PATHOLOGY OF LIVER AND BILIARY SYSTEM

Physiological considerations: At any point of time, 25% of the blood in the body flows through the liver.

Functions of liver

A. Secretion of bile

- ✓ Bile contains pigments and bile salts.
- ✓ Bile pigments are not useful to the body.
- ✓ On the other hand, retention of these (hyperbilirubinemia) is toxic to the body.
- ✓ Bile salts play an important role in digestion, especially of the fats.
- ✓ Bile contains mucin and related substances which helps in emulsification of fats in the bowel.
- ✓ Bile acts as bacteriostatic in intestine.

B. Protein metabolism

- ❖ Uric acid is converted into a harmless allantoin in animals.
- ❖ Highly toxic ammonium salts are detoxified by converting them into urea.
- ❖ The non-nitrogenous residues obtained after deamination of amino acids, are converted into glucose and ketones which are used by the body.

C. Carbohydrate metabolism

- Glycogen is synthesized and stored in the liver.
- Excessive carbohydrates ingested are converted into lipids and stored in the fat depots.
- At times of need, gluconeogenesis from proteins and fats occurs in the liver.

D. Fat metabolism

- ✓ Fats that are characteristics of animals are also synthesized from fatty acids and glycerol by liver.
- ✓ With the assistance of choline, liver is able to transform the depot fats into tissue fats (phospholipids) so that the tissues can utilize them.

E. Erythropoiesis

- In the bird, liver is the site for erythropoiesis.
- In other animals, during fetal life, erythropoiesis occurs in the liver.
- In these animals in severe anemia, erythropoiesis takes place in the liver even in the adult as part of extramedullary hemopoiesis.

F. Iron metabolism

- The reticulo-endothelial cells of the liver are capable of destroying the red blood cells and the minerals released (Fe, Cu and Co) are stored in the liver for use again by the body.

G. Detoxication

- ➢ Some toxic substances, especially putrefactive products from the alimentary tract are detoxified by the liver.
- ➢ Bacterial toxins and hormones produced in excess of requirements are inactivated.

- Many drugs used therapeutically are also made harmless by the liver e.g. Morphine, barbiturates, phenol and camphor.

H. Vitamin metabolism and storage

- ✓ Failure of bile excretion due to hepatic damage interferes with the absorption of fatsoluble vitamins.
- ✓ Vitamin A is stored in the liver
- ✓ Vitamin K is utilized for the formation of prothrombin
- ✓ Some members of the vitamin B group, especially thiamine, riboflavin and niacin are partly metabolized in the liver where they may also be stored.

Liver Function Tests

- The liver has a great reserve power and it has enormous ability to recover from injury.
- So, the tests are not adequate clinically to evaluate the correct state of the health of liver and hence it is not wise to put too much reliance on these tests.
- Since the functions of the liver are carried out by the activity of enzymes, inadequacy or absence of the particular enzyme may affect one function and so a decrease of one function does not mean that other functions are affected.

Effects of liver failure

With severe hepatic diseases, a great many vital processes will be affected. More important pathological conditions met with are:

- ✓ Jaundice due to retention of bile pigments.
- ✓ Bleeding be due to; Lack of absorption of Vitamin K; Failure of prothrombin formation; Lack of formation of fibrinogen.
- ✓ Hypoglycemia: due to impairment of glucose metabolism making the animal weak and irritable
- ✓ Hypoproteinemia: due to failure to synthesize plasma proteins results into generalized edema and emaciation.
- ✓ Anemia due to iron and protein deficiencies: liver stores iron and so in liver diseases iron stores are depleted. In liver diseases protein synthesis also does not occur.
- ✓ Toxemia due to failure of detoxication of proteins and intestinal toxins.
- ✓ Renal failure: Hepatorenal syndrome: In severe hepatic injury, the toxins that are not detoxified are excreted through kidneys resulting into toxic nephrosis.
- ✓ Renal dysfunction leads to uraemia.
- ✓ Pyrexia: The thermoregulatory center is affected by the circulating toxins since they are not detoxified.

DEGENERATIONS OF LIVER

Cloudy swelling

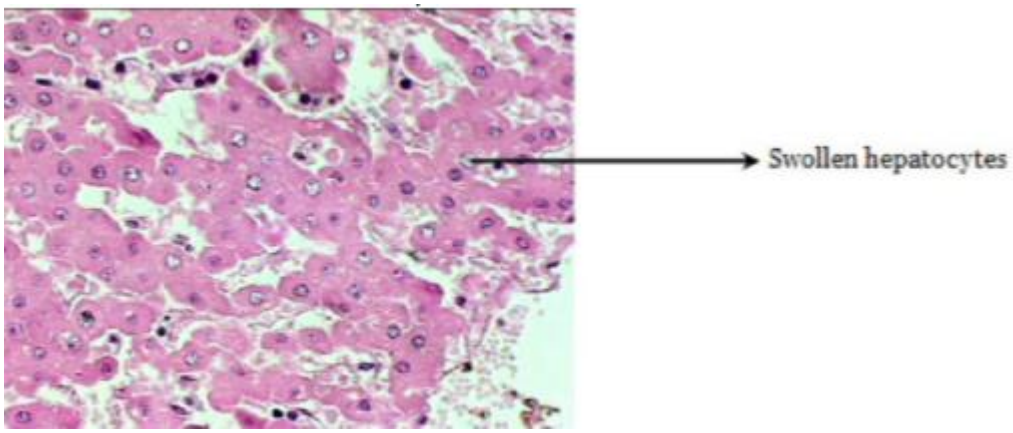
Occurrence: Cloudy swelling is common in the liver.

