Accumulation of lipids
Fatty change

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LEC.5

This refers to abnormal accumulation of fat of triglyceride type within parenchymal cells.

It is an example of reversible (non-lethal) cell injury and is often seen in the liver because of the central role of this organ in fat metabolism.

Free fatty acids are transported to the liver from two sources:

1. **Adipose tissue.**
2. **Ingested food.**

In the liver these fatty acids are esterified to triglycerides.

Release of triglycerides from the liver requires their association with carrier proteins ***(apoproteins)***.

Such complexes circulate in the blood as lipoproteins.

Excess accumulation of triglycerides within the liver (fatty change) may result from defects in any one of the above steps from entry to, till their exit from the hepatocytes.

1- Alcohol may induce a number of such defects through alterations in mitochondrial; and microsomal functions.

2- CCl4 and protein malnutrition act by decreasing apoproteins synthesis.

3- Anoxia (hypoxia) inhibits fatty acid oxidation.

4- Starvation increases fatty acid mobilization from peripheral stores.

Gross features

In the liver mild fatty change shows no gross changes, but with progressive accumulation, the organ enlarges and become increasingly yellow, soft and greasy to touch.

Microscopic features.

In the early stages there are small fat vacuoles around the nucleus.

With progression the vacuoles fuse together creating large clear space that displaces the nucleus to the periphery.

Fatty change may also be seen within myocardial cells e.g. in ischemia and

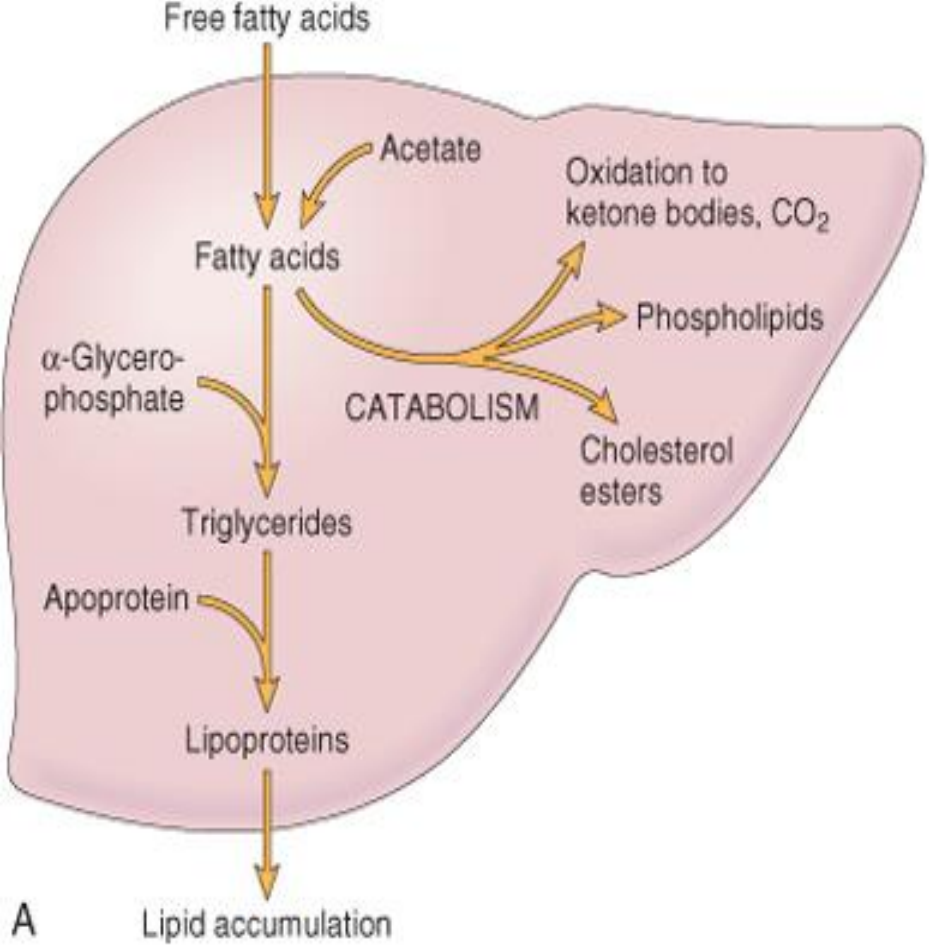
myocarditis.

