Normal anatomy & function

Hepatobiliary Injury and responses

Manifestations of hepatic failure

Developmental anomalies & Miscellaneous lesions

Circulatory disturbances

Metabolic & nutritional disturbances

Infectious diseases of the liver (hepatitis)

Toxin-induced liver diseases

Diseases of uncertain cause

Proliferative lesions of the liver

Diseases of the Gallbladder
Copper Accumulation

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

• Biliary excretion → critical for Cu homeostasis*

• Too much Cu → reactive O₂ species → lipid peroxidation/necrosis of hepatocytes → Cu release into blood → hemolytic crisis

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

Diagnosis: Submit fresh liver for copper quantification

Copper Toxicosis in Sheep

Hemoglobinuric nephrosis
• Bedlington terriers
  • Autosomal recessive disease → impaired biliary excretion of Cu → progressive liver disease
• Similar conditions in other dog breeds
  • Dalmatian, Skye terrier, WHW terrier, Lab
• Increased hepatic copper may occur secondary to liver disease in any breed

Diagnosis: Submit fresh liver for copper quantification

Rhodanine stain
Rubeanic acid stain
**Pigments**

- **Bile**
  - Cholestasis

- **Hemosiderin**
  - Accumulation without liver damage = Hemosiderosis
  - Accumulation resulting in liver damage = Hemochromatosis

- **Parasite hematin**
  - Fluke puke

**METABOLIC DISTURBANCES**

http://vet.uga.edu/vcvm/courses/afip/conf07/wsc23/wsc23_c01_fig02.jpg
METABOLIC DISTURBANCES

**Pigments**

- **Hematin**
  - Pigment from *Fascioloides magna*, liver, ox

**Bile**

- **Cholestasis**

**Hemosiderin**

- Accumulation without liver damage = Hemosiderosis
- Accumulation resulting in liver damage = Hemochromatosis

**Parasite hematin**

- Fluke puke
Hepatosis dietetica

- Disease of Pigs
- Vitamin E/Selenium deficiency
- Hemorrhagic centrilobular to massive necrosis

Areas of massive necrosis and hemorrhage appear as dark regions of different size scattered throughout the liver.
INFECTIONOUS DISEASES OF THE LIVER

**Portals of entry of organisms**

- Hematogenous
  - Portal vein - from the GIT
  - Hepatic artery - sepsis
  - Umbilical vein – newborns
- Ascending (via bile ducts)
- Direct extension

**Infectious Agents**

- Viruses
- Bacteria
- Fungi
- Helminths
- Protozoa

*Image: Dr C Legge*
Infectious Canine Hepatitis (ICH)

**Clinical Signs:**
- Vomiting
- Diarrhea
- Petechiae
- Hemorrhagic Diathesis
- Icterus

**Pathogenesis:**
- Exposure to urine
- Tonsillitis
- Viremia
- Targets hepatocytes, endothelial cells and urinary epithelial cells
INFECTIOUS DISEASES OF THE LIVER – VIRAL INFECTIONS

Infectious Canine Hepatitis (ICH)★

Gross Lesions:
- Enlarged, turgid, friable, congested liver
- Paint brush serosal hemorrhages
- Widespread petechia
- Gall bladder edema*
- Hemorrhagic renal infarcts
- Blue eye*

Etiology: Canine Adenovirus 1

https://instruction.cvhs.okstate.edu/AnatomicPathology/images/dx1-14.JPG

www.nmda.nmsu.edu/animal-and-plant-protection/veterinary-diagnostic-services
Infectious Canine Hepatitis (ICH)

Etiology: Canine Adenovirus 1

Gross Lesions:
- Enlarged, turgid, friable, congested liver
- Paint brush serosal hemorrhages
- Widespread petechiae
- Gall bladder edema*
- Hemorrhagic renal infarcts
- Blue eye*
Histology:
- Centrilobular + single cell necrosis
- Large intranuclear inclusion bodies
  - Hepatocytes, Endothelial cells, Kupffer cells
- Endothelial damage & hemorrhages
- Minimal inflammation

Infectious Canine Hepatitis (ICH) ★

Single cell necrosis of hepatocytes

Eosinophilic intranuclear inclusion bodies (arrows)
Herpesvirus infections

Etiology:
- Equine herpesvirus-1 (EVR)
- Bovine herpesvirus-1 (IBR)
- Canine herpesvirus-1
- Felid herpesvirus-1 (FVR)
- Suid herpesvirus-1 (Pseudorabies)

- Occurs in young animals and fetuses
- Gross lesions
  - Small white foci scattered randomly in the liver = multifocal hepatic necrosis
Herpesvirus infections

**Etiology:**
- Equine herpesvirus-1 (EVR)
- Bovine herpesvirus-1 (IBR)
- Canine herpesvirus-1
- Felid herpesvirus-1 (FVR)
- Suid herpesvirus-1 (Pseudorabies)

**Histologic Lesions**
- Multifocal necrosis with minimal inflammation
- **Intranuclear inclusion bodies** in hepatocytes
Other viruses

- Mutated Feline Enteric Coronavirus (Feline Infectious Peritonitis)
- Porcine circovirus 2
- Adenoviruses of ruminants
- Equine infectious anemia
- Rift valley fever
- Wesselsbron disease
MORPHOLOGIC PATTERNS

Multifocal necrotizing hepatitis

Abscesses

Granulomas

These lesions can look very similar:
- Think about species appropriate differentials!
- When mild – lesions look similar to viral and protozoal infections.
Multifocal necrotizing hepatitis

- Most often occurs in fetuses and neonates

- *Salmonella sp*
- *Listeria monocytogenes*
- *Campylobacter spp*
- *Fusobacterium necrophorum*
- *Actinobacillus sp*
- *Francisella tularensis*
Liver Abscesses

