Lecture 3
Metabolic, nutritional and viral diseases

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VI. Metabolic disturbances

Accumulations of

- Fat
- Glycogen
- Amyloid
- Copper
- Pigments
6.1 Fatty liver – hepatic lipidosis or steatosis

REVIEW

- **Sources of FFA:**
  - Adipose tissue
  - Chylomicrons from gut
  - Hepatic production from AA and glucose (except in ruminants)

- **FFA in liver:**
  - Esterified to triglycerides
  - Used as energy (oxidized)
  - Production of phospholipids & cholesterol
  - Complexed with apoproteins
  - Released as lipoproteins

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*Pathologic Basis of Veterinary Disease (2006), 4th ed., Mosby-Elsevier, chapter 8*
Potential mechanisms of hepatic lipidosis

Rate of accumulation in liver exceeds rate of degradation or secretion into circulation

- Xs dietary intake of fat or carbohydrates
- Xs mobilization of fat from stores (due to ↑ demand)
- ↓ oxidation
- ↑ esterification
- ↓ apoprotein synthesis
- Impaired apoprotein secretion
Gross appearance of hepatic steatosis

Fatty livers, cats (top and bottom)

Fatty livers, dogs (top and bottom)

From Noah's arkive
Histological appearance of hepatic steatosis

In the **microvesicular pattern (acute, toxic)** the hepatocytes are swollen and contain multiple small cytoplasmic vacuoles. The confluence of these vacuoles may give rise to the **macrovesicular pattern (chronic, nutritional or metabolic)**, characterized by large well delineated clear vacuoles that usually displace the nucleus to the periphery.

Fatty liver – Oil-red-O stain
Significance of hepatic lipidosis

Depends on cause, severity and duration

- Reversible in mild cases
- May lead to:
  - Hepatocellular necrosis
  - Fatty cysts
  - Fat embolism
  - Liver rupture → hemoperitoneum
- ↑ susceptibility to toxic damage

Fat embolism, lung. The red dots are fat globules occluding the lumen of alveolar capillaries. Oil-red-O stain

Liver rupture, dog.
Causes/syndromes of lipidosis

6.1.1 Dietary causes

• Dietary excess
• Fasting in obese animals
• Cobalt /vitamin B12 deficiency

6.1.2 Toxic/anoxic injury

• Decreased oxidation of fatty acids
• Decreased formation/secretion of lipoproteins

Hepatic steatosis, aflatoxicosis (aflatoxin B1)
Causes/syndromes of lipidosis

6.1.3 Ketosis

- Xs fat metabolism (↑ energy demand)
- Pregnant ewes (pregnancy toxemia) & lactating dairy cows

6.1.4 Bovine fatty liver syndrome

- Obese animals (peripartum)
- Anorexia
  (retained placenta, metritis, mastitis, parturient paresis, abomasal displacement)
Causes/syndromes of lipidosis

6.1.5 Feline fatty liver syndrome
- Obesity, anorexia & stress
- Icterus, hepatic encephalopathy

6.1.6 Equine hepatic lipidosis
- Obesity, pregnancy & lactation
- Ponies, miniature horses and donkeys
- Hyperlipemia, hepatic rupture, encephalopathy, DIC

6.1.7 Endocrine disorders
- Diabetes & hypothyroidism
6.2 Glycogen accumulation

- Glycogen is normal in hepatocytes
- Excess storage in:
  - Diabetes mellitus
  - Hyperadrenocorticism (steroid induced hepatopathy)
  - Glycogen storage diseases

Glucocorticoid-induced hepatopathy, liver, dog. The liver is enlarged and pale brown to beige. The edges are usually rounded

6.2.1 Glucocorticoid-induced hepatopathy

- Steroids induce glycogen synthetase → hepatic storage
- Enlarged, pale liver due to swollen hepatocytes (midzonal areas)
- PAS stain distinguishes it from fat

Glucocorticoid-induced hepatopathy, liver, dog. Note the swollen hepatocytes (arrows) with extensive cytoplasmic vacuolation. H&E stain.

Glycogen, liver, dog. In this case, glycogen (purplish-red) in each hepatocyte has been pushed to the side of the cell. Periodic acid–Schiff technique.
6.3 Amyloidosis

- Not a single disease entity
- Three types
  - Secondary to prolonged inflammation
  - Primary in plasmacytomas
  - Familial in some breeds
- Most often deposited in
  - Walls of blood vessels
  - Portal connective tissue
  - Space of Disse
- May cause:
  - Hepatomegaly
  - Liver rupture
  - Liver failure

Hepatic amyloidosis, Shar-Pei dog. The perisinusoidal spaces are markedly expanded by the deposition of abundant glassy eosinophilic (hyaline), material-amyloid (A). The plates of hepatocytes are very narrow due to pressure atrophy (arrows). H&E stain.
Hepatic amyloidosis, avian. The liver is pale, enlarged and has rounded edges.