Aetiology:

- ✓ Hypoxia; Poisons; Chemicals- salts of heavy metals – arsenic and lead.
- ✓ Plant toxins – glucosides, saponin.
- ✓ Drugs – carbon tetrachloride which was used as an anthelmintic
- ✓ Bacterial toxins seen in all infectious diseases.
- ✓ Viruses.

Gross pathology: The organ has a dull, parboiled appearance. The liver is enlarged. The capsule is tense. Borders are rounded. Consistency is softer. On section, it bulges at the cutting surface. Lobular markings are indistinct.

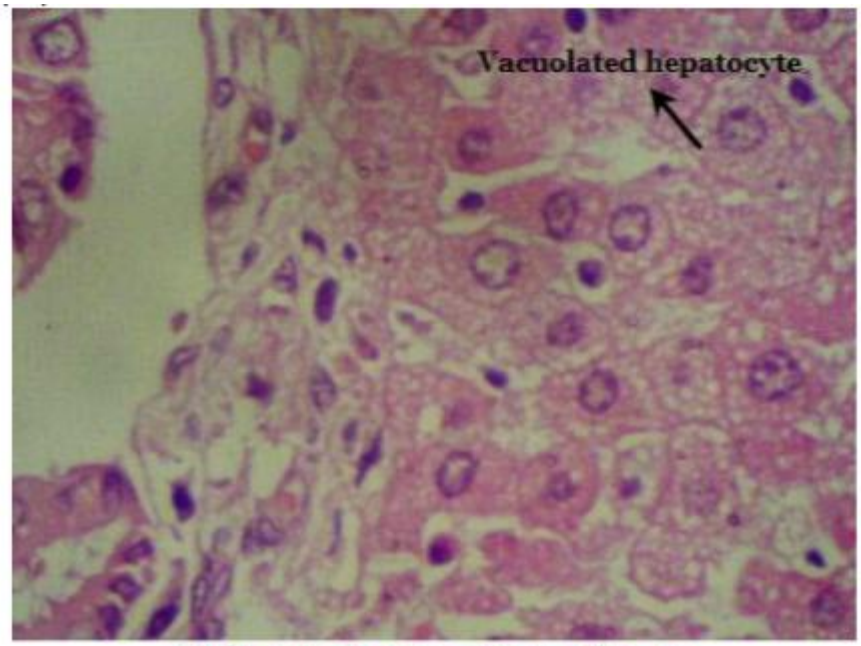
Histopathology: Hepatocytes are swollen and have a pale granular cytoplasm due to swelling of mitochondria. The nuclei may be indistinct**.**



Hydropic degeneration

Etiology: Toxins and septicaemic infections. Ether,chloroform and carbon tetra choloride poisoning.

Gross pathology: Gross lesions are more or less similar to that of cloudy swelling
Histopathology: The cytoplasm of hepatocyte may contain one, two or more vacuoles in the cytoplasm.



Hydropic change - Liver - Sheep

Fatty change

Occurrence: Fatty change in the liver is common in animals.

Aetiology: Hypoxia/anoxia: Chronic venous congestion. Nutritional deficiency: Inadequate choline and apoproteins; Metabolic diseases– Diabetes mellitus in dogs and cats, acetonemia/ketosis in cattle, pregnancy toxaemia in ewes, and deficiency of thyroxine and anterior pituitary hormones. Bacterial toxins; Poisons: Inorganic – phosphorus, arsenic, antimony; Organic - chloroform, carbon tetrachloride, tannic acid, tetrachlorethylene, alkaloids of phytotoxins, aflatoxin and senecios.

Pathogenesis: The liver is too sick to metabolize the dietary as well as the fat brought to it from the depots. Defect may be anywhere in the process from metabolism of fatty acids to the formation and release of lipoproteins.

