Liver and Biliary Slide 1

8-10
Random hepatocellular injury
Equine herpes virus infection, foal
Viral induced lytic necrosis
Other causes salmonellosis, pig septicemia
Massive necrosis involves the entire hepatic lobule
8-21
Intrahepatic biliary obstruction, intestine, dog
Stools lack characteristic dark color produced by bile pigments
End stage liver (cirrhosis)

From chronic phenobarbital
Small firm irregular nodules of regeneration separated by tracts of fibrous CT

Causes
Chronic toxicity
Chronic cholangitis and/or obstruction
Chronic congestion (RHF)
Metabolic disorders (iron, copper)
Chronic hepatitis
Idiopathic
Hepatic encephalopathy
Ammonia/ amines absorbed from GI bypass liver (disease, or shunt) brain (toxicity unknown mechanism)
Metabolic disturbances
Bleeding
Clotting factors (except VII) made in liver
Short half life clotting factors
V, VII, IX, X
Chronic failure
II
Diminished clearance of FDP’s, activated clotting factors and plasminogen factors
Abnormal fibrogen synthesis
Impaired fat absorption
Vitamin K deficiency
Inactive Factors II, VII, IX, X
Hypoalbuminemia
Long half life of albumin

Vascular and hemodynamic alterations
Diffuse fibrosis
Increases resistance to blood flow
Portal hypertension
Acquired portosystemic shunting
Transudation
Ascites
Hepatocutaneous syndrome
Crusting, erosions, ulceration of epidermis, of muzzle, mucocutaneous junctions of face and footpads
Mechanism not understood
Photosensitization
Hair loss, erythema, and necrosis
Photodynamic pigments
Plants
Drugs
Inherited disorders of porphyrin metabolism
Presumed oxidative injury
Primary Photensitization (non-liver)
A photodynamic agent is ingested and absorbed
St Johns Wort
Buckwheat
Tetracycline
Phenothiazone
8-28
Cutaneous necrosis
Photosensitization, skin
Liver failure - cant remove phylloerythrin from portal blood

Secondary Photosensitization (liver)
Herbivores
Impaired excretion of phylloerythrin in bile
Congenital Porphyria (cattle and cats)
Abnormal metabolism of heme
- abnormal excretion and accumulation of porphyrins
- Photodynamic
8-29
Bilobed gallbladder
Liver, cat
Developmental anomaly, no clinical significance
8-30
Distended gallbladder, calf
Common in all species followed prolonged fasting
Biliary cysts, liver, pig

Unilocular cysts replace a portion of the parenchyma in the affected portion of the liver
8-32
Tension lipidosis
Liver, cow
Note the area of fatty infiltration (F)
The ligamentous attachment adjacent to the affected portion (Arrowhead)
Telangiectasis (arrows)
Capsular fibrosis
Liver horse

Numerous fibrous tags on the diaphragmatic surface of the liver
??Thought o be migration tracts of strongyles??
Chronic passive congestion
Liver, dog

Chronic passive congestion in the liver of a dog with a heart base tumor that impeded venous return to the heart.
The liver is enlarged with rounded margins.
Portosystemic shunts
Liver, dog
Note small size but normal color
Histologically, portal areas are abnormal because they lack a portal vein and contain numerous small-caliber arterioles

Intrahepatic shunts
Failure of closure of the ductus venosus at birth
(normally conducts blood from portal vein to caudal vena cava)
Most often in large breed dogs
8-39
Ammonium biurate crystals, urinary bladder

Extrahepatic shunts
Portal vein → caudal vena cava
Portal vein → Azygous vein
All of these are more common in small breed dogs
Elevated ammonium levels
Ammonium biurate crystals in urine
Telangiectasia is a condition in which hepatic sinusoids become dilated and filled with blood.

**Portal Hypertension**

- Intrahepatic arteriovenous shunts
- Direct communication between the hepatic artery and branches of the portal vein
- Portal vein hypoplasia (microvascular dysplasia)
- Abnormally small extrahepatic or intrahepatic portal veins
  - Diminished perfusion
- Proliferation of hepatic arterioles
- Hepatocyte atrophy
- Portal fibrosis and biliary hypertrophy
- Telangiectasis
  - Notable dilation of sinusoids in areas where hepatocytes have been lost
  - Variably sized dark blue foci
Common in cattle and no clinical significance
No inflammation of fibrosis
Glucocorticoid-induced hepatopathy
Liver, dog

Enlarged pale brown to beige liver
Hepatocytes are swollen with extensive cytoplasmic vacuolation
From glycogen accumulation