From Noah’s arkive

Cut section of a kidney with amyloidosis. Lugol's iodine which has affinity for starch demonstrates the presence of amyloid in the glomeruli. Note the dark brown spots in the cortex.
6.4 Copper accumulation

- An essential trace element bound to:
  - Metallothionein in hepatocyte lysosomes
  - Ceruloplasmin in blood

- Biliary excretion $\rightarrow$ critical for Cu homeostasis

- Too much Cu $\rightarrow$ lipid peroxidation/necrosis of hepatocytes $\rightarrow$ Cu release $\rightarrow$ hemolytic crisis

- Copper toxicosis can be due to:
  - Dietary excess in ruminants
  - Molybdenum deficiency
  - Hepatic (cholestatic) disease
  - Hereditary disorders
Copper toxicosis, sheep

**Wool** has a mild yellow discoloration (icterus). The hind limbs are stained with hemoglobin-tinged urine.

**Hemoglobinuric nephrosis**, the kidneys are diffusely dark brown or black due to the presence of hemoglobin.

The liver varies from yellow-brown to orange in color. The abdominal fat is icteric (yellow).

Dark brown urine (hemoglobinuria) within the urinary bladder.
Hereditary Copper Toxicosis

- Bedlington terriers
  - Autosomal recessive disease → impaired biliary excretion of Cu → Levels > 600 ppm dry wt → progressive liver disease
- Similar conditions in other dog breeds
- Wilson’s disease in humans

Copper toxicosis, liver, Bedlington terrier. Abundant copper (red) granules within the cytoplasm of hepatocytes. Rhodanine stain.

Copper toxicosis, liver, Bedlington terrier. Abundant copper (black) granules within the cytoplasm of hepatocytes. Rubeanic acid stain.
6.5 Pigments

- **Bile** (Cholestasis)
- **Hemosiderin** (Hemosiderosis, Hemochromatosis)
- **Lipofuscin**
- **Melanin** (Melanosis)
- **Parasite hematin**

*Hematin pigment from *Fascioloides magna*, liver, ox. Several areas of the liver are black from the pigment excreted by the fluke as it migrated through the organ.

*Hematin* (black pigment) deposited in a fluke migration tract in the liver. H&E stain.
Hemosiderosis, liver, horse (top) and pig (histo). Note many Kupffer cells laden with yellow-brown pigment. H & E stain

Hemosiderosis, liver, human. Hemosiderin is present as fine golden brown (H&E stain, top) and blue (Prussian blue stain, bottom) granules in hepatocytes

6.6 Nutritional diseases of the liver

- **Hepatosis dietetica** in young pigs
  - Vitamin E/Selenium deficiency
  - Hemorrhagic centrilobular to massive necrosis.

- **White liver disease in sheep**
  - Low cobalt intake → low synthesis of vitamin B12 → anemia → fatty liver
Examples of massive necrosis due to vitamin E/Selenium deficiency (hepatosis dietetica), in pigs (left). Areas of hemorrhagic massive necrosis appear as dark regions of different size scattered throughout the liver. *Histo:* Acute centrilobular to massive necrosis is the principal lesion of this disorder.
VII. Infectious hepatitis

- **Routes of infection**
  - Hematogenous (most common)
  - Ascending
  - Direct extension

- **Agents include**
  - Viruses
  - Bacteria
  - Fungi
  - Protozoa
  - Helminths
7.1 Viral infections of the liver

7.1.1 Infectious canine hepatitis (ICH)

- **Synonyms**
  - Rubarth’s disease, Fox encephalitis, Hepatitis contagiosa canis

- **Etiology**
  - Canine adenovirus 1

- **Pathogenesis**
  - Oral exposure to urine → tonsilitis → viremia
  - Tropism for hepatocytes, vascular endothelium & renal epithelium

- **Clinical signs**
  - Vomiting, diarrhea, petechia, hemorrhagic diathesis
ICH - gross lesions

- Paint-brush serosal hemorrhages
- Enlarged, turgid, friable & congested liver
- Gallbladder edema
- Hemorrhagic renal infarcts
- Widespread petechiae
- Blue eye

ICH, paint-brush serosal hemorrhages in the stomach.

ICH, liver dog. Liver is enlarged with rounded edges and diffusely red.

ICH, liver dog. The wall of the gall bladder is markedly thickened due to edema.

ICH, bilateral corneal opacity (blueing) due to edema.
ICH – histological changes

- Periacinar or single cell necrosis

- Large **intranuclear inclusion bodies** (INIB)

- Endothelial damage & hemorrhages

- Minimal inflammation
7.1.2 Herpesvirus infection

- **Lesions**
  - Multifocal hepatic necrosis in young animals & fetuses
  - **INIB**
  - Minimal inflammation

- **Agents**
  - Equine herpesvirus 1 - EVR
  - Bovine herpesvirus 1 - IBR
  - Canine herpesvirus 1
  - Pseudorabies

**Multifocal necrosis, IBR, liver, bovine fetus**

**Intranuclear inclusion body** (arrow), liver, equine fetus, EVR
7.1.3 Other viruses

- Rift valley fever
- Wesselsbron disease
- Infectious feline peritonitis
- Equine infectious anemia
- Adenoviruses of ruminants
- Porcine circovirus 2 (PMWS)

**Focal hepatic necrosis**, Rift Valley fever, liver, sheep. This disease produces randomly distributed focal areas of necrosis in the liver of lambs and fetuses. N = Necrosis and hemorrhage