Lecture 2
Liver failure; developmental anomalies; miscellaneous changes; circulatory disturbances

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III. Hepatic failure

Clinical syndrome that results from inadequate liver function

- It indicates massive reduction of the amount of liver cells or their function
- Result of either acute or chronic liver damage
- Not all functions lost at the same time
Manifestations of liver failure

Consequences of hepatic failure differ somewhat among domestic species. They include:

1. Hepatic encephalopathy
2. Disturbances of bile flow & icterus
3. Metabolic disturbances
4. Vascular and hemodynamic alterations
5. Cutaneous lesions
6. Impaired immune functions

3.1 Hepatic encephalopathy

Hepatic Coma

- Signs vary
  - Depression, behavioral changes
  - Mania, convulsions
- Acute liver disease (horses and ruminants)
- Portosystemic shunts (dogs and cats)
- Chronic liver disease
Pathogenesis of hepatic encephalopathy

- Blood accumulation of neurotoxic substances bypassing the liver and reaching the brain
- Requires shunting of ~ 15% of portal blood
- Main substance is ammonia
- Clinical signs are more severe after feeding

Other factors:
- Imbalance of inhibitory & excitatory amino acid neurotransmitters
- Increased brain concentration of benzodiazepines
3.2 Disturbances of bile flow

- **Cholestasis** - Abnormal accumulation of bile within the liver (intrahepatic), extrahepatic bile ducts or the gallbladder.

- **Icterus** – Yellow discoloration of tissues and body fluids due to hyperbilirubinemia

Yellow discolouration of the oral mucosa (Icterus)
Elevation of bilirubin

Hyperbilirubinemia (> 2 mg/dl) leads to icterus in tissues rich in elastin (sclera, aorta, etc)

Pathogenesis

- Overproduction of bilirubin (prehepatic jaundice)
  - Hemolysis - intra- or extra-vascular

- Decreased uptake, conjugation or secretion of bilirubin (hepatic jaundice)
  - Hepatocellular injury

- Reduced outflow of bile (post hepatic jaundice)
  - Within canaliculi (intrahepatic cholestasis)
  - Extrahepatic bile ducts (extrahepatic cholestasis) or gallbladder
Conjugated vs unconjugated bilirubin

- **Unconjugated (indirect) bilirubin**
  - Toxic to tissues (kernicterus)
  - Not soluble in aqueous solutions
  - Tightly complexed to albumin
  - No urinary excretion

- **Conjugated (direct) bilirubin**
  - Water-soluble
  - Non-toxic
  - Loosely bound to albumin
  - Excreted in urine (bilirubinuria)
Diagnosis of icterus and cholestasis

- **Gross**
  - Generalized yellowish discoloration
  - Yellowish/greenish brown liver

- **Histo**
  - Bile in canaliculi & hepatocytes

- **Clinical chemistry**
  ↑ blood levels of
  - Bilirubin (and choluria)
  - Cholesterol
  - Bile acids

Intrahepatic biliary obstruction, intestine, dog. Bile was unable to reach the intestine and as a result stools lacks the characteristic dark color produced by bile pigments (acholic feces)

Intracellular cholestasis. Note abundant (yellow-brown) pigment inclusions in hepatocytes, human liver.

Canalicular (intrahepatic) cholestasis (arrows)

Illustration of the morphologic features of cholestasis. Cholestatic hepatocytes (1), are dilated with enlarged canalicular spaces (2). Apoptotic cells (3) may be seen, and Kupffer cells often contain regurgitated bile (4).

3.3 Metabolic disturbances of hepatic failure

- Hemorrhagic diathesis
  - ↓ synthesis of clotting factors
  - ↓ clearance of products of clotting
  - ↓ platelet function
  - ↓ absorption of vitamin K
  - Disseminated intravascular coagulation (DIC)

- Intravascular hemolysis
  - Mainly in horses

- Hypoalbuminemia
  - ↓ production
  - Loss in ascites or GIT

Hemoperitoneum, omentum, dog with end-stage liver.
3.4 Vascular and hemodynamic alterations

- Portal hypertension
- Acquired portosystemic shunts
- **Ascites** (dogs and cats)

Due to:

- Portal hypertension
- ↓ colloid osmotic pressure
- Retention of sodium and water (hyperaldosteronism)

**Acquired portosystemic shunts**
secondary to portal hypertension, dog. Note the dilated and tortuous vascular channels (arrows)
3.5 Cutaneous problems

Photosensitization

(Activation of photodynamic pigments by UV light of 290 to 400 nm)

- **Primary**
  - St John’s wort (*Hypericum perforatum*)
  - Chlorpromazine
  - Phenothiazine

- **Secondary (hepatogenous)**
  - Herbivores with impaired excretion of phylloerythrin

- **Congenital**
  - Abnormal metabolism of heme
    - Retention of porphyrins
Hepatocutaneous syndrome (superficial necrolytic dermatitis)

- Rare disease in dogs
- Crusting, erosions & scaling at mucocutaneous junctions and footpads

Superficial necrolytic dermatitis, skin, dog. The epidermis has a trilaminar pattern: (1) parakeratotic layer (P), (2) edema/necrolytic layer (N), and (3) deep epidermal hyperplasia layer (H).