Glycogen accumulations
Diabetes mellitus
Glycogen storage diseases
Glucocorticoid induced hepatocellular degeneration
Swelling of hepatocytes from accumulation of glycogen
Pronounced swelling (midzonal)
Hepatic amyloidosis, liver
Duck
Firm waxy appearance
Pale brownish hue
The perisinusoidal spaces of disse adjacent to the sinusoids are lined with a glassy eosinophilic (hyaline) material-amyloid

Amyloidosis
Any deposition of β-pleated sheets of non-branching fibrils
Amorphous eosinophilic deposits found in space of disse, and along portal tracts and within blood vessel walls
Primary Amyloidosis
AL- Amyloid light chain
☐ Ig light chains
Secondary or Reactive amyloidosis
Prolonged inflammation
Fibrils of Amyloid A (AA)
From SAA (serum amyloid associated protein)
Copper Accumulation
Must be properly sequestered to prevent toxicosis
Serum
Copper bound to ceruloplasmin
Hepatic
Bound to metallothioneine
Excess copper
Initially diffuse
Later in lysosomes
Leads to reactive oxygen species
Lipid peroxidation
Excess Copper
Ruminants
Dietary excess
Sheep eating salt blocks for cattle
Pigs supplements
Pasturing herbivores
Hepatotoxic phytotoxins
Pyrrolizidine alkaloids
Heliotropium
Crotalaria
Secnecio
Prevent hepatocellular proliferation
Results in cholestasis (Copper is in bile)
Hereditary Disorders
Dalmatians
Bedlington terriers
West Highland White terriers
Impaired biliary excretion of copper
Effects
Ruminants
Large build up then quick release
Leads to Hemolysis, hepatocellular necrosis (anemia)
Centrilobular and midzonal
Bedlington terriers
Mutation in MURR1
Chaperone involved in copper excretion
Copper accumulates in centrilobular regions
Ongoing necrosis of hepatocytes
Fibrosis
Hemosiderin
Derived from ferritin
Aggregates
In liver derived from transferrin
In other tissues its from erythrocytes
Hemosiderosis- abundant hemosiderin without affecting organ function
Hemochromstosis- abnormally increased hemosiderin that can cause hepatic dysfunction
Lipofuscin
Incomplete oxidation of lipids
Melanin
Congenital melanosis occurs in ruminant livers
Parasite hematin
Liver flukes- mixture of iron and porphyrin
Fluke exhaust
Infectious canine hepatitis
Hepatic necrosis
Liver, dog
Liver can be slightly enlarged and friable with a blotchy yellow discoloration
Sometimes fibrin is evident on the capsular surface
Canine adenovirus Type 1
Vascular damage
Intranucleasr basophilic inclusions

Infectious canine hepatitis (canine adenovirus 1)
Hepatocytes
Vascular endothelium
Renal epithelium
Disease may be subclinical
Hepatic necrosis and hemorrhage
Urine □ oral
Tonsillitis → LN → Viremia → leukopenia and fever → Liver, endothelium, and mesothelium, kupffer cells
Cytolytic → necrosis
Lesions
Petechiae, ecchymoses, serous effusions into body cavities, fibrin on liver, Zonal necrosis following ischemia
DIC, Type III hypersensitivity Uveitis (Immune complex)
Corneal edema (blue eye)
8-50
Equine herpesvirus hepatitis
Hepatic necrosis random
Eosinophilic intranuclear inclusions

Herpesvirus
Neonates or fetuses
Equine Herpesvirus 1
IBR (Bovine Herpes 1)
Caprine herpesvirus
Canine herpesvirus 1
Feline viral rhinotracheitis
Pseudorabies
Infections
Transplacental
Birth canal
Contact with littermates
Replication in oronasal epithelium → blood via Mononuclear cells → cytolytic infection
Abortigenic viruses
Multifocal pinpoint necrosis of fetal organs

Rift Valley Fever
Mosquito transmitted
Ruminants
Calf mortality, lambs
Abortion of ewes, and cows
Bunyaviridae (Phlebovirus genus)
Africa disease prevalent after rainfall
Centrilobular to massive hepatic necrosis
Petechia and ecchymosis

Wesselbron Disease
Zoonotic
Mosquito transmitted
Newborn lambs and ewe abortion
Flaviviridae
Multifocal necrosis, icterus
Canalicular cholestasis
Adults survive

FIP (corona)
Pyogranulomatous vasculitis
Perivascular lymphocytes and plasma cells