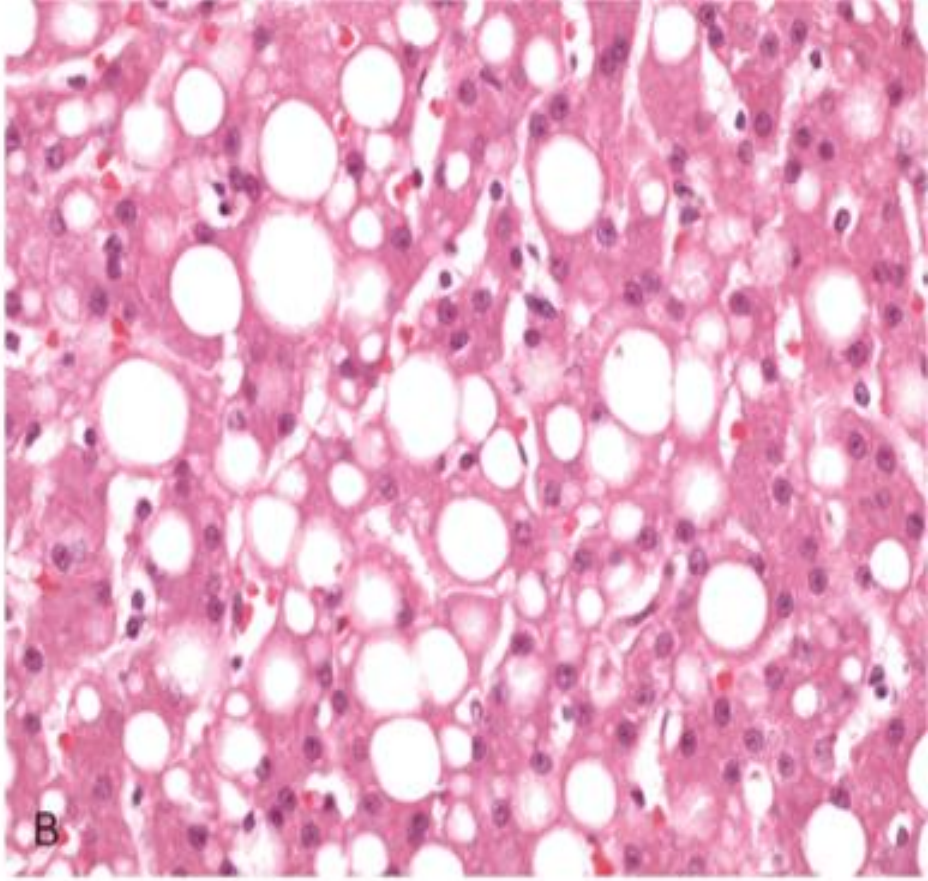
The latter may be seen, as a complication of diphtheria.

The above examples refer to accumulations of triglycerides.

Accumulations may involve cholesterol and its esters within:

1. Smooth muscle cells and macrophages that are located within the intima of arteries in **atherosclerosis.**
2. Macrophages in the acquired and hereditary hyperlipidemias; in such cases the accumulations are usually seen within the subcutaneous connective tissues of the skin and in tendons producing masses known as **xanthomas.**





