Intracellular Degenerations:

- Degeneration is defined the change or decomposition of the chemical components of the cell into a simpler substance, or **Accumulation of Normal Cellular Constituent in Excess such as water, fat, protein , etc.**

Types of Intracellular Degenerations

1- cloudy swelling degeneration

- It is the simplest and most common type of degeneration

- the cell is increased in size and cytoplasm is cloudy or darkened because the accumulation of water droplets and protein granules **in Excess** in the cytoplasm.

-It is called by other names:

- parenchymatous degeneration Because it occurs frequently in parenchymal organs such as the liver, kidneys, spleen, pancreas, and myocardium

- cloudy swelling is also called albuminous degeneration (named so because of the presence of prominent protein granules in the cytoplasm)

Mechanism of cloudy swelling degeneration (PATHOGENESIS)

- Changes in cell membranes, the endoplasmic reticulum, and mitochondria, resulting in disruption of membrane permeability or oxidative phosphorylation.

Or both processes, which leads to a disturbance in the ionic exchange and water between the cell and its environment, where large quantities of potassium ions exit the cell and instead sodium ions enter the cell, taking water with them, which leads to the appearance of water droplets in the cytoplasm.

- As for the accumulation of protein granules in the cytoplasm, it results from the loss of energy necessary for protein metabolism, which leads to a disorder in the process of protein metabolism.

macroscopic appearance or Gross pathology

- The affected organ is increases in size, soft and pale

- A change occurs in the structures of the organs, for example, the liver lobes become unclear

microscopic appearance

1- Cells are swollen with frayed margins; The cytoplasm is granular cloudy appearance or small clear vacuoles

2- Swelling of the renal tubule cells leads to narrowing or closure of the lumen

3- Swollen of liver cells leads to narrowing or closing of the liver sinusoids

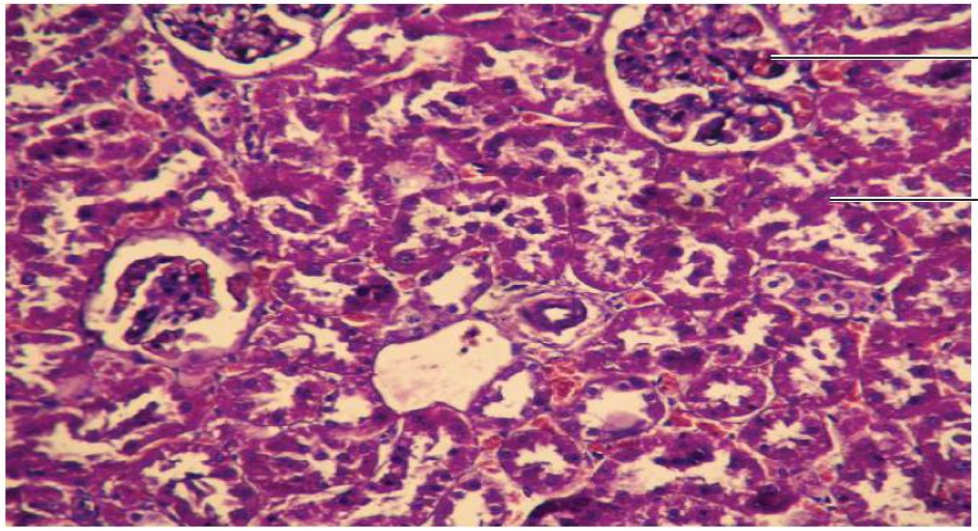


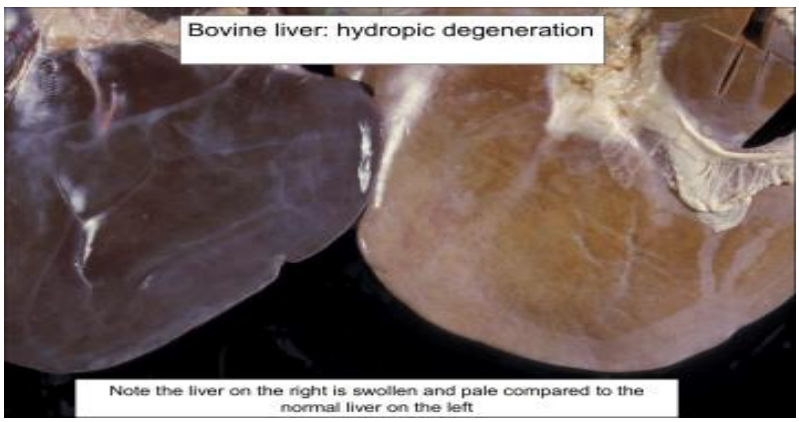
FIGURE 1.13. Section from cloudy swelling kidney showing tubules lined by swollen cells with frayed margins and increased granularity (H&E; 200×).

2- Hydropic degeneration

- It is considered the severe type of cloudy swelling, and the most affected cells are the epithelial cells, especially in the epidermis of the skin and the kidneys

-if Large amounts of clear fluid accumulate in the cytoplasm, is called serous degeneration. Or oedema of cell or granular degeneration.

-if Appearance as one large vacuole (vacuolar degeneration) or Affected cells are ballooned, cytoplasm pale with multiple vacuoles , Vacuoles coalesce and push nucleus towards the periphery (ballooning degeneration)