PCV-2
Hepatocytes and kupffer cells
Mild to severe necrosis
Chronic hepatic abscesses
Corynebacterium pseudotuberculosis
Liver sheep
Thick fibrous capsule and the pale caseous exudate

Liver abscesses and granulomas
Portal vein
Umbilical vein
Hepatic artery
Ascending biliary infection
Parasitic migration
Reticular extension
Adults
Yersinia
Nocardia asteroides
Actinomyces spp
Feedlot cattle
Rumenitis allows Fusobacterium to enter portal circulation
Focal abscesses
Phlebitis thrombosis passive congestion and portal hypertension
Septic embolization of lungs
Mucor from rumen
Hepatic abscesses
*Rhodococcus equi*
Liver goat

More commonly found in foals
Hepatic abscess
Fusobacterium necrophorum
Liver cow

Foci of necrosis and abscess formation
These can erode the wall of the hepatic vein or the caudal vena cava
8-56
Hepatic abscess caudal vena cava cow
Multiple necrotic foci
Disseminated fungal infection (Mucor spp)

Liver cow

Mucor spp enter the portal blood following ulcerative rumenitis and cause focal necrosis inflammation in the liver
Multiple caseous granulomas, tuberculosis
Mycobacterium bovis
Liver
Cow

8-58
Multiple caseous granulomas, tuberculosis
Mycobacterium bovis
Liver
Cow

Tuberculoisis (Mycobacterium bovis)
Eradicated from US
Primary pulmonary disease disseminating to other organs
Zoonotic and infectious to other species
Mycobacterium avium-intracellulare complex
Hematogenous granulomas
Central core of debris, caseation and granulomatous inflammation surrounded by a fibrous capsule
Focal hepatic necrosis
Clostridium hemolyticum
(bacillary hemoglobinuria)
Sharply delineated from adjacent parenchyma

Bacillary Hemoglobinuria (clostridium hemolyticum)
Acute and rapidly fatal
Cattle and sheep
Concurrent Fluke infection
Spores from C hemolyticum reside in Kupffer cells
Bacteria proliferate and release toxins
Phospholipase C → hepatocellular necrosis
And IV hemolysis
Lesions
Sharp demarcation
Surrounded by inflammation
Serous cavities contain serum with fibrin
Icterus hemoglobinemia and –uria

Infectious Necrotic Hepatitis (Black Disease, clostridium novyi usually Type B)
Sheep, cattle, pigs, and horses
Parasitic tracts
Venous congestion
Fluid in pericardium, pleural, and peritoneal cavities
Hepatocellular necrosis, multifocal

Tyzzer’s Disease (Clostridium piliforme)
Obligate intracellular
Foals most often, also calves, cats and dogs
Oral ingestion → GI tract → Portal Vein → Liver → Lesions
Hepatocellular necrosis
Edematous, hemorrhagic LN
Neutrophils and Macrophages

Leptospirosis
Thin spiral motile
Mucous membranes or broken skin
Shed in Urine
Transplacental
Infected cells include:
RBC
Kidney
Liver
IV hemolytic anemia → centrilobular necrosis
Icterus
Hepatic hemorrhage and ascites
Rounded cells with granular cytoplasm (non-specific)
Other bacterial infections
Yersinia pseudotuberculosis
Salmonella spp
Paratyphoid nodules
Discrete accumulations of mixed mononuclear cells
Brucella spp
Haemophilus agni (Sheep)
Pasteurella haemolytica (Sheep)
Arcanobacter pyogenes (bovine fetus and neonate) (formerly Actinomyces pyogenes)
Campylobacter fetus ssp fetus (fetal and neonate lambs)
Actinobacillus equiuli (neonatal foals)
Nocardi a asteroides (dogs)
Yersinia tularensis (Francisella tularensis) (cats and Dogs)

Protozoal Diseases
Multifocal necrosis and inflammation
Neospora sp
Toxoplasma gondii
Neutrophils, macrophages
Free Tachyzooites or cysts containing bradyzoites

Dimorphic Fungal Diseases
Histoplasmosis
Histoplasma capsulatum
Inhalation → Liver
Ingestion → Liver
Multifocal; granulomas, with intralesional yeasts, and intra-histiocytic yeasts PAS positive
Nematodes
Migration tracts
Local hepatocellular necrosis
Inflammation
Replaced with CT scars → Milk spotted Liver
Ascaris suum (pigs)
Stephanurus dentatus (pigs)
Strongylus spp (Horses)
Capillaria hepatica → occasionally in parenchyma of dogs and cats
Dirofilararia immitis
Vena caval syndrome (Postcaval syndrome)
DIC
IV hemolysis
Acute liver failure

