[A QUICK SUMMARY]

[Pathology, 5th lec]

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**INTRACELLULAR ACCUMULATION MECHANISMS:**

1. **Inadequate removal of a normal substance**
   - Normal endogenous material
   - Inadequately removed
   - Accumulate
   - *E.g.* fatty change → liver

2. **Accumulation of an abnormal endogenous substance**
   - Misfolding protein
   - Accumulated in the ER
   - *E.g.* α1-antitrypsin deficiency disease

3. **Failure to degrade a metabolite due to inherited enzyme deficiencies**
   - Genetic mutation
   - Enzymatic deficiency
   - Accumulate of metabolites
   - *E.g.* Lysosomal storage diseases

4. **Deposition and accumulation of an abnormal exogenous substance**
   - Abnormal exogenous substances
   - Deposition in the cell
   - *E.g.* carbon deposition in the lung

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**FATTY CHANGE (STEATOSIS)**

*Causes:* Toxins (ex. Carbon tetrachloride) / Protein malnutrition / Diabetes mellitus (DM) / Obesity / Anoxia

*Where:* In the liver (organ involved in fat metabolism) heart, kidney, muscles

*Mechanism:* Deposition of triglycerides in the cells

*E.X.*: Alcohol abuse and DM + obesity >>> fatty liver disease.

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**CHOLESTEROL AND CHOLESTERYL ESTERS DEPOSITION**

*Causes:* Increased intake or decreased catabolism of these cholesterol and cholesterol esters.

*Where:* Walls of the blood vessels

*Mechanism:* Phagocytes and microphages uptake the fat >>> overloaded with lipids (triglycerides, cholesterol, and cholesterol esters).

*E.X.*: Atherosclerosis predispose to: coronary heart disease or cerebrovascular accidents.

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**GLYCOGEN DEPOSITION**

*Causes:* Abnormality in the glucose or glycogen metabolism

*E.X.*: Glycogen storage disease:

*Where:* Liver

*Mechanism:* Inherited abnormality in the metabolism of glycogen

*E.X.*: Diabetes mellitus (DM):

*Where:* Renal tubular cells, heart cells, or vessel cells of the pancreas
### Nephrotic Syndrome
- Lose large amount of **albumin** in the urine
- Increase reabsorption by the kidney
- Deposition of proteins in the **proximal convoluted tubules**
- Pinkish color droplets

### Russell Bodies in Plasma Cells
- Excessive amounts of immunoglobulin production in the **plasma cells**
- Deposited in the **ER** of the plasma cells
- Pinkish color droplets

### Alcoholic Hyaline in Liver
- In the **liver** cells of alcoholic patients

### Neurofibrillary Tangles in Neurons
- In the neurons of patients with Alzheimer's disease

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### Pigments

#### Exogenous
- **Carbon**
  - **Causes**: Aging and atrophy
  - **Where**: Heart, liver, and brain cells
  - **Color under the L.M**: Brown-yellow granular pigment
  - **E.X**: Brown atrophy: Excessive amount of lipofuscin pigment turns brown in color (atrophy)

#### Endogenous
- **Melanin Pigment**
  - **Causes**: Melanocyte in the skin
  - **Where**: In the dermal macrophages and adjacent keratinocytes at the basal cell layer of the skin
  - **Color**: Large amount in the skin >> Deep colored skin / Small amount >> Fair colored skin
  - **E.X**: Freckles

- **Hemosiderin Pigment**
  - **Causes**: Excessive deposition of iron either in physiologic or pathologic ways
  - **Where**: Physiologic: Tissues have a rabid red blood cell turnover like in macrophages & phagocytes of the bone marrow, spleen or liver
    - **Pathologic**: Check below
  - **Color under the L.M**: Brown granular pigment

#### Lipofuscin Pigment
- Wear-and-tear pigment

### Diseases
- **Anthracosis** [in lung]
- **Causes**: Air pollution or cool dust
- **Mechanism**: Alveolar macrophages ingest the carbon → Lymphatic channels → Tracheobronchial LN
- **Color under the L.M**: Black granular pigment [inside the macrophages]

### Others
- It is an indication of a previous free radical injury
  - Peroxidation of the membranes and damage to the lipids
- Melanin offers protection against UV light & colorizes the skin
- **Pathologic deposition**:
  1. **Bruise**: After a localized hemorrhage
  2. **Hemosiderosis**: Causes: Hemochromatosis, hemolytic anemias, repeated blood transfusions
- **Iron + Apoferritin = Ferritin Micelles**
Pathologic calcification = Abnormal deposition of calcium salts + smaller amounts of Iron, magnesium & other minerals.
Aging is associated with a progressive decline in the life span and functional capacity of cells. Replicative senescence is a progressive decrease in the number of divisions that a cell can undergo.

**Cellular Aging**

- **Environmental and metabolic insults**: Radiation, UV light, toxins, ROS
- **Lowering Cell's capacity to repair any damage**
- **Accumulation of mutations in DNA**: Defective DNA repair
- **Telomere shortening**: The cell goes into cell cycle arrest
- **Proteins, damaged proteins**: Less chaperones, more proteins degradation, less # of proteins
- **Decreased cell functions, cell loss**: Due to less activity of the telomerase enzyme

**Telomerase**
- Short repeats of DNA at the end of the chromosomes, which protect the coding material of chromosome at both ends & ensure complete replication of them
- Progressive shortening upon replication (aging)
- Telomere length is maintained by telomerase enzyme.
- Telomerase expressed in germline cells, low levels in stem cells, but absent in most somatic cells.
- Telomerase is reactivated in cancer cells.

**Anti-aging - slowing of aging (elixir of youth)**
- Calorie restriction improve immunity reduce IGF
- Physical activity: Stress accelerates aging
- Precise mechanisms underlying these effects remain to be defined
- Persistent inflammation, chronic metabolic diseases, accelerates aging