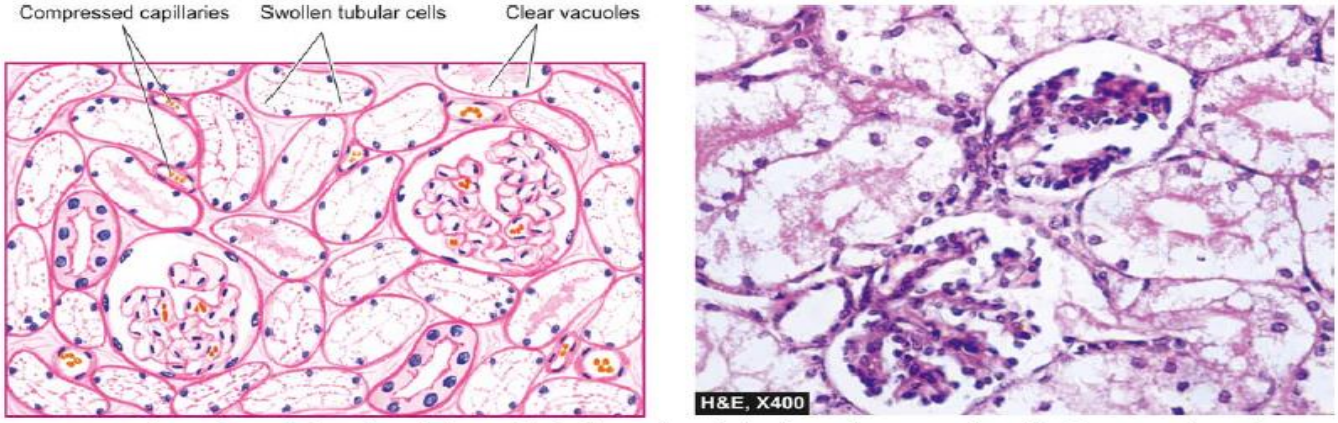


Figure 2.7 Hydropic change kidney. The tubular epithelial cells are distended with cytoplasmic vacuoles while the interstitial vasculature is compressed. The nuclei of affected tubules are pale.

3- Fatty degeneration or fatty change or STEATOSIS

- The term fatty change is used to refer to fatty degeneration and fatty infiltration at the same time because of the difficulty in determining the origin of the fats that are seen in the cytoplasm of the cells.

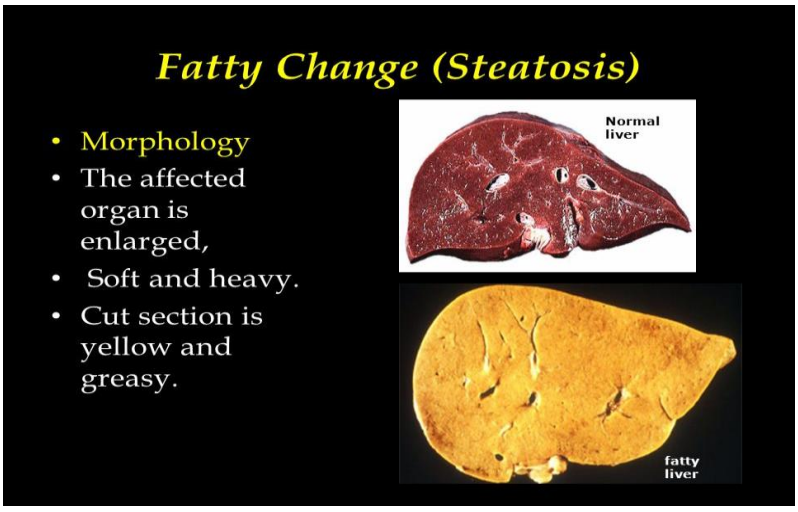
-The fatty change describe abnormal accumulations of triglycerides within parenchymal cells.

macroscopic appearance or Gross morphology

- In diffuse fatty change the organ such as liver or kidney and heart increase in size and are pale or yellow in color,

- soft and greasy in texture, and it is fragile and easy to tear

- In the case of fatty change resulting from lack of oxygen, the distribution of fat in the heart is in the form of spots or yellow parallel lines, and this gives the heart muscle an appearance that resembles the skin of a tiger.



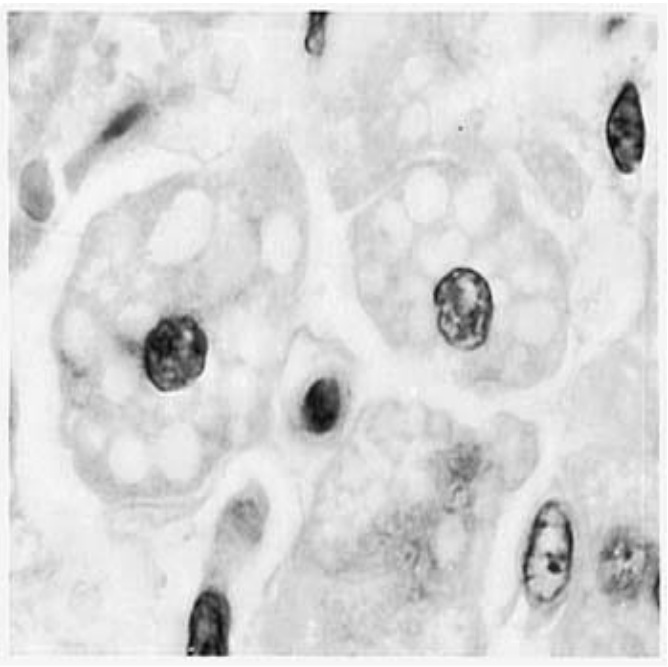
microscopic appearance

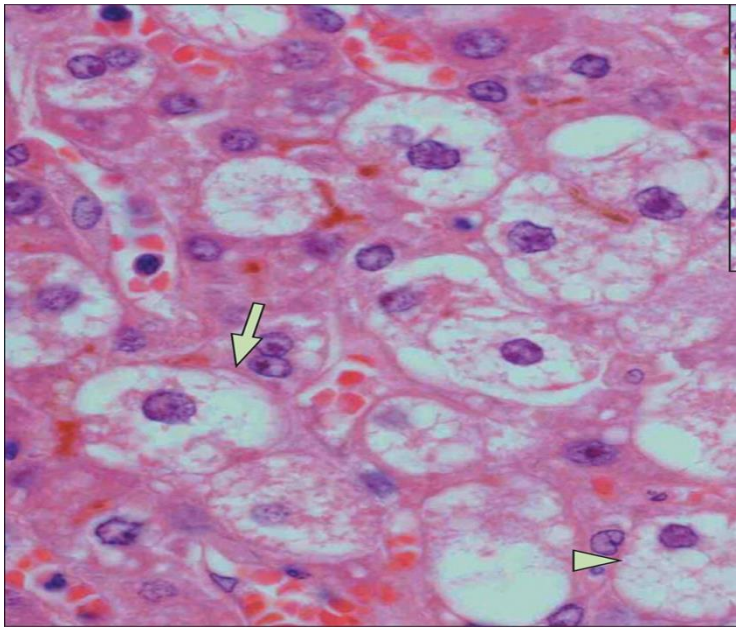
-- It is not possible to notice the fat droplets with the light microscopic preparation methods because the solutions used in them dissolve the fat, leaving vacuoles or spaces that were occupied by the fat in the cells, so special dyeing methods are used for fats such as Sudan black dyes and using the freezing method.