Cestodes
Taenia
Ova ingested by intermediate host → embryos → penetrate GI wall → Blood → anywhere in body → Larvae encyst in liver
Adults live in GI (Taenia hydatigena)
The intermediate stage (Cysticercus tenuicollis) in peritoneal cavity of many species (horses, ruminants, pigs)

Hydatid
Echinococcus granulosus
Canids are definitive hosts
Intermediate hosts are many and develop hydatid cysts (including humans)
Life cycle
Adults pass proglottids in feces → contaminate pasture → sheep ingest ova → embryos develop into hydatid cysts anywhere in body → rarely cause clinical signs
Cestode adults living in Hepatobiliary system
Stilesia hepatica
Stilesia globipunctata
Thyanosoma actinoides
All can inhabit the bile duct of ruminants

Trematodes
Fasciola hepatica
Adults are leaf shaped → eggs in bile → Snail intermediate hosts → larvae
develop in snail → cercariae leave the snail → encyst on herbiage → develop into
infectious metacercariae → ingested by ruminants → penetrate wall of duodenum
→ peritoneal cavity → Liver → migrate → reside in Bile ducts

Migration tarcts
Acute peritonitis, hepatic abscess
Clostridium spores proliferate (haemolyticum or novyi)
Cholangitis by adult flukes
Periductular fibrosis, and cholestasis
Fasciola magna
8-60

Tyzzer's disease
Clostridium piliforme
Liver-horse

1-2 mm foci

Filamentous bacterium in the cytoplasm

Tyzzer's Disease (Clostridium piliforme, formerly Bacillus piliformis)
Obligate intracellular parasite
Penetrate portal venous drainage
Enter the liver

Lesions
Lymph nodes hemorrhagic, edematous
Random pale hepatocellular necrosis
Variable neutrophils and mononuclear cells

Leptospirosis
Motile spiral bacteria
Mucous membrane entry
Or skin if damaged
Sources are contaminated bedding and soil
Transplacental infection
Infects
RBC
Kidney
Liver
IV hemolytic anemia
Leptospira toxins act on hepatocytes
Hepatocellular necrosis
Dissociation of hepatocytes
Rounded, eosinophilic cytoplasm, dark shrunken hyperbasophilic nuclei
Kupffer cells have hemosiderin

Other Bacterial Infections
Systemic Bacteremia
Yersinia pseudotuberculosis
Salmonella spp
Brucella
Pasteurella haemolytica- sheep
Haemophilus agni
Arcanobacter pyogenes (Actinomyces)- bovine fetus and neonate
Actinobacillus equi – foals
Nocardia asteroides- dogs
Yersinia (Francisella) tularensis- cats and dogs
Hepatic salmonellosis
Liver, cow
Random 1-2 mm foci of necrosis

Salmonella septicemia

In pigs necrotic foci are infiltrated by macrophages and form discrete granulomas termed paratyphoid nodules

Salmonella
Paratyphoid nodules
Salmonella spp

Protozoal diseases
Toxoplasma
Neospora
MF necrosis and inflammation
Neutrophils
Macrophages
Tachyzoites
Encysted bradyzoites
Hepatic histoplasmosis
Liver, dog
Histoplasma capsulatum

Liver enlarged pale mohogany from diffuse hypertrophy and proliferation of kupffer cells

Dimorphic Fungal Diseases
Histoplasmosis (Histoplasma capsulatum)
Soil dwelling
Inhalation
Pulmonary □ dissemination □ Liver
MF granulomas
Intralesional yeasts
INtrahistiocytic yeasts, PAS positive
Ingestion
Capsular and portal fibrosis (milk spotted liver)
Ascaris suum larval migration

Nematodes
Migration → necrotic tracts
Capsular scars → Milk spotted liver
Ascaris suum
Walled off abscess or granuloma
Stephanurus dentatus – pigs
Strongylus spp – Horse
Capillaria hepatica – dogs and cats
8-64
Dirofilaria
Vena caval syndrome
Rapidly fatal condition

Nematodes cont
Dirofilaria immitis
Caval syndrome
Vena caval syndrome
Postcaval syndrome
DIC
IV hemolysis
Acute liver failure
8-65
Cysticercosis liver
Cut surface, sheep
Thick fibrous capsule usually indicates the death of the larva

