Intracellular accumulation substances

There are four main pathways of abnormal intracellular accumulations:

- Inadequate removal of a normal substance secondary to defects in mechanisms of packaging and transport.
- Accumulation of an abnormal endogenous substance as a result of genetic or acquired defects in folding, packaging, transport, or secretion.
- Failure to degrade a metabolite due to inherited enzyme deficiencies.
- Deposition and accumulation of an abnormal exogenous substance due to defect in enzymatic machinery that degrade the substance or defect in transporing it to other sites.

Depositions of lipids

Fatty Change (Steatosis) refers to any abnormal accumulation of triglycerides within parenchymal cells resulting from excessive intake or defective transport (often because of defects in synthesis of transport proteins) leading to reversible cell injury. Alcohol abuse and diabetes associated with obesity are the most common causes of fatty change in the liver.

Cholesterol deposition

It occurs in macrophages and smooth muscle cells of vessel walls in atherosclerosis, Cellular cholesterol is important in regulated normal cell membrane synthesis but defective catabolism and excessive intake leading to intracellular accumulation in phagocytic cells in several different pathologic processes such as atherosclerosis.

Deposition of proteins

Protein accumulations are much less common than lipid accumulations; as a result from cells excessive amounts synthesize (ex: amyloidosis, alcoholic hyaline in the liver and Russal bodies)

Deposition of glycogen

Excessive intracellular deposits of glycogen are associated with abnormalities in the metabolism of either glucose or glycogen (diabetes mellitus , glycogen storage diseases).

Deposition of pigments

Pigments are colored substances that are either exogenouscoming from outside the body, such as carbon, or endogenous synthesized within the body itself, such as lipofuscin, melanin, and certain derivatives of hemoglobin.

• *Lipofuscin,* or "wear-and-tear pigment," is an insoluble brownish-yellow granular intracellular material that accumulates in a variety of tissues as a function of age or atrophy.. It is not injurious to the cell but is a marker of past free radical injury.

• *Melanin* is an endogenous, brown-black pigment that is synthesized by melanocytes located in the epidermis and acts as a screen against harmful ultraviolet radiation.

• *Hemosiderin* is a hemoglobin-derived granular pigment that is golden yellow to brown accumulates in tissues when there is a local or systemic excess of iron.

Pathologic calcifications

Dystrophic calcification refers to deposition of calcium at sites of cell injury and necrosis and metastatic calcification refers to deposition of calcium in normal tissues, caused by hypercalcemia (excessive parathyroid hormone)

Ageing

Cellular aging is the result of a progressive decline in the life span and functional capacity of cells. Several mechanisms are thought to be responsible for cellular aging:

- Accumulation of DNA damage: defective DNA repair mechanisms (free radicals effect,
- Replicative senescence: reduced capacity of cells to divide secondary to progressive shortening of chromosomal ends (telomeres) Telomere length is maintained by an enzyme called telomerase.
- Other factors: progressive accumulation of metabolic damage, Defective protein homeostasis, calorie restriction