Footpad. Note the fissure (arrow) and crusts. The crusting is due largely to the parakeratosis.

IV. Developmental anomalies

4.1 Congenital cysts

Congenital cysts most likely originated from embryonic bile ducts; common in calves.
IV. Miscellaneous changes

4.2 Displacements

- Ventral hernia
- Diaphragmatic hernia
- Torsion of lobes
  - Swine and dogs
  - Infarction, shock, death

4.4 Rupture

- Trauma
- Enlarged liver

Multiple linear lacerations of the hepatic capsule and parenchyma, dog
Incidental lesions

4.4 Tension lipidosis
Focal areas in cattle & horses near mesenteric attachments

4.5 Capsular Fibrosis
• Resolution of peritonitis
• Parasitic migration??
  *(Perihepatitis filamentosa)*
4.5 Postmortem changes

Will be discussed in a lab/tutorial
V. Circulatory disturbances

Grouped according whether blood flow into, through, or from the liver is impaired

5.1 Impaired blood flow into the liver

- Any impairment of blood flow through the portal vein (or hepatic artery) before it enters the liver

- Possible sequelae:
  - Prehepatic portal hypertension
  - Liver infarcts

5.1.1 Portal vein hypoplasia (microvascular dysplasia)
- Congenital
5.2 Impaired blood flow through the liver

- ↑ resistance of blood flow within the sinusoids
  - cirrhosis,
  - diffuse fibrosis,
  - amyloidosis

- Sequella:
  - **Intrahepatic** portal hypertension

5.2.1 Intrahepatic arteriovenous shunts

- Direct communications between the hepatic artery and portal vein (congenital)

*WSAVA Standards for Clinical and Histological Diagnosis of Canine and Feline Liver Diseases. Saunders Elsevier - 2006*
5.3 Hepatic venous outflow obstruction

- Conditions that lead to ↑ resistance to venous outflow in the hepatic vein or cava
  - Thrombosis of the hepatic vein (Budd-Chiari syndrome)
  - Veno-occlusive disease
  - Passive congestion

- Sequella:
  - **Posthepatic** portal hypertension

5.3.1 Hepatic veno-occlusive disease

- Occlusion of central vein due to fibrosis
- Pyrrolizidine alkaloids
- Vitamin A toxicity in captive cats

Veno-occlusive disease. A reticulin stain reveals the parenchyma framework of the lobule and the marked deposition of collagen within the lumen of the central vein.
5.3.2 Passive congestion

- Acute
  - Slight enlargement of liver
  - Prominent reticular pattern

- Chronic
  - Nutmeg appearance
    - Centrilobular congestion
    - Midzonal /periportal fatty change
    - Later, centrilobular fibrosis & hemosiderosis

Chronic passive congestion (nutmeg liver), cut surface, cow. Inset: Cut surface of a nutmeg for comparison

Chronic passive congestion, dog. The liver is enlarged with rounded edges
Microscopic lesions in chronic passive congestion, liver

Centrilobular (periacinar) congestion

Centrilobular fibrosis (arrows). Dog.

Courtesy of Dr. Bildfell, Oregon State University
5.4 Other vascular (or circulatory) disorders

5.4.1 Congenital portosystemic shunt

- Intrahepatic
- Extrahepatic
- Hepatic encephalopathy
- Hepatic atrophy

Portosystemic shunt, liver dog. Note the small size (atrophy) of the liver (up under the rib cage).

Congenital portosystemic shunt, liver dog. The portal area is abnormal because it lacks a portal vein and contain numerous arterioles (arrows).
5.4.2 Telangiectasis

- Focal areas with dilated sinusoids filled with blood

- **Gross**
  - 1-5 mm, dark-red foci, often multiple

- **Histo**
  - Cavernous dilation of sinusoids
  - Loss of hepatocytes

- Incidental (cattle & cats)

5.4.3 Anemia

- Centrilobular or paracentral necrosis
5.4.4 Infarction

Infarction not common because of dual blood supply

- Thrombosis of hepatic artery
- Torsion of hepatic lobe
- Mycotic rumenitis
- Hepatic vein thrombosis

Hemorrhagic infarcts secondary to mycotic rumenitis, cow

Liver infarct, human