Cestodes
Taenia
Adults in GI tract of carnivores (innocuous)
Intermediate host
Ova ingested □ Embryo □ Penetrate gut □ Blood □ disseminated □ Parasitic cysts □ Cysts ingested by definitive host (dogs)
Taenia hydatigena (Adult)
Cysticercus tenuicollis (intermediate stage)
Peritoneal cavity of horses, ruminants, pigs
Immature cysticerci migrate
Echinococcus granulosus (Adult, dogs)
Hydatid cysts (intermediate, sheep)
Adults pass proglottids in feces → Ova ingested by sheep → any organ develops hydatid cysts (liver and lungs) → Cysts less than 10cm diameter
Cestode adults
Stilesia hepatica
Stilesia globipunctata
Thysanosoma actinoides
All can inhabit the bile duct of ruminants
Fasciola hepatica infection
Chronic intrahepatic cholangitis
Ducts become prominent by fibrosis

Trematodes
Fasciola hepatica
Sheep
Cattle
Snails are intermediate hosts
Adults live in biliary system → eggs in bile → feces → Larvae develop in snail → cercaria leave snail → encyst on herbiage → develop into metacercariae → Ingested by ruminants → penetrate duodenum → enter peritoneal cavity → Liver → migrate within liver → reside in bile ducts.
Hemorrhagic tracts → repair by fibrosis
Acute peritonitis
Hepatic abscess
Death
Clostridium hemolyticum, novyi
Spores proliferate in necrotic tissue
Cholangitis by adults
Bile duct obstruction
Periductular fibrosis
Ectasia of ducts
Fasciola gigantica- adults in bile ducts
Fascioloides magna- adults in parenchyma
Migrate → damage
Enclosed by fibrous CT
Other Bile Duct Parasites
Dicrocelium dendriticum- horses, Rum, Pigs, Dogs, Cats
Eurytrema pancreaticum, coelomaticum – ruminants
Opisthorchis tenuicollis – Pigs, dogs, cats
Opisthorchis viverrini – dogs, cats
PSeudamphistomum truncatum
Metorchis conjunctus, albidus
Parametorchis complexus
Concinnum procyonis
Playnosomum fastosum – dogs and cats
Fluke migration tracts
Fasciolodiasis, liver

Migration of fascioloides magna through the bovine liver
Produces extensive parenchymal damage

Inflammatory Disorders of the biliary tract

**Neutrophilic cholangitis (Ascending bacteria)**
Neutrophils in lumen or epithelium
Rupture of affected ducts can lead to hepatic abscess
Ascending bacterial infections

**Lymphocytic Cholangitis (Unknown)**
Cats
> 4yrs
Icterus from intrahepatic cholestasis
Can involve bile ducts directly
Inflammation around periphery of ducts
Portal inflammation
Bile duct proliferation
Hepatic or biliary fibrosis
Unknown cause
**Destructive Cholangitis (TMS drug in dogs)**
Necrosis of the bile duct epithelium
Inflammation around necrosis
Within portal area
TMS in dogs
8-72
Hepatosis dietetica, liver
Hemorrhagic centrilobular necrosis
Massive necrosis

Hepatosis Dietetica (Vit E/ Se)
Young rapidly growing pigs
Oxidative injury → hepatocyte necrosis
Massive necrosis
Distended, deep red, friable
Hemorrhagic centrilobular to massive necrosis
Post necrotic scarring

White Liver Disease
Pale fatty livers
Sheep
Insufficient cobalt
Cofactor in B12 enzyme action → anemia
Chronic pyrrolizidine hepatotoxicity
Cow
Fibrotic and sometimes distorted liver
Irregular capsular surface
Greatly enlarged hepatocytes (megalocytes) in the persisting parenchyma

Non-Hepatocyte Toxins
Bile duct epithelium
TMS
Sporidesmin
Kupffer cells
Endotoxin
Endothelial cells
Arsenicals
Hepatic stellate cells
Vitamin A Excess
Phase 1 Toxins (centrilobular necrosis)
P450 High energy conversions- forms covalent bonds with enzymes and nucleic acids
CCl3 radical
Acetaminophen

Blue Green Algae (Cyanobacteria)
Pre-formed toxins
Microcystin LR
Dead and dying organisms
Hemorrhagic gastroenteritis
Red Swollen hemorrhagic liver
Zonal or massive necrosis is evident