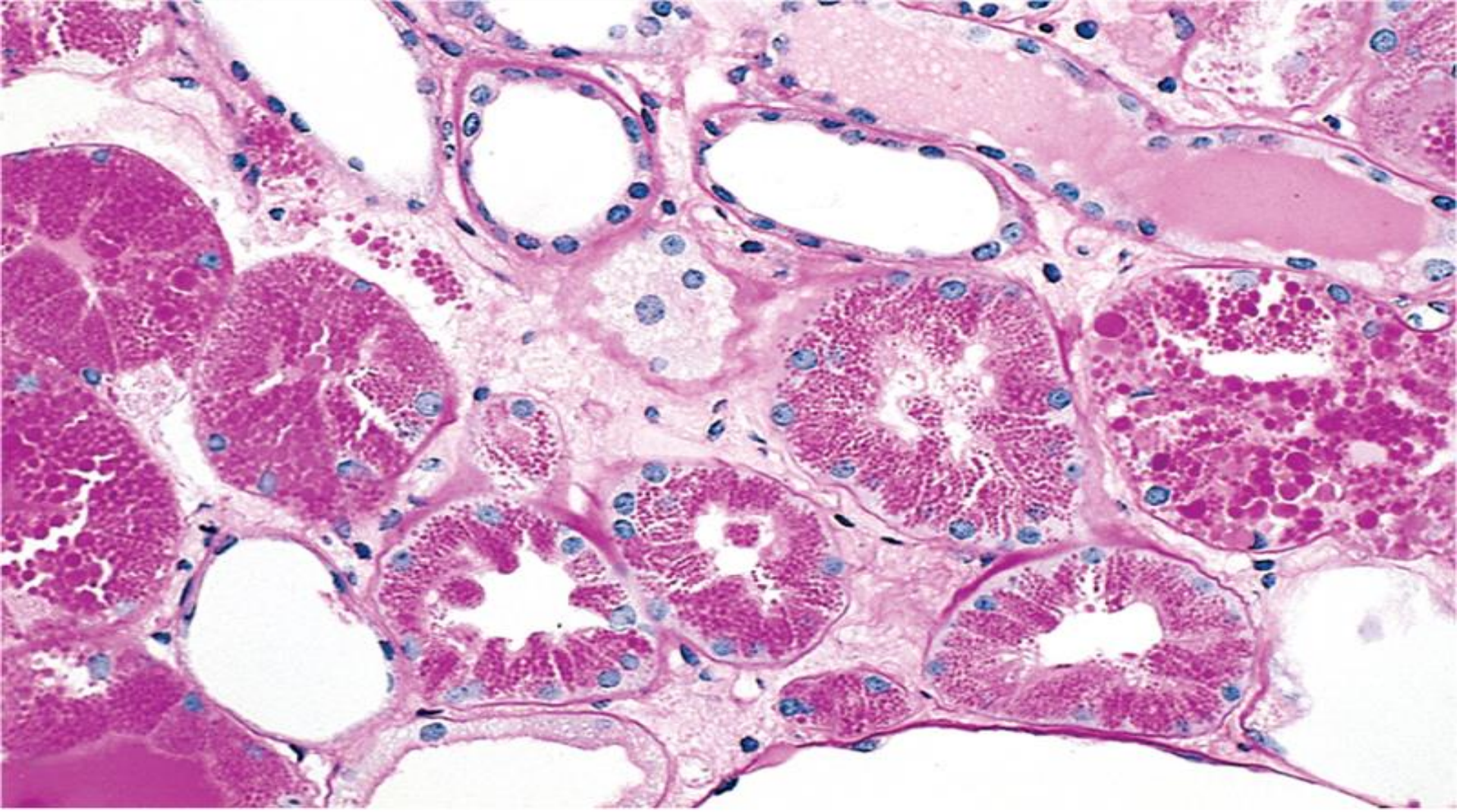
Fatty liver. A, The possible mechanisms leading to accumulation of triglycerides in fatty liver. Defects in any of the steps of uptake, catabolism, or secretion can lead to lipid accumulation. B, High-power detail of fatty change of the liver. In most cells the well-preserved nucleus is squeezed into the displaced rim of cytoplasm about the fat vacuole.

Protein accumulations

This occurs principally in the:

1- Epithelial cells of proximal convoluted renal tubules e.g. in cases of proteinuria.

2- Plasma cells, these cells are actively engaged in immunoglobulin synthesis (antibody-formation) and may become overloaded with its own products.



Protein reabsorption droplets in the renal tubular epithelium.

Glycogen accumulations

Accumulation of glycogen within the cytoplasm is seen as clear cytoplasmic vacuoles.

PAS (periodic acid-Schiff reagent) stain is routinely used for its demonstration (appears as red to violet in color).