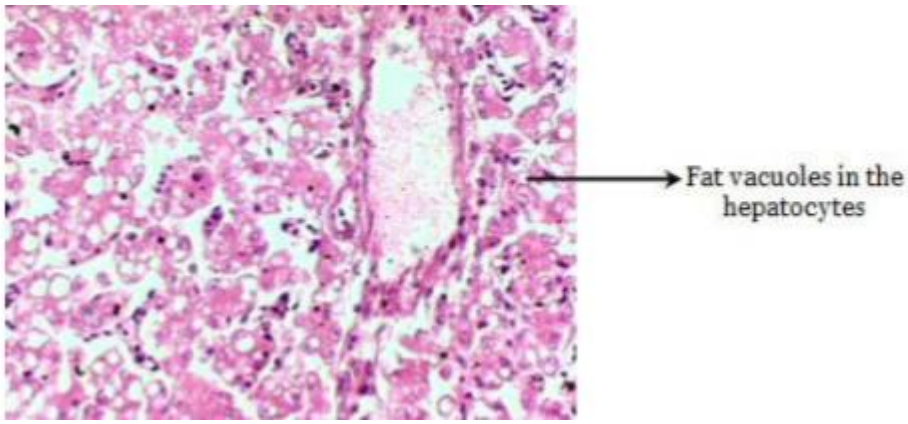
Gross pathology

- ✓ The liver is enlarged with round margins, has a smooth surface and is pale or yellowish.
- ✓ Consistency is friable.
- ✓ On section it bulges on the cut surface.
- ✓ Fat droplets are seen on the blade.
- ✓ Very fatty livers as in pregnancy toxemia of sheep, float in water.

Mottled and enlarged liver - Chicken

Histopathology

- The hepatic parenchymal cells contain fat droplets, either as a single large globule or as multiple small globules.
- If single and large the nucleus may be pushed to a side.
- The sinusoids are compressed and so appear ischaemic.
- Usually the distribution of the lesions in the liver may be diffuse or zonal.
- In chronic venous congestion, the lesion is in the centrilobular hepatocytes.
- In poisoning, when poison is brought through the portal vein, the fatty changes are found at the periphery of the lobule.
- Rupture of affected hepatocytes may give rise to fatty cysts.



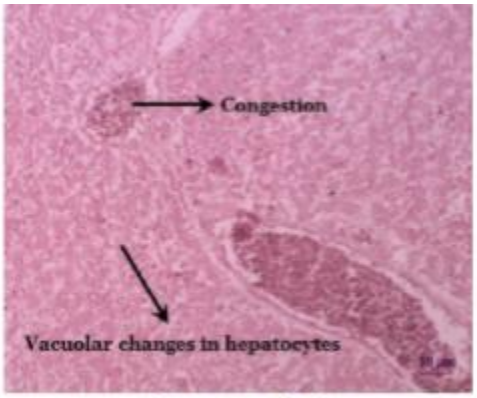
HEPATITIS

- Hepatitis is an alterative inflammation of liver in which the various degenerative processes like cloudy swelling, fatty change and necrosis are caused by irritants which also produce inflammation.
- Besides, in liver, these degenerative changes are accompanied by lymphocytic or leucocytic infiltrations typical of an inflammatory reaction.

- Hepatitis is classified as alternative inflammation because the inflammatory process is caused by the same etiological agents that also produce degeneration and so alteration in the parenchymatous cells is produced.
- Hepatitis may be either infectious, non-infectious or toxic.
- This may again be acute or chronic. The chronic variety is usually called Cirrhosis.

ACUTE TOXIC HEPATITIS

This is characterized by necrosis which is usually preceded by degenerative changes like cloudy swelling and fatty changes.



Acute toxic hepatitis - Chicken

Hepatic necrosis is classified as per anatomical distribution into:

- Focal necrosis
- Centrilobular necrosis
- Midzonal necrosis.
- Periportal necrosis
- Diffuse necrosis
- Paracentral necrosis

FOCAL NECROSIS; In this variety, numerous small necrotic areas are seen scattered in the liver and may be found in any part of the lobule.

Aetiology

- ✓ Obstruction of biliary passages
- ✓ Bacterial – in bacteremic or septicemic affections – Pasteurellosis, Johne's disease, Salmonellosis, Tularemia, Listeriosis in new-born.
- ✓ Viral – as in equine viral rhinopneumonitis in the foetus.
- ✓ Due to parasitic migration.

CENTRILOBULAR NECROSIS

Definition: In this condition, the cells nearest to the central vein are affected.

Aetiology

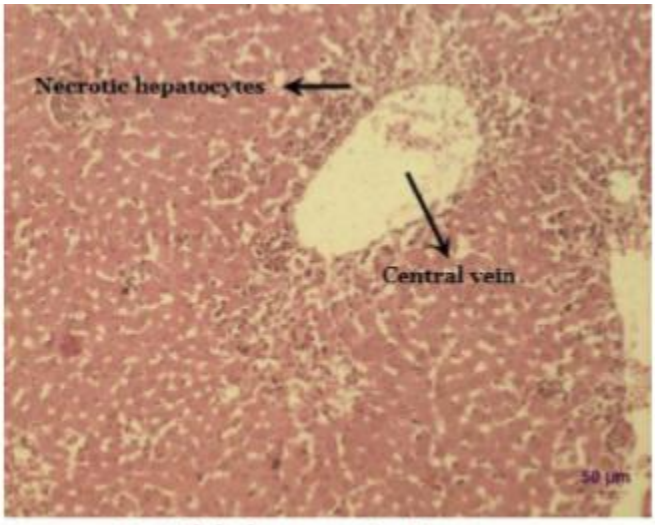
- Anoxia
- Low atmospheric pressure
- Acute hemorrhagic anemia
- Shock – due to reduced blood pressure, reduced oxygen tension and reduced volume flow.
- Congestive cardiac failure
- Toxins o Blood borne especially carbon tetrachloride.

