Deposition and pigmentation

Intracellular accumulation

Under some circumstances, cells may accumulate abnormal amounts of various substances, which may be harmless or may cause varying degrees of injury. The substance may be located in the cytoplasm, within organelles (typically lysosomes), or in the nucleus.

The main pathway are:

1. Inadequate removal of normal substance secondary to defect in mechanism of package & transport (Ex: Fatty changes in the liver)
2. Accumulation of an abnormal endogenous substance because of genetic or acquired defect in its folding, packages, transport or secretion (Ex: alpha- anti- trypsin deficiency).
3. Failure to degrade a metabolite due to inherited enzyme deficiency. The resulting disorder called storage disease.
4. Deposition and accumulation of abnormal exogenous substance because the cell has neither enzymatic machinery to degrade the substance nor the ability to transported it to another sites (Ex: accumulation of carbon &silica particles).

Note : Figure in last page

Steatosis (Fatty Change)

The terms steatosis and fatty change describe abnormal accumulations of triglycerides within parenchymal cells. Fatty Change is often seen in the liver because it is the major organ involved in fat metabolism, but it also occurs in heart & skeletal muscle.

* Alcohol abuse & diabetes with obesity are the most common causes of fatty changes in the liver.

*It results from excessive entry or defective metabolism and export of lipid

Morphology:

Fatty change is most often seen in the liver and heart. In all organs fatty change appears as clear vacuoles within parenchymal cells.

Protein

Protein accumulation much less common than lipid.

It occurs when excesses are presented to the cells or if the cells synthesize excessive amount. Ex: in nephrotic syndrome: there is heavy protein leakage lead to much larger reabsorption of the protein that accumulate as pink hyaline cytoplasmic droplets

Glycogen

Deposition of glycogen usually associated with abnormality in metabolism of glucose or glycogen.

Ex.: Poorly controlled diabetes mellitus the glycogen accumulate in renal tubules, cardiac myocytes &B cell islets of Langerhans in the pancreas.

Other Ex. Glycogen storage disease (group of genetic disease)

Pigmentation

Pigment: are colored substances that are either:

1- Exogenous coming from outside the body such as carbon.

2- Endogenous that synthesis inside the body such as melanin.

1. Carbon:

is the most common exogenous substances when inhaled phagocytosed by alveolar macrophages & transported to the regional tracheobronchial lymph nodes.

2. Lipofuscin:

represents complexes of lipid & protein that appear as an insoluble brownish- yellow granular intracellular material that accumulate in verity of tissues (heart, liver & brain), as a function of age or atrophy.

3. Melanin:

is an endogenous brown- black pigments that synthesized by melanocytes located in the epidermis & act as a screen against harmful ultraviolet radiation.

4. Hemosiderin:

is a hemoglobin derived granular pigments that is golden- yellow to brown & accumulated in tissues when there is excess of iron.

- Although the accumulation of hemosiderin is pathological, there is a small amount of this pigment normally seen in phagocytes of the bone marrow & spleen where aging red cells are degraded.

Pathologic Calcification

1. DYSTROPHIC CALCIFICATION:

There is deposition of calcium salt in dead or dying tissue & occurs in absence of derangement in calcium metabolism (normal serum levels of calcium)

*It is encountered in areas of cell injury or necrosis.

*It is almost always present in the atheroma of advanced atherosclerosis. It also commonly develops in aging or damaged heart valves.

2. METASTATIC CALCIFICATION:

In which there is deposition of calcium salt in normal tissues & it is almost always secondary to derangement in calcium metabolism (hypercalcemia).

Causes of Hypercalcemia:

1. Increased secretion of parathyroid hormone (hyperparathyroidism)

2. Destruction of bone tissues, secondary to primary tumors of bone marrow e.g., multiple myeloma, leukemia

3. vitamin D-related disorders including vitamin D intoxication, sarcoidosis.

4. Renal failure: which causes retention of phosphate and lead to secondary hyperparathyroidism.

Amyloidosis

Is a condition associated with a number of inherited & inflammatory disorders in which extracellular deposits of fibrillary proteins are responsible for tissue damage & functional compromise

Pathogenesis:

Amyloidosis results from abnormal folding of proteins which are deposited as fibrils in extracellular tissue & disrupt normal function.

- Normally misfolded proteins are degraded intracellularly by proteasomes or extracellularly by macrophages.

On biochemical form of amyloid proteins:

1. **AL (Amyloid light chain) protein**: it is produced by plasma cells & is made up of complete immunoglobulin light chain.

2. **AA (amyloid associated) fibrils**: it is non- immunoglobulin protein derived from larger serum precursor called SAA (Serum Amyloid Associated) protein that synthesized in the liver.

3. **AB amyloid**: it is derived from larger transmembrane glycoprotein called Amyloid Precursor protein (APP), it is usually found in cerebral lesions of Alzheimer disease

Morphologically

In general small amounts are not recognized grossly on cut surface.

- When amyloid accumulate in large amounts, the organ frequently is enlarged & tissue appears grey, waxy & firm in consistency.