- Single or multiple
- Often follows chemical rumenitis and TRP in cattle

- *Fusobacterium necrophorum*
- *Trueperella pyogenes*
- Streptococci and Staphylococci
- *Corynebacterium pseudotuberculosis*
- *Rhodococcus equi*
Liver Abscesses

- Single or multiple
- Often follows chemical rumenitis and TRP in cattle

- *Fusobacterium necrophorum*
- *Trueperella pyogenes*
- Streptococci and Staphylococci
- *Corynebacterium pseudotuberculosis*
- *Rhodococcus equi*

Sheep, Hepatic abscess, *Corynebacterium pseudotuberculosis*
Liver Abscesses

Sheep, *Corynebacterium pseudotuberculosis*

**Significance**
- Incidental finding
- Become encapsulated and sterile
- Cause fibrous adhesions
Liver Abscesses

Significance

- Break into hepatic vein or vena cava
  - Thrombophlebitis
  - Endocarditis
  - Pulmonary aneurysms
  - Lung abscesses
- Generalized infection in young
- Rupture and toxemia
Hepatic Granulomas

INFECTIOUS DISEASES OF THE LIVER – BACTERIAL INFECTIONS

Tuberculosis, cattle
Mycobacterium bovis

Johne’s Disease
Mycobacterium avium paratuberculosis

www.askjc.org/wsc0/wsc/images/2010/101003-3.jpg
Lesion
• Single large area of hepatic necrosis
• Rapid autolysis

Bacillary Hemoglobinuria

• Cattle & sheep – acute and highly fatal
• Pathogenesis:

Etiology: *Clostridium hemolyticum*

Liver injury by migrating flukes
Anaerobic environment
Germination of *Cl hemolyticum* spores (latent in the liver)
Release exotoxins
Liver necrosis and intravascular hemolysis
Hemoglobinuria

Lesion

Noah’s arkive
Black Disease (Infectious Necrotic Hepatitis)

- Etiology: *Clostridium novyi*
- Sheep, cattle, pigs, horses
- Pathogenesis:
  - Liver injury by migrating flukes
  - Anaerobic environment
  - Germination of *Cl novyi* spores (latent in the liver)
  - Release exotoxins
  - Liver necrosis and Vascular damage
  - Subcutaneous hemorrhage

Lesion
- Multifocal hepatic necrosis
- Subcutaneous congestion and hemorrhage
**Tyzzer’s Disease**

**Affects:**
- Rodents
- Immunocompromised or young foals, calves, kittens, puppies

**Lesions**
- Multifocal necrotizing hepatitis
- Necrotizing colitis

**Etiology:** *Clostridium piliforme*
**Tyzzer’s Disease**

**Etiology:** *Clostridium pilliforme*

**Diagnosis:**
- Difficult to culture *
- Histology:
  - Bundles of long bacilli in hepatocytes
Mycotic infections may cause:

- Hemorrhagic infarcts
  - Cattle – resulting from mycotic rumenitis

- Granulomatous hepatitis
  - *Blastomyces dermatitidis*
  - *Histoplasma capsulatum*
Nematodes

*Ascaris suum*

- Adults live in the intestine of pigs
- Larvae migrate through the liver
- Tunnel → hemorrhage → eosinophilic infiltration/coagulative necrosis → fibrosis
- Multifocal fibrosis = “Milk spots"

Other nematodes that migrate through liver:
- *Stephanurus dentatus* – pigs
- *Strongylus vulgaris* – horse
Nematodes

*Dirofilaria immitis*

- Fatal vena caval (postcaval) syndrome in heavy infections
  - DIC, Intravascular hemolysis, acute hepatic failure
Cysticercosis

- Adult tapeworm in GIT
- Larval tapeworms (cysticerci) encysted within tissues or on serosal surfaces
- Usually incidental

Cestodes

*Taenia spp*

**Cysticercosis**

- Cysticercosis (T. hydatigena), liver, pig
- Cysticercosis ((Taenia sp), liver, pocupine

INFECTIOUS DISEASES OF THE LIVER – PARASITIC INFECTIONS
**Cestodes**

*Echinococcus granulosus*

**Hydatosis**
- Adult tapeworm in canid GIT
- Larval form encysts in viscera – sheep, many species
- Zoonotic – people can get hydatid cysts

Cestodes with adult form in biliary tract:
- *Stilesia hepatica*
- *Thysanosoma actinoides*
INFECTIOUS DISEASES OF THE LIVER – PARASITIC INFECTIONS

Trematodes

- *Fasciola hepatica*
- *Fasciola gigantica*
- *Fascioloides magna* (marked with an asterisk)
- *Dicrocoelium*
- *Opisthorchis*
- *Platynosum*
Lesions

- Immature flukes: Hemorrhage/necrosis during migration
  - +/- activate Clostridial spores
- Adults: mechanical/chemical irritation/physical obstruction
  - Fibrosing cholangitis (pipestem liver) - *F. hepatica*
  - Parenchymal cysts and Pigment - *F. magna*
- Blood loss
Protozoa

- Histomoniasis in turkeys*
- Coccidiosis (rabbits)*
- Leishmaniasis
- Toxoplasmosis
- Neosporosis
Protozoa

Histomoniasis
“Black head”

*Histomonas meleagris*

- Turkeys > Chickens
- Typhlitis
- Target-like areas of Hepatic necrosis
- Transmitted in the ova of *Heterakis gallinarum*
Hepatic Coccidiosis

*Protozoa*

- *Eimeria stiedae*

  - Coccidia reside in biliary epithelial cells - rabbits
  - Proliferative cholangitis
Questions?