Gross pathology:

- ✓ The liver is enlarged and paler than normal. In severe cases the organ may be dark red due to venous stasis.
- ✓ The lobular markings are exaggerated. This is due to the difference in color at the center and periphery. When congestion of the central part is present, the periphery is paler due to degenerative changes in the cells.
- ✓ On the other hand, if necrosis of the cells in the center occurs, then the center will be pale while the periphery is darker.

Histopathology

- ➢ The cells round about the central veins have disappeared, blood taking up their places.
- ➢ In area nearer to the periphery of lobule, the cells may show fatty changes or cloudy swelling.



Centrilobular necrosis - Liver

PERIPORTAL NECROSIS: In this condition the cells adjoining the portal tract become necrotic.

Aetiology: Here the toxins should have been conveyed by the portal vein; This is more commonly seen in phosphorus poisoning.

Histopathology: Inflammation of the portal triads results in cirrhosis similar to portal cirrhosis.

MASSIVE NECROSIS / ACUTE YELLOW ATROPHY:

In this condition, there is necrosis of considerable number of the cells in a lobule. This may be a severe manifestation of various types of necrosis described above.

Etiology

- Dietetic: Deficiency of sulphur-containg amino acids, Tocopherols and Selenium.
- Poisons: Carbon tetrachloride, chloroform, phosphorus.

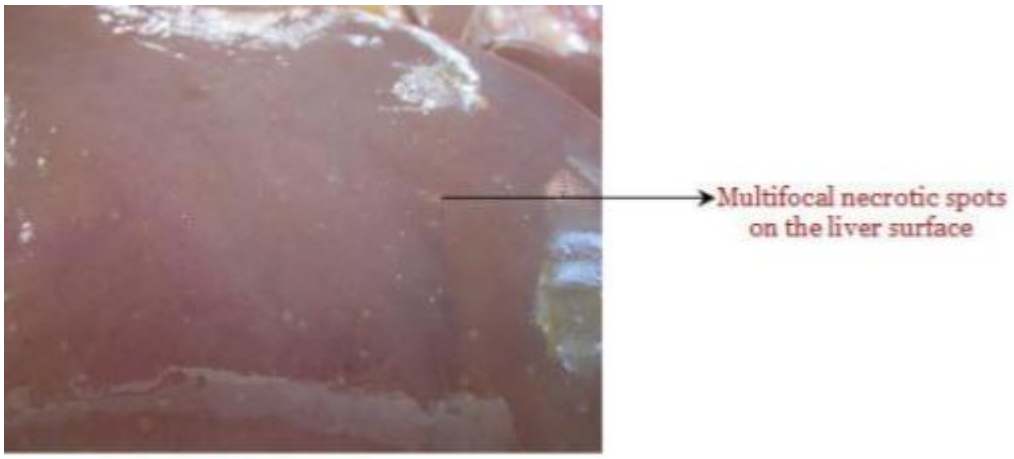
Gross pathology: The liver is yellow and smaller in size.

Histopathology: There is fatty change and necrosis of hepatocytes with loss of parenchyma.

SAW DUST LIVER

The foci of necrosis may be few or many, and appear to the naked eye as though saw dust is sprinkled on the liver.

Aetiology: In well-fed young cattle, at postmortem, focal necrosis of the liver is commonly seen.
Pathogenesis: Here the irritant is borne by the portal veins from the gut and so the lesions are found nearer the portal areas.
Clinical signs: The animals do not manifest any symptoms while alive.
Histopathology: These spots are evidently scars resulting from inflammatory reaction. The lesion consists of hepatic cells which have undergone coagulative necrosis. There is also infiltration by lymphocytes and neutrophils.



Sawdust liver in a cow

PATHOLOGY OF CIRRHOSIS

CIRRHOSIS:

- Cirrhosis of the liver is chronic hepatitis characterized by degeneration and hyperplasia of hepatic cells and fibrosis.
- The stimulus for the fibroblastic proliferation is some irritant, chronic and severe enough to produce degeneration and necrosis of the parenchymatous cells.
- The irritant may reach the liver through (a) The portal vein (b) hepatic artery and (c) Bile ducts.