Pyrrolizidine Alkaloids
Alkaloids ingested → convert to pyrrolic esters by Cyt P450 → Esters are all alkylating agents → Cytosolic and nuclear proteins and nucleic acids.
Pigs>>horses>Cattle>>Sheep
Chronic intoxication
Hepatic fibrosis
Megalocytes (anti-mitotic effects, prevent cell division not nucleic acid synthesis)
Also occurs with aflatoxins and notrosamines
Biliary proliferation
Nodular regeneration
Cycasin
Non-toxic glycoside → deconjugated by bacteria → release toxic metabolite
Methylazoxymethanol → Portal vein → hepatic metabolism → Alkylating agents
Mitoinhibitory
Hyperchromasia
Hepatic fibrosis
Nervous disease
Progressive proprioceptive deficits
Axonal degeneration in dorsal funiculus and spinocerebellar tracts and corticospinal tracts
More common in sheep
Acute GI dysfunction
Centrilobular hepatic necrosis
Chronic hepatic aflatoxicosis
Postnecrotic scarring, pig
Shrunken and fibrotic liver from collapse of areas of massive necrosis and condensation of fibrous stroma

Mycotoxins
Aflatoxins
Aspergillus flavus
Aflatoxin B1 - most common and most potent
Toxin and carcinogen
P450 → toxic intermediates → bind cellular DNA, RNA, or proteins → toxic, carcinogenic, teratogenic
Sheep more resistant
Acute intoxication not common in cattle and horses (needs too big dose)
Acute intoxication in dogs
Hemorrhagic centrilobular to massive necrosis
Lipidosis and biliary proliferation
Chronic Intoxication
Firm pale livers
Lipidosis
Necrosis
Biliary hyperplasia
Centrilobular to bridging fibrosis
Cellulare atypia
Sporidesmin
Pithomyces chartarum
Grows well in dead rye grass
Necrosis of Biliary Epithelium
Sheep, less in cattle
Cholestasis
Failure to excrete phylloerythrin □ Photosensitization
□ facial eczema
Acute- bile stained livers
Prominent small caliber bile ducts
Dilated bile ducts
Fibrosis and narrowing of bile ducts (chronic cholangitis)
Atrophy and fibrosis of left liver lobe
Phomopsins
Phomopsis leptostromiformis (Grows on lupine)
Chronic atrophy and fibrosis of liver
Diffuse MF hepatocyte necrosis with metaphase mitoses
Diffuse fibrosis and bilary hyperplasia
Photosensitization may occur
Mushrooms
Amanita phalloides (Death cap)
Fatal liver necrosis
Toxic cyclopeptides
Amatoxin (octapeptide) □ Inhibits RNA Pol II □ Hemorrhage □ Shrunken liver
Lipidosis
Centrilobular to massive necrosis
Phalloidin
Toxic heptapeptide
Disrupts actin filaments

HEPATOXIC CHEMICALS
Phosphorus
White Phosphorus
Rodenticide
Direct toxin- periportal necrosis
CCL4
Centrilobular necrosis and lipidosis
Cresols/ or Cotton seed meal
Pigs ingest (from asphalt shingles and clay pigeons)
Centrilobular to Massive necrosis (Similar to Hepatosis dietetica)
Metals
Copper
IV Hemolytic anemia $\rightarrow$ centrilobular necrosis
Free radicals $\rightarrow$ Centrilobular necrosis
Iron
Hemochromatosis
Iron dextran intoxication of Piglets
Ferrous Fumarate intox Foals
Massive Hepatic necrosis
Bile Duct Hyperplasia
Hepatotoxic Therapeutic Drugs
Glucuronyl transferase deficiency
Cats
Acetaminophen toxicity
Carprofen
Labradors more often
Acute hepatic necrosis
Diazepam
Acute fatal hepatic injury in SOME CATS
Phenobarbitol, Phenytoin, Primidone
Chronic toxicity - nodular regeneration and fibrosis
Unknown mechanisms
Equine Serum hepatitis
Horse liver
Small, flabby, pale, discolored
Most hepatocytes are necrotic
Theiler’s disease
Tetanus antitoxin
Pregnant mare gonadotropin

Equine Serum Hepatitis (Theiler's Disease)
Equine antisera
Tetanus antitoxin (Not TETANUS TOXOID)
Pregnant mare serum gonadotropin
No infectious agent has been identified
Hepatic failure
Hepatic Encephalopathy
Icterus
IV Hemolysis
Small, Flabby Livers
Green to brown
Diffuse Centrilobular degeneration, enhanced lobular
8-76
Chronic active hepatitis
Scattered regenerative nodules
Extensive fibrosis

Canine Chronic Hepatitis (Chronic Active Hepatitis)
Causes unknown
Leptospira
Canine Adenovirus I
Copper Toxicosis of Dalmatians, Bedlington, WHWT
Hepatic nodular hyperplasia
Liver
Dog