Types of Fatty Liver

Acute Fatty Liver

Acute fatty liver is a rare but serious condition associated with acute liver failure. In acute fatty liver, triglyceride accumulates as small, membrane-bound droplets in the cytoplasm (microvacuolar fatty change) and nuclei are centrally located



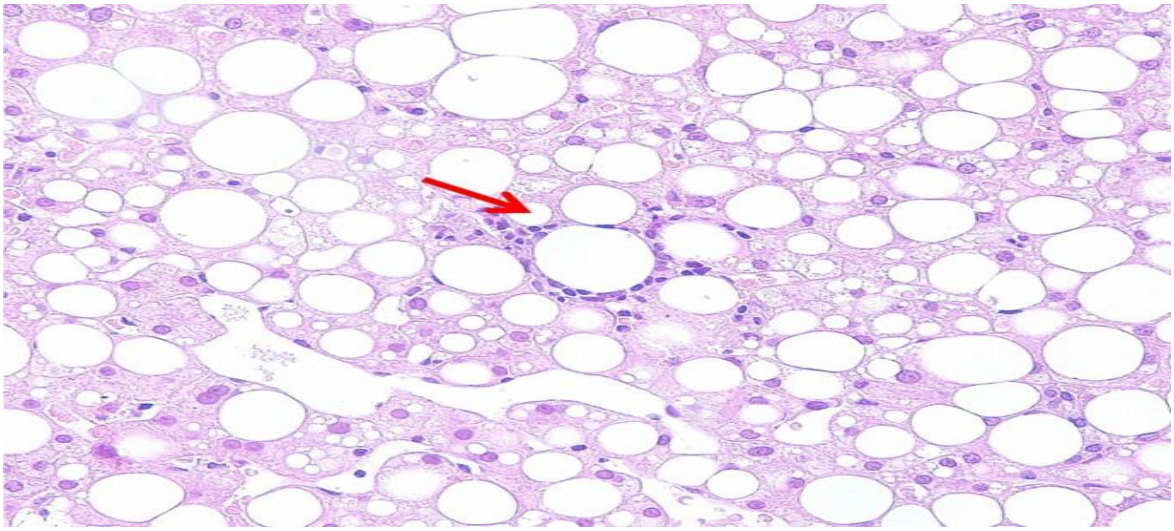


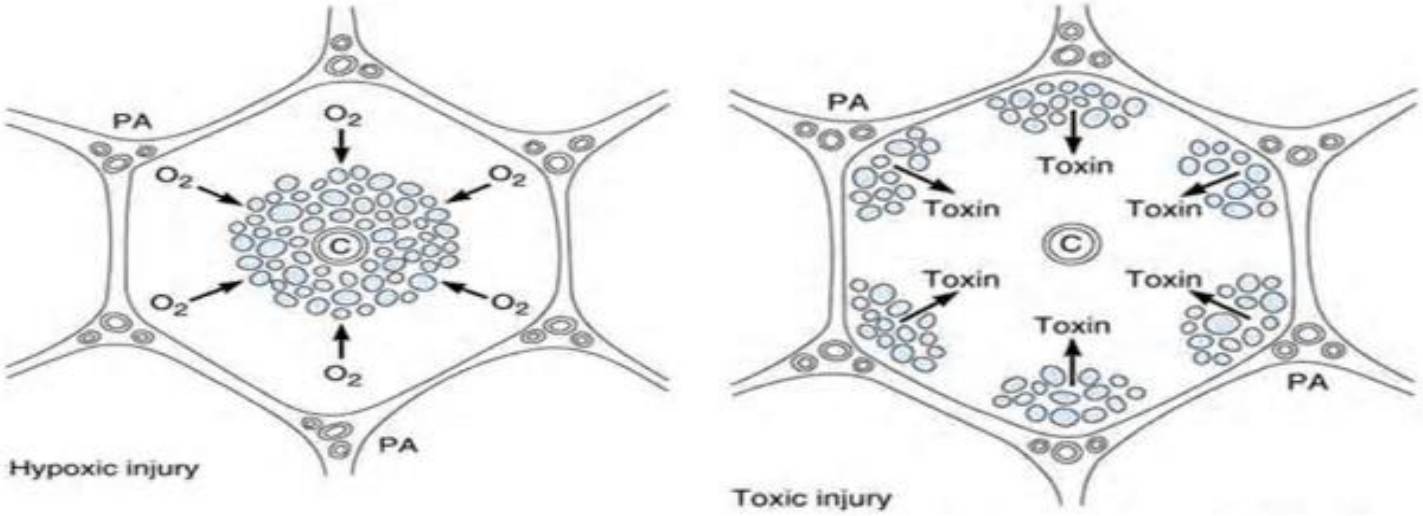
Chronic Fatty Liver

-Chronic fatty liver is much more common. It is associated with chronic alcoholism, malnutrition, and several hepatotoxins.

- Fat droplets in the cytoplasm fuse to form progressively larger globules (macrovacuolar fatty change).

-The large fat globules in the cytoplasm appear as empty spaces that have displaced the nucleus to the side. The degree of fatty change varies from slight to marked .





Distribution of fatty change (tinted circles) in the liver in hypoxic and toxic liver injuries. In hypoxic injury, fatty change is centrizonal; in toxic injury, fatty change occurs around the portal areas. The rules relating to this distribution, which are dependent on the mode of entry of oxygen and toxins into the liver lobule, are not without exception. Carbon tetrachloride, for example, causes centrizonal fatty change.