The classification of cirrhosis:

- Portal or nodular cirrhosis
- Multinodular or Atrophic or Gindrinker's or Laennec's cirrhosis
- Biliary cirrhosis (Monolobular or hypertrophic cirrhosis)

Portal or nodular cirrhosis

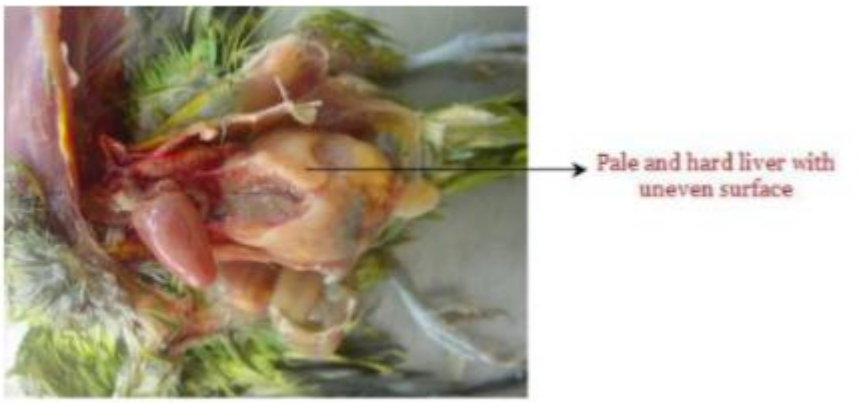
Aetiology: The irritant is mild and acting for a long time. Usually, the causes are the same as described for acute focal toxic hepatitis. Toxic plants: Crotalaria saggitalis in horses; plants of Senecio family in horses, cattle and sheep; Atalaya intermedia in horses; Amsinckia intermedia (tar weed) in horses, swine and cattle; plants containing high selenium content-in horses. (Wheat loco weed). Chemicals: Pitch in tar paper, repeated exposure to chloroform, carbon tetrachloride

Pathogenesis

- When the irritant is conveyed via the portal veins, changes are first at the periphery of the lobules –area next to the portal tract.
- The following changes take place: o Stimulation of the interlobular connective tissue to proliferate
- Depending upon the severity of the irritant degeneration or necrosis of the hepatic tissue.
- New irregular blood vessels are formed which anastomose with the network of the portal vein and hepatic artery resulting into arterio-venous shunts. Thus ischaemia of some parts of the liver occurs leading to further hepatic necrosis.
- Infiltration of lymphocytes and macrophages occur into the islands of Glisson.
- Hyperplasia of the surviving hepatocytes replaces the destroyed cells.
- The newly formed after maturation contracts, interfering with blood circulation.
- Due to resultant ischaemia, hyperplasia does not progress further.
- As the fibrous tissue grows into the lobule, the hepatic cells become atrophied.
- The fibrosis constricts the central vein impeding the out flow of blood, thereby rendering the irritant to stay longer in the liver.

- Growth of the fibrous tissue into the lobule divides the parenchyma into small islands of hepatic cells-pseudolobulation.
- In the new fibrous tissue, especially in the portal areas, new bile ducts are formed. These are not functional, lacking an outlet and so stasis of bile occurs.
- If irritant enters the liver through the hepatic artery, changes of damage are first noticed in the tissues of portal canal and inter-lobular connective tissue.
- The features here are: lymphocytic infiltration, proliferation of the connective tissue slowly encroaches into the lobule which produces changes as described above.

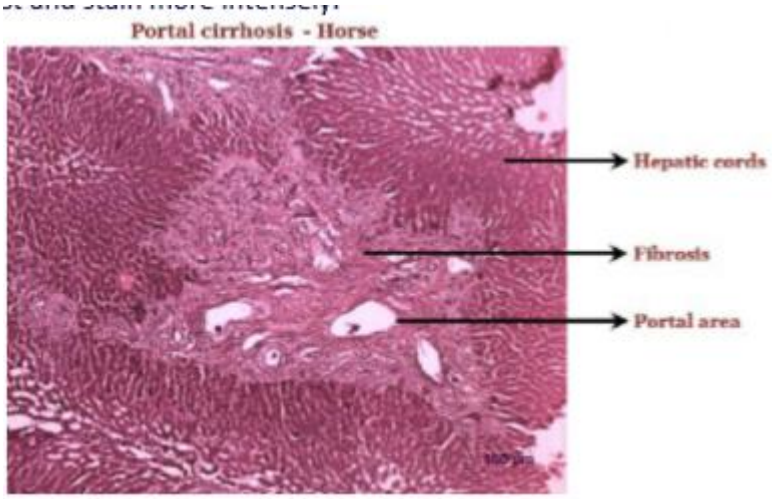
Gross pathology: In the early stages the liver may be large. But as the condition progresses, due to atrophy of the parenchyma, the liver is reduced in size. Due to biliary stasis, the color of the organ is tawny or yellowish-gray or green and it is to this color that the name "Cirrhosis" was first applied. The liver surface is uneven and nodular (Hobnail liver). The liver is hard and firm.



Cirrhosis of liver in a budgerigar

Histopathology

- The architecture of the liver is lost.
- The characteristic picture is the increase in fibrous tissue within and around the lobules.
- In the portal area small new bile ducts and inflammatory cells (lymphocytes and macrophages) are presen
- The parenchymatous cells show various stages of degeneration - cloudy swelling, fatty change and even necrosis.
- Hyperplasia that is present gives nodularity to the organ. These regenerating young cells are plump, robust and stain more intensely.