8-77
Hepatic nodular hyperplasia
Liver
Dog

Hepatocellular Nodular Hyperplasia
Not Nodular regeneration
Well demarcated from parenchyma
Compress normal liver
Lobular pattern is distorted
Increased hepatocytes
Decreased portal tracts
Decreased central veins
Variable sized hepatocytes
Frequently contain glycogen or lipid
Starts in Dogs 6 yrs old
Hepatocellular adenoma
Liver, dog

Discreet masses of hepatocytes that compress adjacent normal parenchyma

Hepatocellular Adenoma
Benign
Single, Unencapsulated, red brown masses
Compressive
Pedunculated or spherical
Well differentiated hepatocytes forming Plates 2-3 cells thick, and abut normal adjacent hepatocytes at right angles
Portal tracts and veins scarce
Similar to Nodular Hyperplasia
Hepatocellular carcinoma
Liver, dog

Hepatocellular Carcinoma
Malignant
Uncommon
Solitary, may involve entire lobe
Well demarcated
Friable, gray-white, or yellow-brown tissue, subdivided into lobules by multiple fibrous bands
Irregular plates (trabeculae) 3+ cells thick
Patterns found in one tumor
Trabecular
Pseudoglandular
Solid
Cells range from atypical to bizarre
Metastasis
LN in abdomen
Lungs
Seeding peritoneum
8-80
Cholangiocellular carcinoma
Liver, dog
Multiple nodules some are umbilicated

Cholangiocellular Adenoma
Most common primary neoplasm of cats
Discrete firm gray to white masses
Well differentiated bile duct epithelium
Gland like
Tubules
Narrow lumen
Or distended by cystic fluid
Cystic Variants
Bile Duct Cystadenoma
Non-encapsulated multilocular cystic structure
Stroma is fibrovascular with moderate amounts of collagen
Cholangiocellular Carcinoma
Malignant
Arise from intrahepatic ducts
All species
Single or multiple masses
Umbilicated
Unencapsulated
Can be well differentiated- tubular or acinar
Can have squamous differentiation
Abundant deposition of collagen is Schirrous response
Metastasis common
LN, Lungs, Peritoneum

Carcinoids
Uncommon
Believed to arise from Neuroendocrine cells in the Biliary Epithelium
Single masses
Intrahepatic metastasis can occur (Multinodular)
Cells
Small
Elongated
Spindle shaped
Ribbons or rosettes
IHC
Chromogranin A
8-82
Hepatic lymphoma
Cow, nodular pattern

Lymphoma
Expand the liver
Diffuse infiltrative
Nodular variants
Can have enhanced lobular appearance
Centrilobular degeneration (anemia)
Portal and Periportal (lymphomas)
Sinusoidal (Myeloproliferative disorders)
8-83
Choleliths
Pig gallbladder

Cholelithiasis
May become obstructive

Cholecystitis
Viral
Rift Valley Fever (ruminants)
Canine Hepatitis (edema and hemorrhage in GB)
Salmonella dublin
Fibrinous cholecystitis
Ascending Biliary Bacteria
Acute or chronic cholecystitis
Chronic Cholecystitis
Prolonged bacterial
Cholelithiasis
Flukes
May cause rupture
Bile peritonitis (life threatening)
8-84
Fibrinous cholecystitis
Cow gallbladder
Salmonella enteritidis- dublin
Fibrinous cast sloughed into lumen
Cystic mucinous hyperplasia
Dog gallbladder
The gall bladder mucosa is thickened and contains multiple mucous cysts

Gall Bladder Mucocoele
Distended gall bladder
Filled with mucus
Often signs of biliary obstruction
Small breeds most affected
Usually hyperplastic mucosa

Cystic Mucinous Hyperplasia of the GB
Dogs and Sheep
Mucosa is grey to white
Spongelike mucosa
Polypoid masses
Variably sized cystic spaces in mucosa
Cysts contain mucus

Adenoma of GB
Young Cattle
Multinodular or Papillary
Loose CT Stalk

Carcinoma of GB
Rare
Mucin secreting epithelial cells
May invade the liver
Metastasis to LN or other sites
Adenoma
Dog gallbladder

Papillary projections of proliferating mucosa bulge into the lumen
8-87
Pancreatic atrophy/hypoplasia
Dog Pancreas
Remnants indicate by arrows
Autosomal recessive in GSD

Exocrine Pancreatic Atrophy (Juvenile Pancreatic Atrophy)
Autosomal Recessive
Small Pancreas
Islands of normal tissue remain
May be autoimmune pancreatitis
Signs
Maldigestion secondary to exocrine pancreatic insufficiency
Rapid Weight Loss
Atrophic cells may contain Lipofuscin which is not seen in hypoplasia of calves

