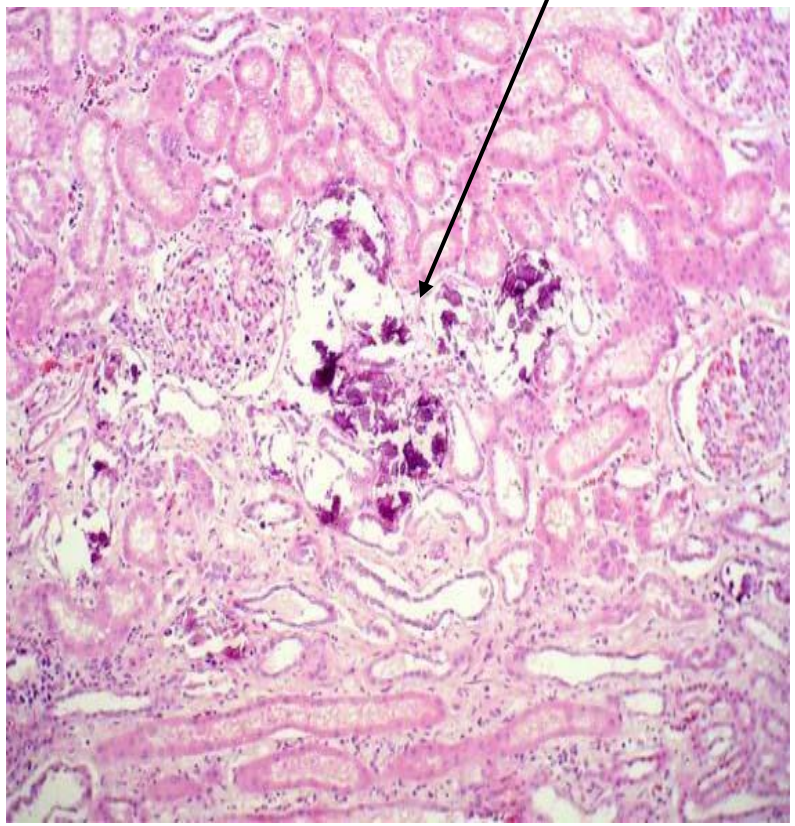
- Hyperparathyroidism (primary and parathyroid hormone related protein) Or secondary
  Parathyroid hormone involved the calcium metabolism regulation , increase the absorption of calcium from the gut
- Bone destruction (metastasis, MM, leukemia, Pagets, immobilization) → If the tumor enters the bone, it will release calcium from it to the bloodstream

Multiple myeloma

- Vit-D intoxication, High dose
- Sarcoidosis. Inflammatory Disease
- Renal failure with 2ry hyperparathyroidism.

## #Where deposition happens?

- VESSELS, LUNG, KIDNEY




kidney

# For any feedback, scan the code or click on it.

Corrections from previous versions:

| Versions | Slide # and Place of Error | Before Correction | After Correction |
|---|---|---|---|
| V0 → V1 | 4 | The captions for the top right and bottom left are in the wrong places. | The captions had been swapped. |
| V1 → V2 | | | |

# Additional Resources:

# رسالة من الفريق العلمي:

Reference Used:

قالَ ابنُ الجَوزيّ-رحِمهُ الله -
يا أخي، لا يبيعُ الباقيَ بِالفاني إلّا خاسِرٌ،
وإيّاكَ والأنسَ بِمَن تَرحَلُ عنهُ، فتبقى كالحائِرِ.
رفيقُ التّقوى رَفيقٌ صادِقٌ، ورفيقُ المعاصي غادِرٌ.
مَهرُ الآخرةِ يَسيرٌ :قلبٌ مُخلِصٌ ولِسانٌ ذاكِرٌ ☘!