Pathogenesis of Fatty Liver

Various mechanisms are involved in excess accumulation of triglyceride in the liver

From peripheral stores FFA enters into liver during starvation and diabetes:

1- Defective metabolism of lipids: This may be due to:

— Increased synthesis of fatty acids by liver

— Decreased oxidation of fatty acids into ketone bodies resulting in increased esterification of fatty acids into triglycerides.
— Decreased synthesis of apoproteins (e.g. in CCl4 and protein malnutrition) causes decreased formation of lipoproteins from triglycerides.
2- Defective excretion of lipoproteins: Fatty liver may also develop due to defect in excretion of lipoproteins from liver into the blood

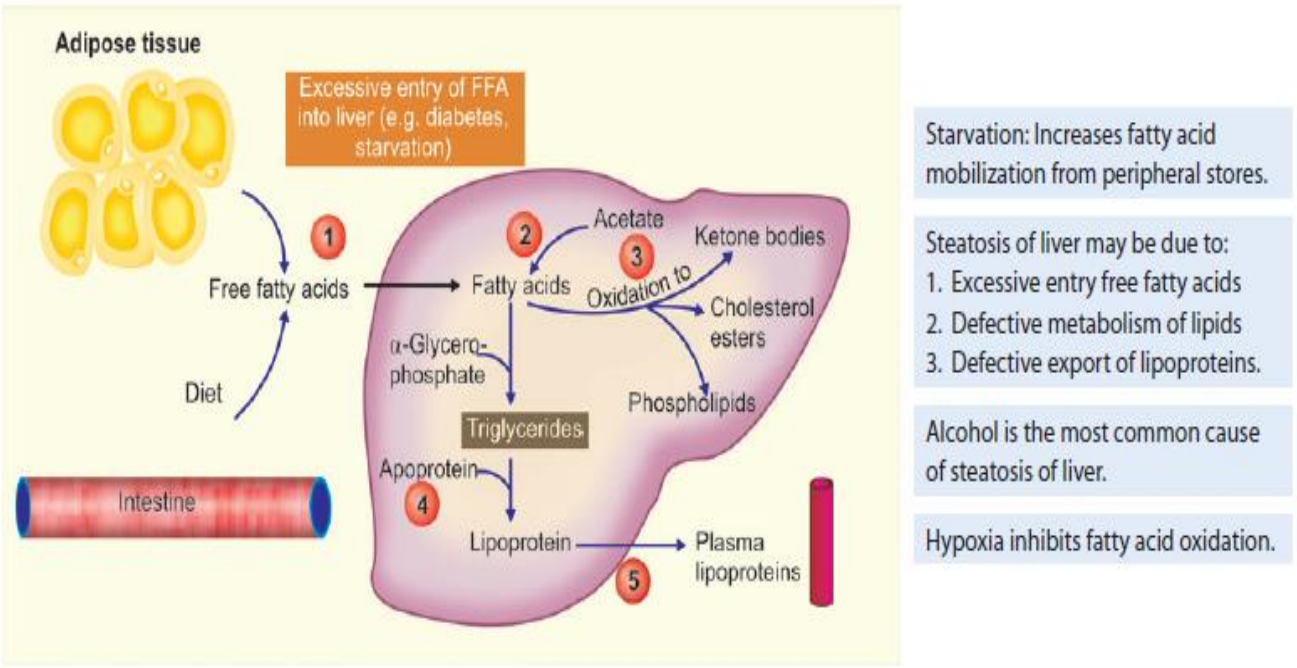


Fig. 1.13: Various mechanisms that can produce accumulation of triglycerides in fatty liver

4- hyaline droplet degeneration (reabsorption droplets)

- Intracellular accumulations of proteins usually appear as homogeneous (glassy) rounded, eosinophilic droplets, aggregates in the cytoplasm duo to reabsorption of large amounts of protein from the glomerular filtration .

- occur in epithelial cells of renal tubules, and it can occur in the other organs.

macroscopic appearance

-The affected organ is larger , pale and hard texture.

microscopic appearance

- Clear transparent droplets ,stain red or pink with eosin (eosinophilic) and dark red with van gieson are observed in the cells

- swelling of cells and narrowing of luman ,and these droplets may burst and thus fill the renal tubule cavities

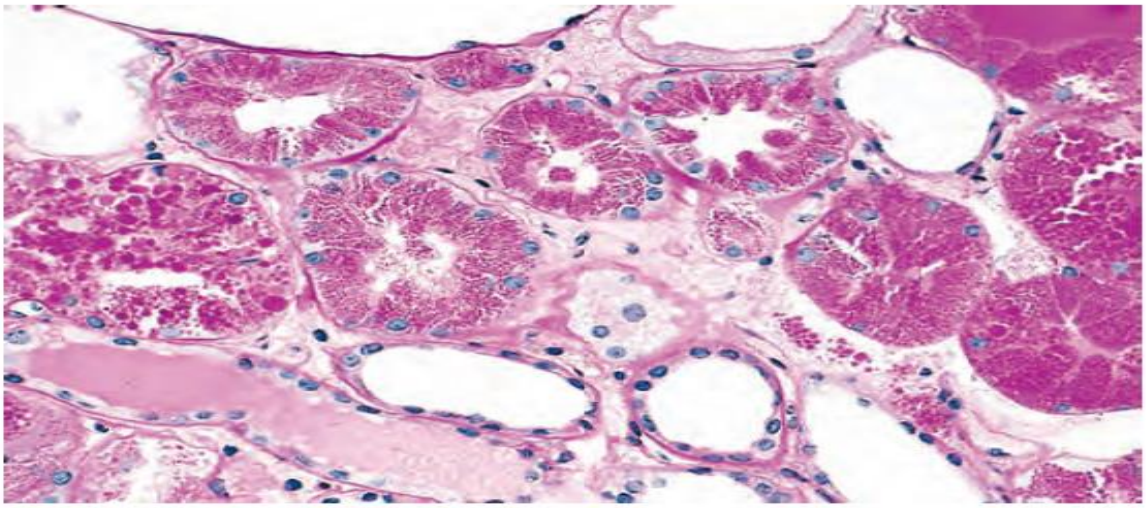


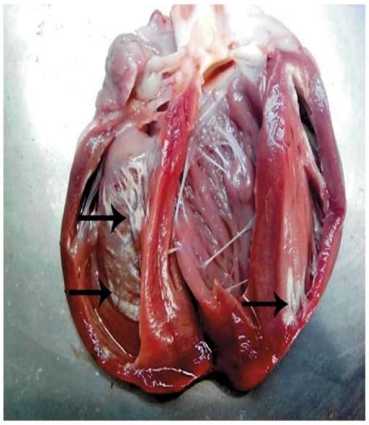
Figure 2-32 Protein reabsorption droplets in the renal tubular epithelium.