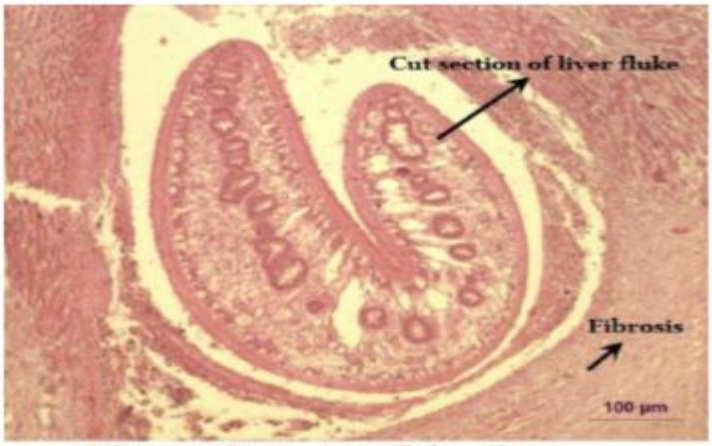
Biliary cirrhosis (monolobular or hypertrophic cirrhosis): Liver flukes that inhabit the bile ducts do not cause extensive cirrhosis but only a local fibrosis.

Aetiology: The causes are:

- Cholangitis-the inflammatory exudate clogs the bile ducts o Stone in the common bile duct.
- Obstruction of biliary passages by flukes (Chlonorchis sinesis) and ascarids.
- Stricture of the bile duct.
- Extramural pressure on the bile ducts from tumour of pancreas

Gross pathology: The liver is enlarged, greenish and the surface is either smooth or finely granular.

Histopathology: Here, the connective tissue encircles individual lobules (hence monolobular). The bile ducts may be dilated and tortuous. There is great infiltration of the connective tissue with chronic inflammatory cells. Newly formed non-functional bile ducts are also found. Hepatic cells reveal degenerative changes.



Biliary cirrhosis - Liver fluke - Sheep

SEQUELAE / EFFECTS OF CIRRHOSIS

- Due to disturbance in portal circulation Ascites: due to: Increased hydrostatic pressure in portal veins due to compression of veins and distortion of the portal and hepatic veins as well as sinusoids. The effect is more in portal cirrhosis.
- Decreased colloid osmotic pressure due to decreased production of plasma proteins, particularly albumin.
- Hormones are not inactivated by a damaged liver. Hence mineralocorticoids and the anti-diuretic hormone leads to retention of sodium chloride and generalised oedema.
- Varicosity and rupture of esophageal veins may lead to hematemesis.
- Splenomegaly.
- Chronic gastroenteritis as a result of chronic venous congestion of abdominal viscera.
- Toxins – exogenous or endogenous are normally detoxified by the liver. If this is not done, the toxins affect the brain, producing degenerative changes resulting in "walking disease" in horses.
- Jaundice – due to pressure on the bile canaliculi by the compressed cord cells (by fibrous tissue). So there is obstructive jaundice resulting in digestive disturbances.

ABSCESSES OF THE LIVER

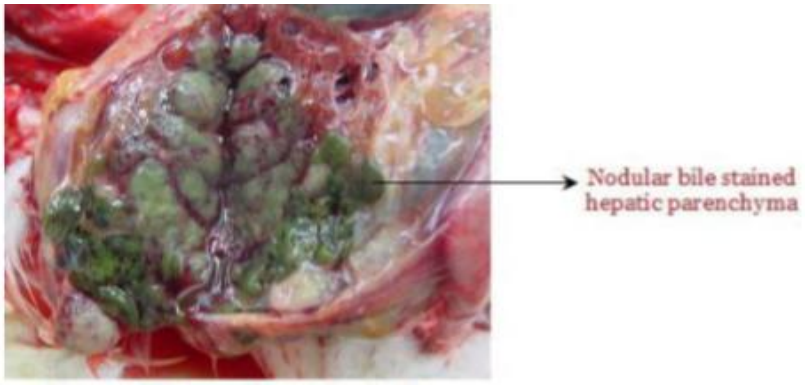
- Infection by pyogenic bacteria cause abscesses in liver.
- The bacteria enter the liver by way of portal veins and hepatic arteries mostly.
- Infection may also occur from the umbilical vein in the young animal.
- In the adult and older cattle, infection may occur from traumatic reticulitis.
- In countries where cattle are fattened for slaughter, abcesses are frequently encountered in the liver.
- The cause is Fusobacterium necrophorum, which gains entry through the portal vein. In these animals, highly concentrate diet produces ruminal disturbances, resulting into ulcers.

