Normal anatomy & function
Hepatobiliary injury and responses
Manifestations of hepatic failure
Developmental anomalies and 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 and bile ducts
Copper Accumulation

• Cu is an essential trace element bound to:
  • Metallothionein in hepatocyte lysosomes
  • Ceruloplasmin in blood
• Biliary excretion → critical for Cu homeostasis*
• Too much Cu → reactive O$_2$ species → lipid peroxidation/necrosis of hepatocytes → Cu release into blood → hemolytic crisis

Dietary excess may occur as a result of:
• Treatment for Cu deficiency (iatrogenic)
• Use of Cu containing fertilizers on crops
• Use of feed/ mineral block intended for a different species

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

*METABOLIC DISTURBANCES

Image: David Tyner, (Flickr)
Copper Accumulation

Pathogenesis

METABOLIC DISTURBANCES

Hemolysis

Oxidative damage

Hepatic necrosis

Cu

Cu

Cu

Cu

Cu

Cu

Cu

Cu

Cu

Cu
Copper Accumulation
Pathogenesis / Lesions

Diagnosis: Submit fresh liver for copper quantification

Hemoglobinuric nephrosis
Hereditary Copper Toxicosis - Dogs

- Bedlington terriers
  - Autosomal recessive disease → impaired biliary excretion of Cu → progressive liver disease with necrosis → cirrhosis
- Similar conditions in other dog breeds
  - Dalmatians, Skye terriers, WHW terriers, Labs
- Increased hepatic copper may occur secondary to liver disease in any breed

Diagnosis: Biopsy and submit liver for copper quantification
**Pigments**

**Bile**
- Cholestasis

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

**Parasite hematin**
- Fluke puke

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http://vet.uga.edu/ivcm/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 young pigs
- Etiology: ~ 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
- May have gallbladder edema
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**

**Types of Infectious Agents**

- Viruses
- Bacteria
- Fungi
- Helminths
- Protozoa

*Image: Dr C Legge*
**Pathogenesis:**

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

**Etiology:** Canine Adenovirus 1

**Exposure to urine**

**Tonsillitis**

**Viremia**

Targets hepatocytes, endothelial cells and urinary epithelial cells
Infectious Canine Hepatitis (ICH)

Etiology: Canine Adenovirus 1

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

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

www.nmda.nmsu.edu/animal-and-plant-protection/veterinary-diagnostic-services
Gross Lesions:
- Enlarged, turgid, friable, congested liver
- Widespread petechia and ecchymoses
- Gall bladder edema*
- Hemorrhagic renal infarcts
- Blue eye*

Etiology: Canine Adenovirus 1
Infectious Canine Hepatitis (ICH)

Histology:
- Centrilobular + single cell necrosis
- Large intranuclear inclusion bodies
  - Hepatocytes, Endothelial cells, Kupffer cells
- Endothelial damage & hemorrhages
- Minimal inflammation

Single cell necrosis of hepatocytes

Eosinophilic intranuclear inclusion bodies
Infections in neonatal animals and fetuses with herpesviruses often results in:

- Abortion
- Neonatal death
- Multifocal necrosis in multiple organs

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 (FIP)
- Porcine circovirus 2
- Adenoviruses of ruminants
- Equine infectious anemia
- Rift valley fever
- Wesselsbron disease
BACTERIAL INFECTIONS CAUSE:

- 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*

Listeriosis, *Listeria monocytogenes*, Chinchilla

Tularemia, *Francisella tularensis*, beaver

Necrobacillosis, *Fusobacterium necrophorum*, lamb
Hepatic Granulomas

**Tuberculosis, cattle**

*Mycobacterium bovis*

Epitheliod macrophages

Multinucleated giant cells
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

Significance of abscesses:
- Incidental finding
- Become encapsulated and sterile
- Cause fibrous adhesions

Sheep, *Corynebacterium pseudotuberculosis*
Liver Abscesses

Significance of abscesses:
- Break into vena cava
  - Thrombophlebitis
    - Endocarditis
    - Pulmonary aneurysms
    - Lung abscesses
- Generalized infection (sepsis)

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Bacillary Hemoglobinuria

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

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

Lesion
- Single large area of hepatic necrosis
- Rapid autolysis

Etiology: *Clostridium haemolyticum*
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

Etiology: *Clostridium piliforme*

Pathologic Basis of Veterinary Disease, 5th ed., Mosby-Elsevier

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

Lesions
- Multifocal necrotizing hepatitis and colitis
INFECTIOUS DISEASES OF THE LIVER – BACTERIAL INFECTIONS

**Tyzzer’s Disease**

Etiology: *Clostridium pilliforme*

**Diagnosis:**
- Difficult to culture *
- Histology:
  - Bundles of long bacilli in hepatocytes

Warthin-Starry stain

*Pathologic Basis of Veterinary Disease, 5th ed., Mosby-Elsevier*
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 $\rightarrow$ hemorrhage $\rightarrow$ eosinophilic infiltration/coagulative necrosis $\rightarrow$ fibrosis
  - Multifocal fibrosis = “Milk spots”
Nematodes

**Dirofilaria immitis**

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

**Echinococcus granulosus**

**Hydatosis**

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

**Echinococcus multilocularis**

**Alveolar echinococcosis**

- Adult tapeworm in canid GIT
  - Larval form encysts in viscera – rodents, many species (accidental hosts)
  - Zoonotic – people can get alveolar hydatid cysts

- In Canada, was mostly restricted to the northern tundra and south AB, MB, SK
- A few cases have occurred in Ontario recently in dogs as intermediate hosts
Cysticercosis

- Adult tapeworm in GIT
- Larval tapeworms (cysticerci) encysted within tissues or on serosal surfaces
- Usually incidental
INFECTIOUS DISEASES OF THE LIVER – PARASITIC INFECTIONS

Trematodes

- *Fasciola hepatica*
- *Fasciola gigantica*
- *Fascioloides magna*
- *Dicrocoelium*
- *Opisthorchis*
- *Platynosum*

Cholangitis, *Fasciola hepatica*, liver, cow

UNAM-FMVZ PATOLOGIA

Fasciola hepatica
INFECTIOUS DISEASES OF THE LIVER – PARASITIC INFECTIONS

**Trematodes**

- Immature flukes: Hemorrhage/necrosis during migration
  - May activate Clostridial spores if present
- Adults: Cause mechanical/chemical irritation/physical obstruction
  - Fibrosing cholangitis (pipestem liver) - *F hepatica*
  - Parenchymal cysts and pigment - *F magna*
Histomoniasis
“Black head”

Histomonas meleagrisid

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

Hepatic Coccidiosis

*Eimeria stiedae*

- Disease of rabbits
- Coccidia live in biliary epithelial cells
- Proliferative cholangitis
Questions?