5- hyaline degeneration or Zenker's degeneration

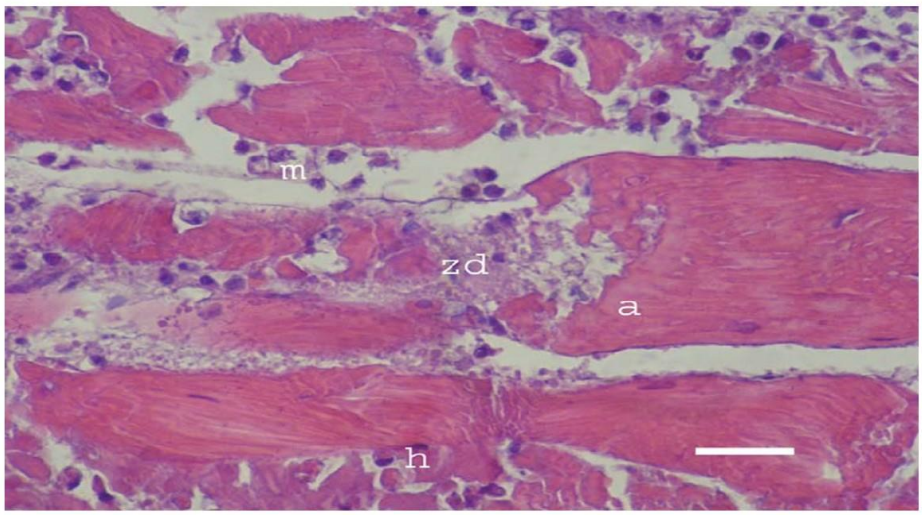
- **Zenker's degeneration** also called **Zenker's necrosis or** or waxy hyaline degeneration **because its associated with** Coagulative necrosis of striated muscles(cardiac and skeletal muscles).

- **Grossly**, the muscles appear pale and friable due to coagulation of sarcoplasm protein

-**microscopically**, the muscle fibres are swollen, with loss of cross striations, and show a homogeneous, glassy, pink or eosinophilic appearance in routine histologic sections stained with hematoxylin and eosin. small hemorrhage and Coagulative necrosis occurs



Zenker's necrosis in heart muscle (black arrow)



Degenerative necrotic changes (Zenker's degeneration) (zd), increased acidophilia (a), heterophil leukocytes (h) and macrophages (m) among dead muscle tissue, Haematoxylin-eosin, bar: 35 µm

6-hyaline degeneration of plasma cells

- - Russell bodies is Excessive immunoglobulins in endoplasmic reticulum in certain plasma cells engaged in active synthesis of immunoglobulins

- When multiple inculsions are seen in a plasma cell, then it is called as **mott cell.**

- Russell bodies are large and globular of varying size, and become packed into the cell's cytoplasm pushing the nucleus to the edge of the cell, and are found in the peripheral areas of tumors.

- **Dutcher and Russell bodies** are both intracytoplasmic spherical inclusions of the same origin, i.e., an abnormal accumulation of immunoglobulin. Dutcher bodies invaginate into or overlie the nucleus (intranuclear pseudo inclusions) whereas Russell bodies are clearly seen to be within the cytoplasm. They occur in neoplastic plasma or plasmacytoid cells, in multiple myeloma and in other B-cell neoplasms.

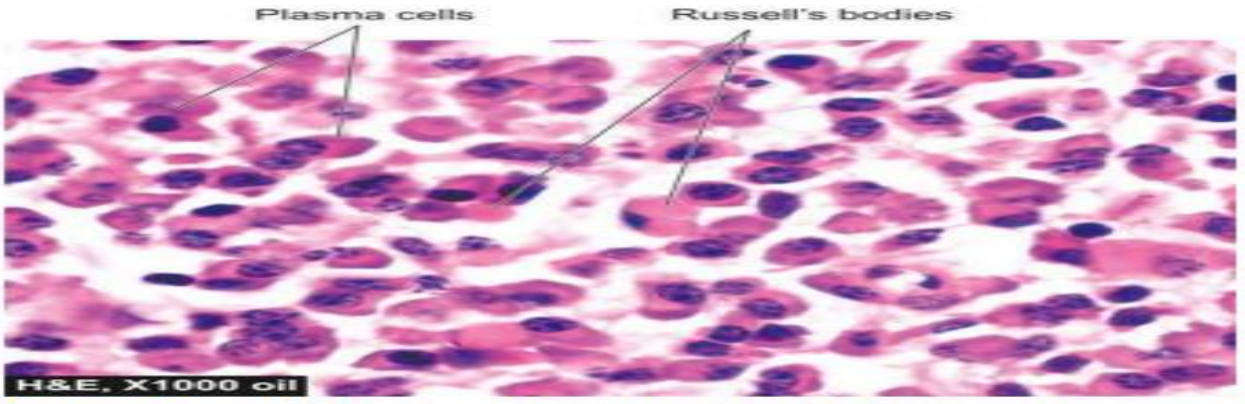
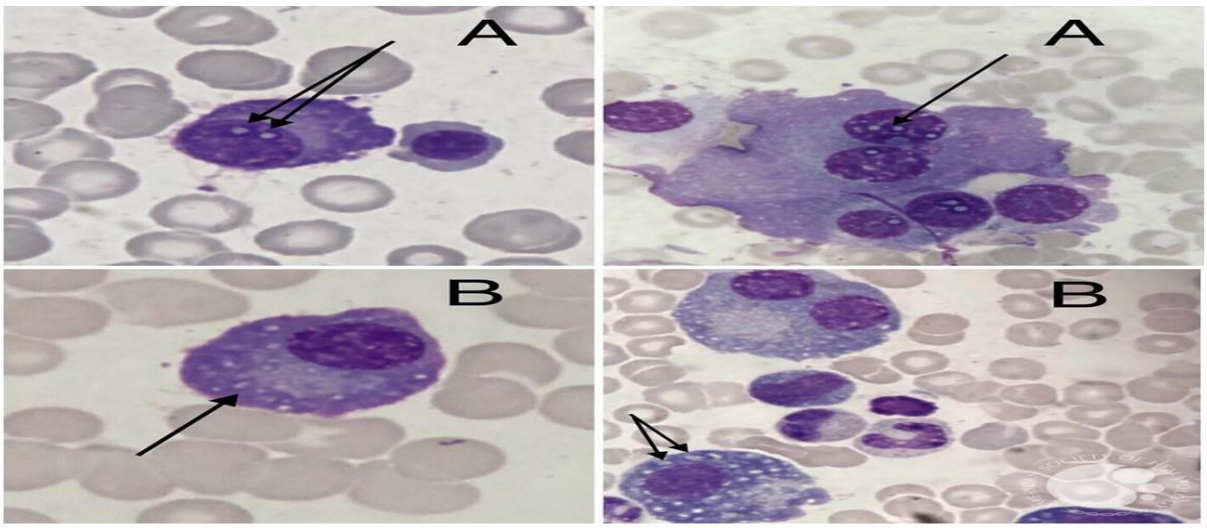