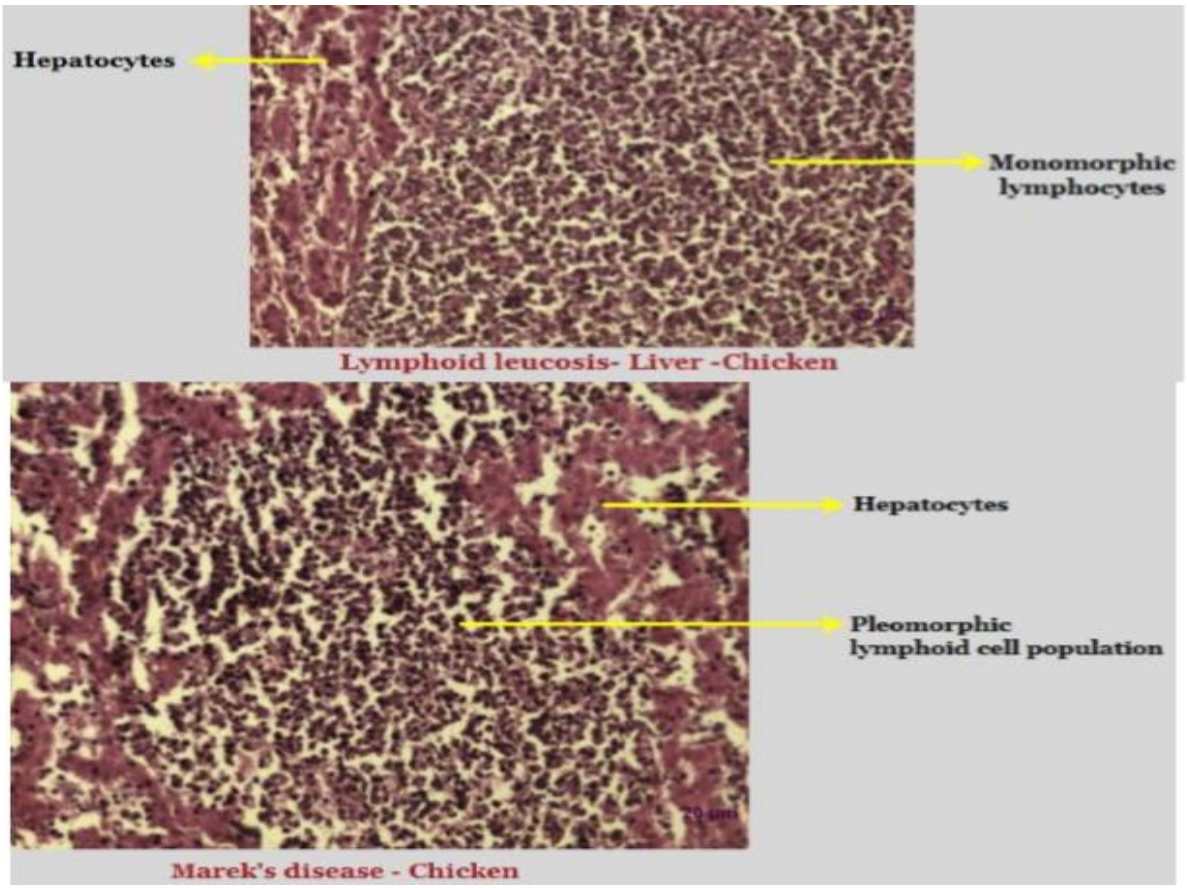
- From infected ulcers, Fusobacterium necrophorum reaches the liver, where it produces first coagulative necrosis and subsequently abscess on liquefaction.

Neoplasms of liver

Tumours of the liver may be primary (arising from the liver parenchyma and bile ducts) or secondary metastases from elsewhere.

Primary neoplasms: The most common primary tumours are hepatomas, hepatocellular carcinomas and cholangiocellular carcinoma. In dogs, hemangiomas are common. Primary fibroma may also be found in the liver. In chicken, lymphoid leucosis and Marek's disease primarily affect liver.





Secondary

- ✓ Metastases of any malignant tumor may be found in the liver.
- ✓ Metastases of lymphocytoma and pancreatic carcinoma are mostly seen
- ✓ In the cow, metastases of uterine carcinoma are common.
- ✓ Mammary gland carcinoma in the dog metastasizes in the liver.

CHOLANGITIS

Inflammation of bile duct is called cholangitis.

Aetiology: Mostly liver fluke infection, Hepatic coccidiosis by Eimeria stiedae in rabbits

Pathogenesis: Cholangitis is caused by the irritation of the spines on the cuticle of the parasites as well as the toxins liberated by the liver flukes.