Ectopic Pancreatic Tissue
Duodenum, small bowel, stomach, spleen, gallbladder, mesentery of the dog and cat (Choristoma - normal tissue in abnormal location)
8-88
Pacinian corpuscles
Cat pancreas
1mm clear foci
Normal

Pacinian Corpuscles
Interlobular septa- normal structures

Autolysis
Very Rapid Post mortem
Color changes to dark red or green

Pancreatic calculi
Uncommon in Cattle
Pancreaolithiasis

Stromal Fat cell Infiltration
Infiltration of the interstitial CT by fat cells
Obese cats
Pancreas itself unaffected
Illusion that pancreas is replaced by fat

Pancreatic Degeneration
Starvation
Loss of Zymogen Granules
Obstruction of Pancreatic ducts
Neoplasm
Chronic Inflammation
Fibrosis
Parasites
Pancreoliths

Pancreatic Pseudocysts
Fluid filled nonepithelialized fibrous sacs
Contain cellular debris and pancreatic enzymes
Folows pancreatic inflammation

Acute Pancreatic Necrosis
Routes of Injury
Ducts
Obstruction → Interstitial edema → compromises blood flow → ischemic damage to acinar cells
Ascarids
flukes
Calculi- ruminants
Blood
Toxins
cassia occidentalis
T-2 mycotoxin - Pigs
Zinc - Dogs, veal calves, sheep
Steroids
Inappropriate activation of enzymes
Trauma
Role of Trypsin
Activates elastase and Phospholipase A
Activates Kallikrein
→ kinin, and complement system, clotting → thrombosis and hemorrhage
Pancreatic secretions
Trypsin
Chymotrypsin
Elastase
Aminopeptidase
Lipase
Phospholipase
Amylase
Nucleases
Zymogen granules
Contain the enzyme in inactivated forms
Trypsinogen is only activated once in the lumen of the SI (via duodenal enteropeptidase)
Acute pancreatic necrosis
Acute pancreatitis
Dog
Expansion of pancreas by hemorrhage and edema
Fibrinous exudate and edema in interlobular septa and inflammatory exudate

Acute Pancreatic necrosis Cont…
Gross Lesions
Proteolytic degradation of parenchyma
Hemorrhage
Necrosis of peripancreatic fat
Edema of the interstitium
Coagulation necrosis- gray-white
Necrosis and hemorrhage – blue black
Fat necrosis- saponification, chalky white foci
Fibrous adhesions
Microscopic appearance
Hemorrhage
Leukocyte infiltrates
Coagulation necrosis
Fibrinous exudate in interlobular septa
Necrosis and inflammation of fat
Distinct Syndromes
Cats
Acute pancreatic necrosis
Suppurative Pancreatitis
Secondary to ascending bacteria
Systemic Effects
Dogs
Inflammatory mediators
Activated enzymes
Vascular injury → hemorrhage → shock → DIC
Liver Damage
Healing
Fibrosis
Regeneration is modest
Replication of acinar cells
Precursor cells from adjacent ducts
8-90
Chronic pancreatitis
Dog
Prominent lobules due to fibrosis
Fat necrosis/ mineralization

Chronic Pancreatitis
Fibrosis
Parenchymal atrophy
Obstruction of pancreatic ducts
Chronic Inflammation
Lymphoplasmacytic (dog)
Results from repeated mild episodes of acute pancreatic necrosis

Signs
Exocrine pancreatic Insufficiency
Endocrine Pancreatic Insufficiency (Diabetes Mellitus)

Parasitic Infections
Flukes
Opisthorchiidae (Opisthorchis and Metorchis)
Dicrocoeliidae (Eurytrema, concinnum, Dicrocelium)
Nematodes
Ascarids
8-91
Pancreatic nodular exocrine hyperplasia
Dog
Hyperplastic nodules are acini lacking zymogen granules

Pancreatic Nodular Hyperplasia
Dogs, cats, cattle
No clinical significance
Unencapsulated aggregates of acinar cells +/- zymogen granules

Pancreatic adenoma
Rare
Cat
Like hyperplastic nodules but single and larger
Pancreatic carcinoma
Composed of pancreatic epithelial cells and scirrhoues CT.
Carcinma tends to form crude acini that invade adjacent tissue

Pancreatic Carcinoma
*Uncommon*
Single or multiple nodules
Grey or yellow tissue
Gritty when cut
Can Seed peritoneum
Metastasis to LN
Microscopic features
Well differentiated adenocarcinoma
With tubular patters
Undifferentiated carcinoma
Solid patterns