Figure 2.8 Intracellular hyaline as Russell's bodies in the plasma cells. The cytoplasm shows pink homogeneous globular material due to accumulated immunoglobulins.



Dutcher and Russell bodies are both intracytoplasmic spherical inclusions of the same origin, i.e., an abnormal accumulation of immunoglobulin. Dutcher bodies (Figures A- arrows) invaginate into or overlie the nucleus (intranuclear pseudo inclusions) whereas Russell (Figures B- arrows) bodies are clearly seen to be within the cytoplasm. They occur in neoplastic plasma or plasmacytoid cells, in multiple myeloma and in other B-cell neoplasms.

Extracellular degenerations

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1- Mucoid change or mucinous degeneration

- Mucoid change is deposition of mucinous material in epithelial and connective tissues in excessive amounts.

- Mucin is normally produced by epithelial cells of mucous membranes (mucous cells)and mucous glands, as well as by some connective tissues such as ground substance in the umbilical cord.

- connective tissue mucin is termed myxoid and epithelial mucus is called mucin .

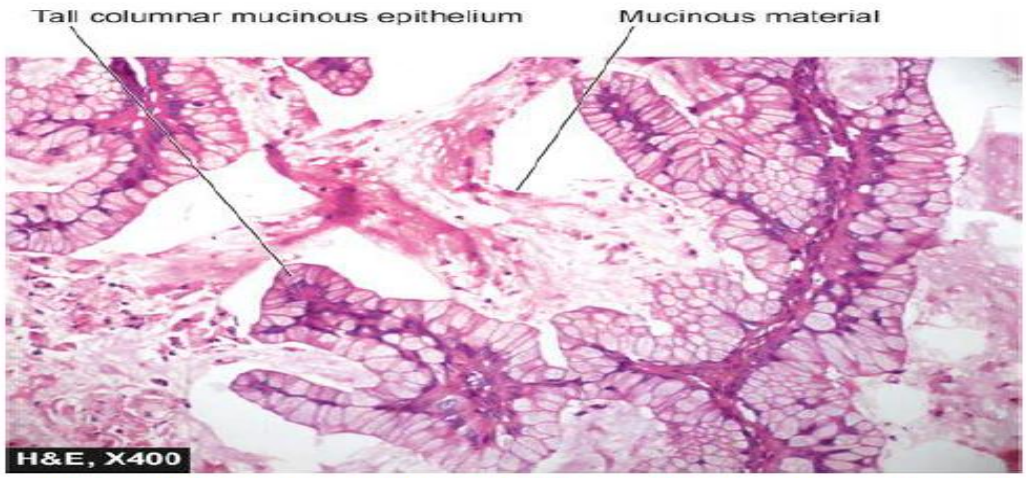
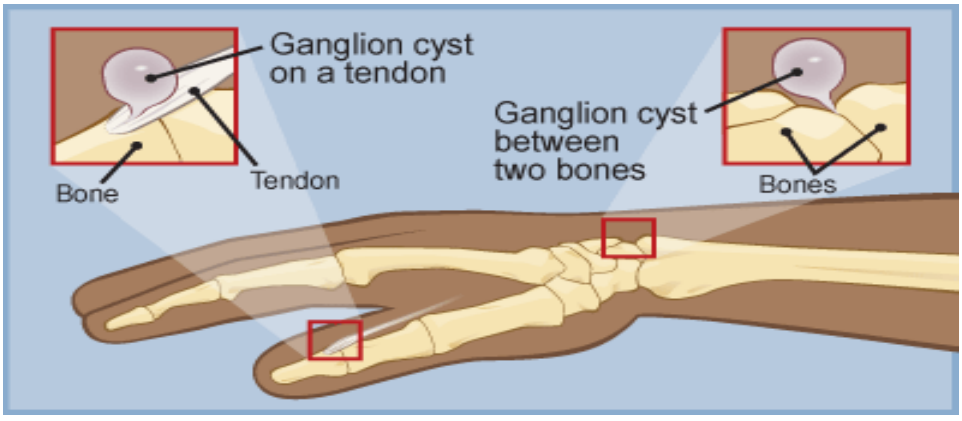


Figure 2.10 Epithelial mucin. Mucinous cystadenoma of the ovary showing intracytoplasmic mucinous material in the epithelial cells lining the cyst.

Macroscopic appearance

- The connective tissues affected are shrunken, soft and fragile in texture
- best example of Myxoid change: in the synovium in ganglion (ganglion cysts) on the wrist. Ganglion cysts are soft, gel-like masses that often change size, usually develops near a joint or tendon, its cause is unknown, but may be due to trauma or underlying arthritis, when the synovial fluid that surrounds a joint or tendon leaks out and collects in a sac.