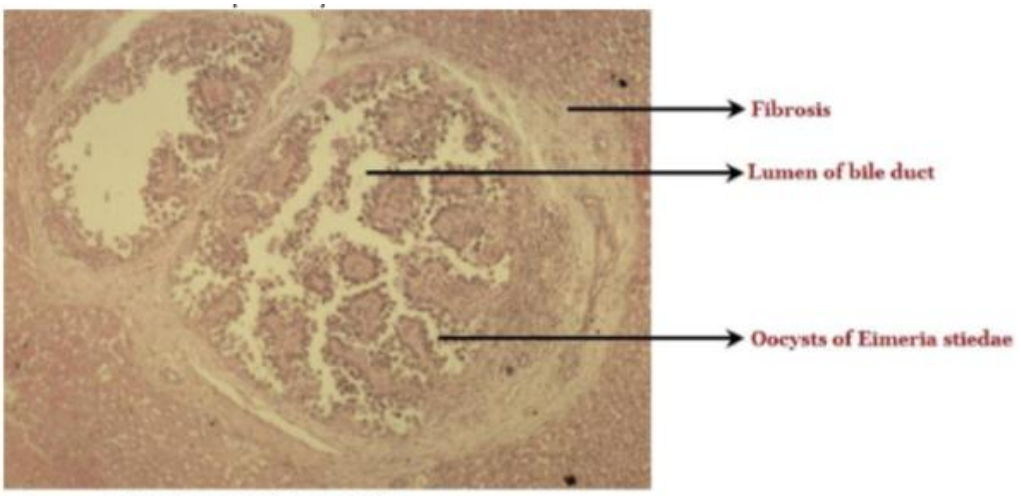
Gross pathology:

- ✓ The lumen of the bile duct is dilated and its wall is thickened due to fibrous tissue proliferation around it.

- ✓ These ducts stand out as thick cords.
- ✓ In some cases, calcification makes them hard (Clay pipe appearance)

Histopathology:

- ❖ The bile duct mucosa is hyperplastic with papillary projections.
- ❖ The bile duct wall is infiltrated by macrophages and lymphocytes.
- ❖ The lumen contains mucus.
- ❖ The fibrous tissue proliferates around the walls of the bile ducts and may extend to a short distance into the parenchyma of the liver.



Hepatic coccidiosis rabbit

CHOLECYSTITIS: Inflammation of gall bladder is called cholecystitis. It is caused when stasis of bile occurs by the presence of foreign bodies, parasites. Extramural pressure on bile duct E.Coli and Salmonella are frequently associated with cholecystitis. Infection is usually ascending from the duodenum. The retained bile itself acts as an irritant. Usually the catarrhal variety is noticed with congested mucosa and increased secretion of mucus by the glands.

CHOLELITHIASIS

Occurrence: Gall stones or choleliths are not as common in animals as in man. These are found mostly in cattle.

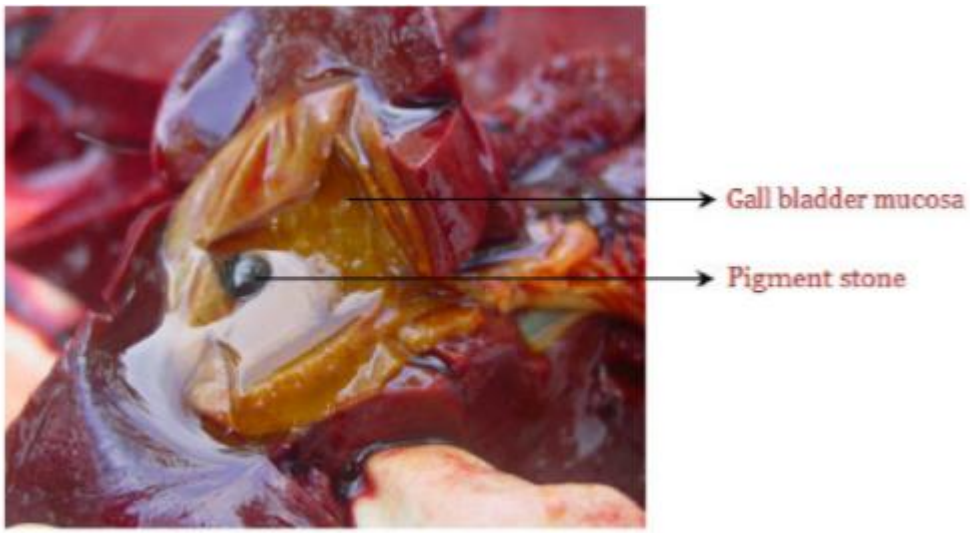
Etiology: Almost always gall stones occur as a result of cholescystitis.

Pathogenesis: The dead cells, bacteria or mucus may form the nuclei for development of cholelithiasis. Sand particles and food materials that may reach the gall bladder through the bile duct from the duodenum during violent peristalsis may also form nuclei of the choleliths.

Cholesterol is normally held in solution by loose combination with bile salts. This combination may be easily broken up. In cholecystitis, the bile salts are rapidly absorbed leaving the cholesterol which is precipitated. Gall stones are composed of cholesterol, bilirubin, bile salts, calcium and organic matrix.

Gross pathology

- The gall stones may be found in the gall bladder or bile ducts but unlike in man, bile ducts are more often affected because of frequency of parasitic involvement.
- They may arise in the bile passages of the liver
- The larger ones may be faceted due to rubbing against one another.
- These may be dark brown or yellowish-green in color.
- They are light and friable



Cholelith - Pigment type in a bitch