- On histological examination: the amyloid deposition is extracellular between cells often closely adjacent to the basement membranes.

- The most commonly used staining technique is **Congo red** which appear under light microscope as a pink or red color to amyloid deposits.

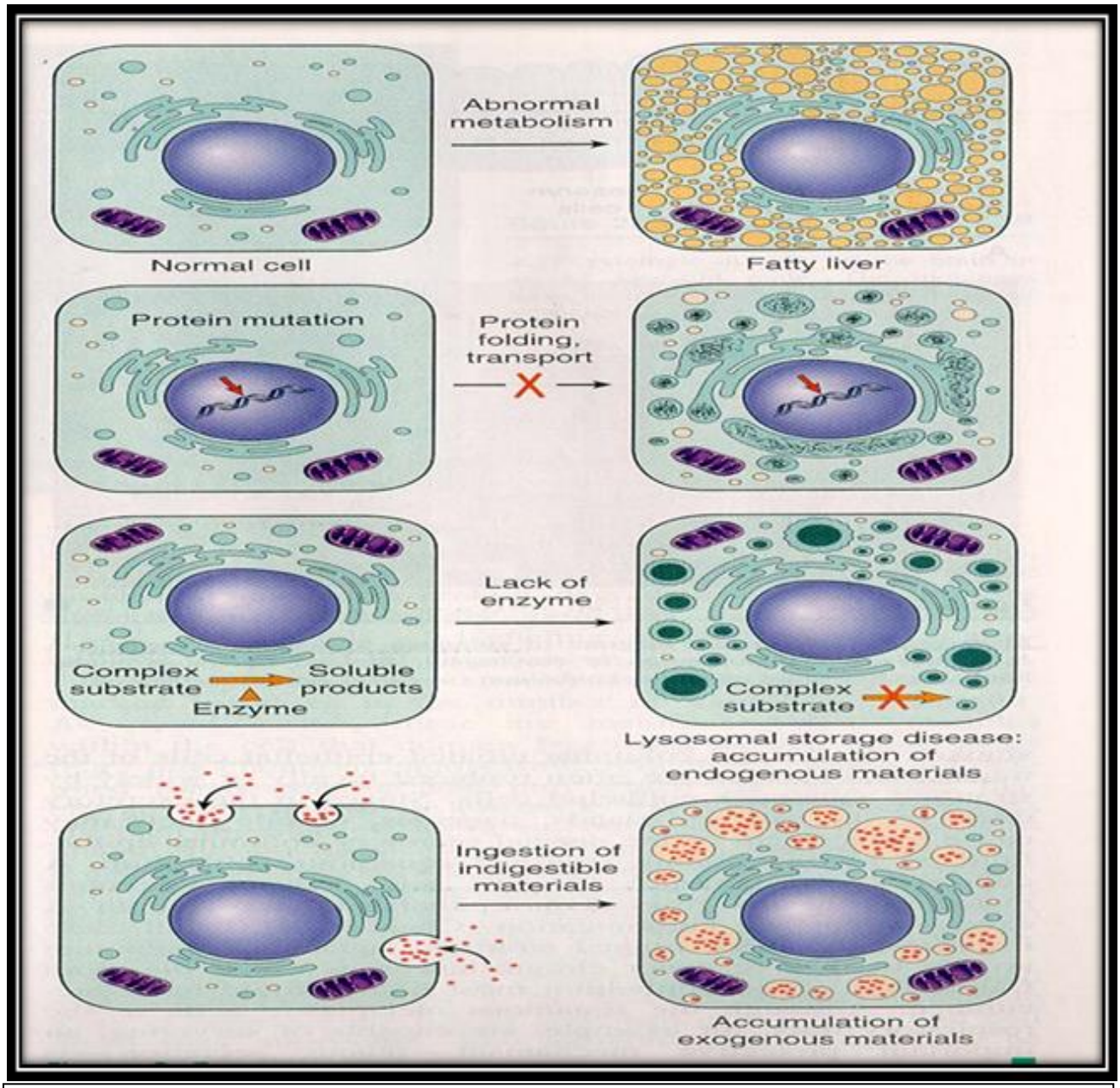
The pattern of organ involvement:

* **In kidney**: the amyloid deposits are found in the glomeruli & also are present in the interstitial tubules as well as in the wall of the blood vessels.

* **In spleen**: has two patterns, either the deposits are limited to the splenic follicles produce granules (sago spleen).

Or amyloidosis may principally involve the splenic sinus & may extended to the splenic pulps with formation of sheet like deposits (Lardaceous spleen)

* **In the heart**: the deposits typically are found throughout the myocardium beginning between myocardial fibers & causing their pressure atrophy.



Mechanisms of intracellular accumulation: *(1)* Abnormal metabolism, as in fatty change in the liver. *(2)* Mutations causing alterations in protein folding and transport, so that defective molecules accumulate intracellularly. *(3)* A deficiency of critical enzymes responsible for breaking down certain compounds, causing substrates to accumulate in lysosomes, as in lysosomal storage diseases. *(4)* An inability to degrade phagocytosed particles, as in carbon pigment accumlation