Microscopic appearance

- The shape and structure of the tissue becomes similar to the mucoid connective tissue of umbilical cord, which is called Wharton gel
- degradation and disorganization of collagen fibers and the deposition of a mucoid substance within those fibers, and there are a small number of fibroblasts and a large amount of mucin between these cells .
  --Both epithelial and connective tissue mucin are stained by alcian blue. However, epithelial mucin stains positively with periodic acid-Schiff (PAS), while connective tissue mucin is PAS negative but is, instead, stained positively with colloidal iron

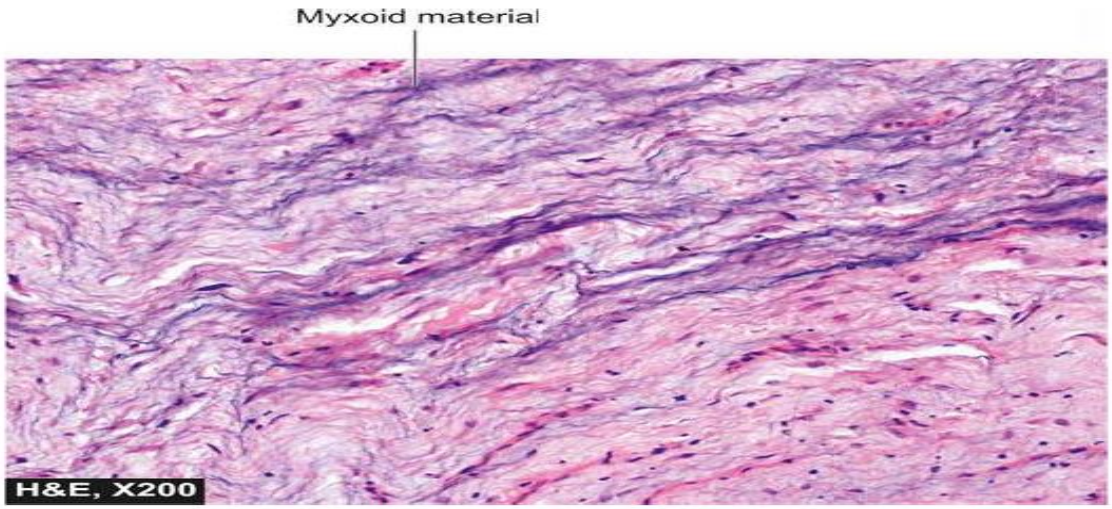


Figure 2.11 Connective tissue mucin (myxoid change) in neurofibroma.

2- Hyaline degeneration of connective tissue or extracellular hyaline

- Hyaline degeneration as deposition of a glassy, homogenous, eosinophilic material in connective tissues,**Seen in** Old scars, Walls of blood vessels affected by arteriosclerosis (hyaline arteriosclerosis), and In some tumors (hyaline degeneration in leiomyoma, also known as a fibroid, is a benign smooth muscle tumor)

Macroscopic appearance :Changes cannot be seen by naked eye

Microscopic appearance

- The transformation of connective tissue into glassy homogeneous material ,containing a small number of cells .
- Does not contain capillary blood vessels
- appear as eosinophilic in H&E staining section and red color with van kison dye.

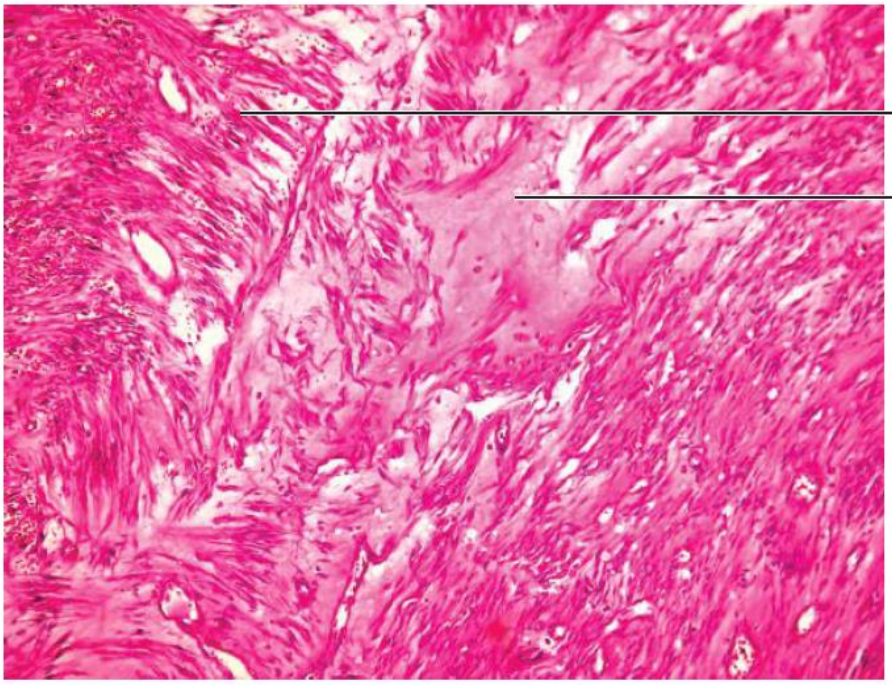


FIGURE 1.15. Hyaline degeneration in a leiomyoma (H&E; 200×).

3-Amyloid degeneration or amyloidosis

- Amyloid is a pathologic fibrillar protein (misfolded proteins)deposited in the extracellular space around the blood vessels in various tissues and organs of the body in variety of clinical condition.

Pathogenesis

- Amyloidosis results from abnormal folding of proteins, which become insoluble, aggregate, and deposit as fibrils in extracellular tissues. Normally, misfolded proteins are degraded intracellularly in proteasomes, or extracellularly by macrophages. It appears that in amyloidosis, these quality control mechanisms fail, leading to accumulation of a misfolded protein outside cells.