Diabetes mellitus causes glycogen accumulation within the epithelial cells of distal renal tubules producing virtual clearing of their cytoplasm.

Similar accumulations occur in the cells of the liver, heart and islet cells of Langerhans within the pancreas.

In **glycogen storage diseases** there is genetically determined defects in certain enzymes concerned with glycogen metabolism; glycogen (normal and abnormal) cannot be metabolized.

This leads to massive accumulation of glycogen within the cells with subsequent cell injury.

Accumulations of complex lipids and carbohydrates

These accumulate principally within the reticulo-endothelial cells.

Examples include:

1. Mucopolysaccharidoses.
2. Gaucher disease.
3. Tay-Sachs disease.
4. Niemann-piek disease.

The abnormal metabolites in all the above storage diseases overflow into the blood to be taken up by the reticulo-endothelial cells.

These cells become distended with foamy cytoplasm.

There is often massive hepatomegaly.

Pigments

These are colored substances and are either normal constituents of the body e.g. **melanin** or abnormal that accumulate under certain situations.

The abnormal pigments are either endogenous or exogenous.

The most common exogenous pigment is **carbon** (coal dust).

When this is inhaled it is picked up by macrophages within the alveoli then transported via lymphatics to regional lymph nodes in the hila of the lungs.

Accumulation of this carbon pigment causes black discoloration of lung tissue, a condition called **anthracosis**.

In coal miners and in those living *in* heavily polluted atmosphere the deposition may be very marked and associated with fibrosis and emphysema ***(coal worker's pneumoconiosis).***

Tattooing is a form of exogenous pigmentation of the skin. The pigment inoculated is taken up by dermal macrophages.

Endogenous pigments

1. Lipofuscin.
2. Melanin.
3. Derivatives of hemoglobin.

Lipofuscin (lipochrome pigment)

This is a yellow-brown (fuscus = brown), intra-cytoplasmic pigment, which is seen in cells undergoing slow atrophy:

1. Particularly prominent in the cells of the liver and heart of the elderly. ***(Brown atrophy of the heart).***
2. Patients with severe malnutrition and cancer cachexia.

Melanin: This is an endogenous, nonhemoglobin-derived, brown-black pigment (melas = black).

This skin pigment is produced by the oxidation of tyrosine through the help of the enzyme tyrosinase within melanocytes.

Hemosiderin:

This is a hemoglobin-derived, golden-yellow to brown granules.

Excess iron in the body causes hemosiderin to accumulate within cells.

Excess deposition of hemosiderin is termed **hemosiderosis,** when there is no tissue injury or damage.

On the other hand, when there is associated tissue damage the condition is known as **hemochromatosis**

Hemosiderosis is either localized or systemic (generalized).

Localized hemosiderosis result from local hemorrhage e.g. the common bruise, pulmonary or cerebral hemorrhage.

Systemic hemosiderosis occurs whenever there is systemic iron overload. Here the deposition is seen in many organs and tissues such as the liver.