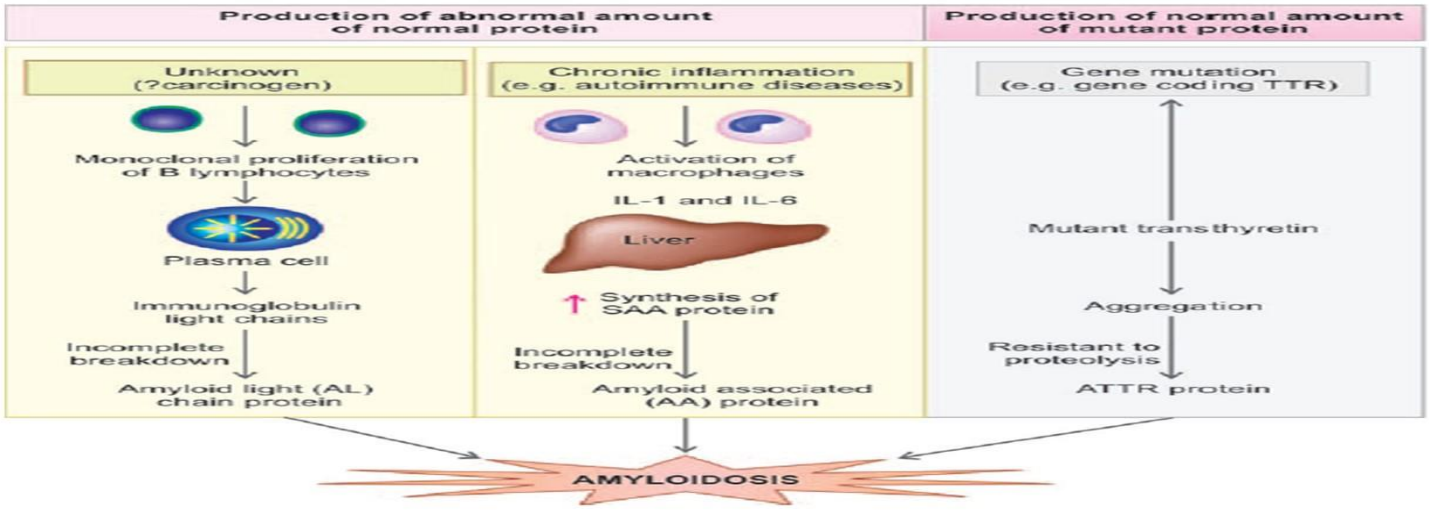


Fig. 6.25: Pathogenesis of amyloidosis. AL protein is seen in association with B lymphocyte and plasma cell proliferation which secrete immunoglobulin light chains that are amyloidogenic. AA protein is seen in variety of diseases associated with the activation of macrophages, which in turn leads to the synthesis and release of SAA. The SAA is converted to AA protein. ATTR protein is due to mutant proteins which aggregate and deposit as amyloid
Abbreviation: SAA, serum amyloid; ATTR, transthyretin

Macroscopic appearance or Gross features

- Oversized the organ ,pale color, soft ,and rubbery texture

Amyloidosis of spleen. Compare with normal spleen at the bottom.

Microscopic appearance or Microscopic features

- With the light microscope and hematoxylin and eosin stains, amyloid appears as an amorphous, eosinophilic, hyaline,

- To differentiate amyloid from other hyaline materials (e.g., collagen, fibrin), a variety of histochemical techniques are used. most widely used is the Congo red stain, which under light microscope a pink or red color to tissue deposits

- in liver , the accumulation of amyloid is observed in the space between the hepatic sinuses and the hepatic cords
- in spleen , amyloid aggregates around the endothelial reticulocytes and around the central artery, and from these sites it extends to surround the spleen pulp
- in kidney , amyloid accumulates in the glomeruli around the capillary blood vessel as well as around the blood vessels in the interdisciplinary tissue between the renal tubules

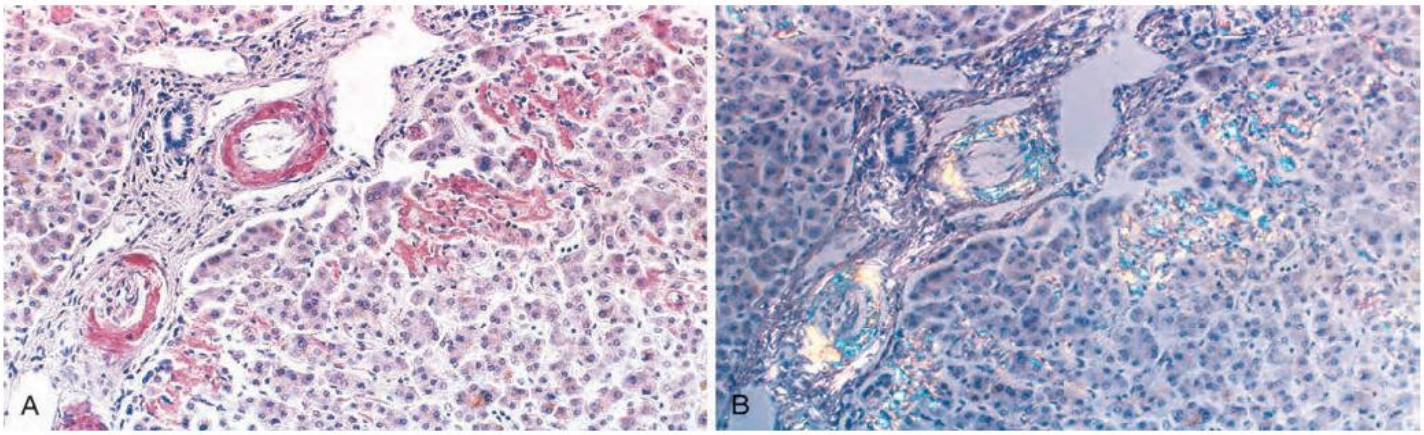


Figure 6-46 Amyloidosis. **A,** A section of the liver stained with Congo red reveals pink-red deposits of amyloid in the walls of blood vessels and along sinusoids. **B,** Note the yellow-green birefringence of the deposits when observed by polarizing microscope. (Courtesy Dr. Trace Worrell and Sandy Hinton, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

Glycogen infiltration (INTRACELLULAR ACCUMULATION OF GLYCOGEN)

-Excessive intracellular deposits of glycogen are seen in patients with an abnormality in either glucose or glycogen metabolism.

- Glycogen infiltration appears in some tumors, some infections and around necrotic tissues

-Glycogen deposits in diabetes mellitus are seen in epithelium of distal portion of proximal convoluted tubule and descending loop of Henle, in the hepatocytes, in beta cells of pancreatic islets, and in cardiac muscle cells.

Macroscopic appearance

- Glycogenic infiltration cannot be seen visually in the tissue, but if the amount is large, the organ is enlarged and pale in color.

Microscopic appearance

-the glycogen masses appear as clear vacuoles within the cytoplasm. Glycogen dissolves in aqueous fixatives; thus, it is most readily identified when tissues are fixed in absolute alcohol. and staining the section with Best carmine or the PAS reaction imparts a rose-to-violet color to the glycogen,