This is associated with

1. Increased absorption of iron.
2. Impaired utilization of iron.
3. Hemolytic anemias.
4. Excessive blood transfusion.

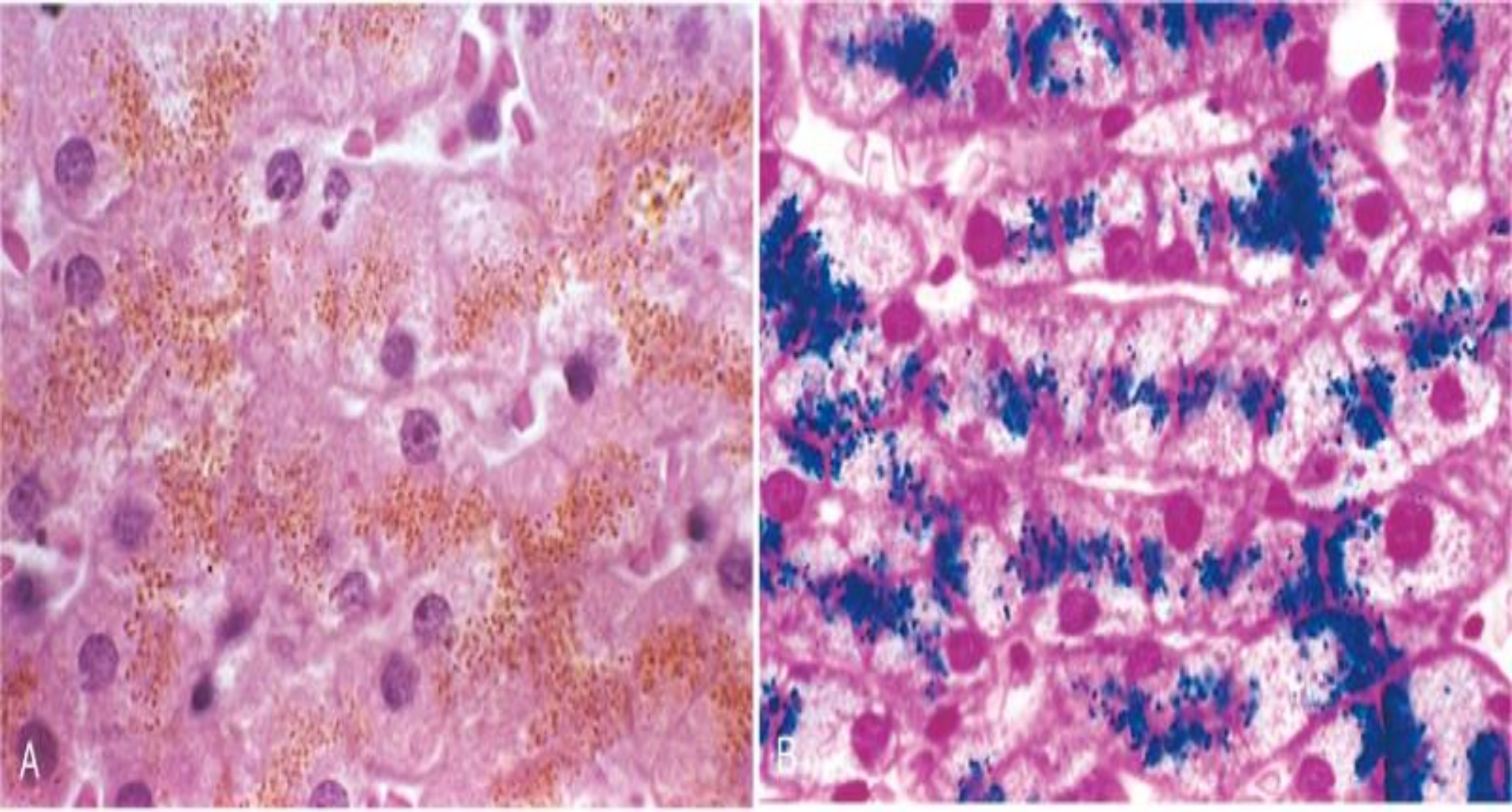
In systemic hemosiderosis, hemosiderin accumulates first within the reticuloendothelial cells of various organs and tissues.

With progression accumulation is seen in the parenchymal cells principally of the liver, pancreas, heart and endocrine organs.

In most instances the accumulated hemosiderin does not damage the parenchymal cells.

However, in the more extreme accumulations, in a disease called ***hemochromatosis,*** there is an associated liver, heart and pancreatic damage.

This results in liver cirrhosis, heart failure and diabetes mellitus.



Hemosiderin granules in liver cells. A, H&E section showing golden-brown, finely granular pigment. B, Prussian blue reaction, specific for iron.

Bilirubin:

This is a normal major pigment of bile, which is derived from hemoglobin (but contains no iron).

The conversion to bile occurs within hepatocytes.

Jaundice:

Results from excess bilirubin pigment that is distributed throughout all tissues and body fluids.

In the liver, particularly when there is obstruction to the bile flow (e.g. obstruction of the common bile duct by a stone, tumor or biliary atresia) bilirubin is seen within bile canaliculi, kupffer cells and hepatocytes as green-brown globular deposits.

This imparts greenish color to the liver grossly.