Normal structure and function

- lobulated gland; synthesizes more protein on a wt-for-wt basis than any other tissue;
- a ductal system drains secretions into the duodenum through one or two main pancreatic ducts
- portal system of blood capillaries from islets of endocrine pancreas to much of the acinar tissue of exocrine pancreas;
- digestive enzymes are released as proenzymes;
- limited regenerative ability of the parenchyma.
Pancreatic acini, showing the radial orientation of the pyramidal exocrine acinar cells. The cytoplasm is devoted to the synthesis and packaging of digestive enzymes for secretion into a central lumen.

1. Developmental anomalies of the pancreas

1.1 Ectopic pancreatic tissue

- dislocated portions of duodenal buds during embryonic development.
- found as small nodules embedded in the submucosa or muscularis of a variety of abdominal organs or tissues.
- usually incidental, in humans has been associated with local inflammation, bleeding, and tumor development.

[Image of an organ with a small nodule indicated by an arrow]
1.2 Pancreatic hypoplasia

- sporadic in dogs and calves;
- defect of acinar tissue; (endocrine tissue generally normal).

**Pancreatic hypoplasia, dog.** Virtually no pancreatic tissue is present. Pancreatic remnants are indicated by arrows.

**Pancreatic hypoplasia, dog.** An island of (primitive or immature) exocrine pancreatic tissue surrounded by loose connective tissue.

http://w3.vet.cornell.edu
in dogs, also called Juvenile Pancreatic Atrophy;

**distinction between hypoplasia and atrophy may be difficult**;

grossly, marked decrease in amount of pancreatic tissue;

microscopically, some evidence of ongoing degeneration / atrophy of parenchyma.

Pancreatic hypoplasia, dogs. Virtually no pancreatic tissue is present. Pancreatic remnants are indicated by arrows.
2. Degeneration and atrophy

2.1 Pancreatic atrophy

- occurs as a consequence of a variety of local and systemic diseases → atrophy
- causes include:
  - protein-calorie deficiency (atrophy also evident in other organs / tissues, e.g. muscle mass, liver).
  - obstruction of pancreatic ducts → parenchymal inflammation and fibrosis, which may not be uniform along the organ; islets of endocrine pancreas fare better.

Segmental pancreatic atrophy, adult dog.
There is a portion of normal pancreas (n) and a contiguous area of atrophy (arrows).
2.2 Pancreatic lithiasis

- often incidentally in cattle (rare in other species).
- calculi consist mainly of calcium carbonate and calcium phosphate.
- may be a consequence of local inflammation.

Mild pancreatic fibrosis and calculi, bull. The pancreatic duct has been opened to show multiple calculi.
3. Inflammation

3.1 Acute pancreatitis/acute pancreatic necrosis

- important disease in **dogs**
- The predominance of necrosis over inflammation in most instances supports using the term of acute pancreatic necrosis over acute pancreatitis
- Pathogenesis in dogs is still obscure, but basic cause is activation of pancreatic digestive enzymes and consequent autodigestion …. 
- possible factors involved:
  - obese females, after high-fat meal;
  - surgical manipulation, combined with hypotension;
  - certain drugs;
  - familial predisposition in some breeds.
- death may be acute, or the disease may smolder until almost complete destruction of the organ.
Acute pancreatitis in humans (cont’d)

• important disease commonly associated with biliary calculi or alcohol abuse;
• Hemorrhagic pancreatitis is the most severe form variant (which is rare in dogs);
• basic cause is reflux of duodenal content into the pancreatic duct → activation of pancreatic enzymes;
• in early stages of the disease, lesions are **centrilobular**.

**Acute pancreatitis.** The pancreas has been sectioned longitudinally to reveal dark areas of hemorrhage in the head of the organ and a focal area of pale fat necrosis in the peripancreatic fat (arrow).
Three proposed pathways in the pathogenesis of acute pancreatitis
Interrelationships between the four **plasma mediator systems** triggered by activation of factor XII (Hageman factor). Note that thrombin induces inflammation by binding to protease-activated receptors (principally PAR-1) on platelets, endothelium, smooth muscle cells, and other cells. HMWK, high molecular weight kininogen.
Acute pancreatitis/pancreatic necrosis (cont’d)

- gross lesions are either locally extensive or multifocal.
- in early stages of the disease, lesions are perilobular, which also corresponds to the periphery of the blood circulation.
Acute pancreatitis, dogs. Early stage that shows expansion of the pancreas by clear gelatinous material (edema) and areas of hemorrhage (top). Multifocal areas of necrosis covered by fibrin (yellow material) and hyperemia (bottom) may also been found.
Acute pancreatitis/pancreatic necrosis (cont’d)

Hemorrhagic pancreatitis secondary to DIC (Disseminated Intravascular Coagulation) in a dog.

Multifocal fat necrosis (chalky-white areas scattered throughout the abdominal fat, pancreatitis, cats (left & right). Pancreas (p)
Acute pancreatitis/pancreatic necrosis (cont’d)

- necrosis of parenchyma and adjacent adipose tissue; severe inflammation.

**Acute pancreatitis.** The microscopic field shows a region of fat necrosis on the right (f) and focal pancreatic parenchymal necrosis (n, *center*).
3.2 Chronic interstitial pancreatitis

- **in dogs**, usually the sequel of repeated mild episodes of acute pancreatitis:
  - subclinical or, if severe, can result in exocrine / endocrine insufficiency (common cause of diabetes mellitus).

- **in cats**, cholangitis usually coexists with chronic interstitial pancreatitis, because the pancreatic and biliary ducts fuse prior to entering the duodenum.
Chronic interstitial pancreatitis (cont’d)

- characterized by parenchymal atrophy, fibrosis, and chronic inflammation.

Chronic pancreatitis in an older cat. The organ is shrunken and nodular as a result of interstitial fibrosis and nodular hyperplasia

*Histo:* Chronic pancreatitis, pancreas, dogs.
Remaining exocrine pancreatic cells are separated into small lobules by abundant fibrous connective tissue (F), which contains chronic inflammatory cells (arrow).

Comparison of the sequelae of acute and chronic pancreatitis in humans

- **Acute pancreatitis**
  - shock, acute respiratory distress syndrome, acute renal failure
  - disseminated intravascular coagulation
  - pancreatic pseudocysts and abscesses
  - duodenal obstruction

- **Chronic pancreatitis**
  - pancreatic pseudocysts
  - pancreatic duct obstruction
  - maldigestion, steatorrhea
  - secondary diabetes mellitus

(Robbins and Cotran Pathologic Basis of Disease. 2005)
Sequelae of chronic pancreatitis

Pseudocyst (p). A: Cavitated area (p). B: Necroinflammatory tissue lining the cavity

Chronic pancreatitis (horse, bottom, right). Fibrosis (F) and ductal dilation (d)

Atrophy (a), fibrosis (F) and cystic dilation of ducts (d)
### 3.3 Parasitic infections/diseases of pancreas

**Strongylus equinus granulomas**, pancreas horse. Several hard yellow nodules (arrows) scattered.

http://w3.vet.cornell.edu/nst/nst.asp

**Chronic pancreatitis.** Cross section of a parasite (*Eurytrema* spp, arrow) in a dilated, thick walled duct (d) and small round lobules (L) caught in the connective tissue (F).

Trematodes (flukes) inhabiting pancreatic ducts
4.1 Hyperplastic and neoplastic conditions

4.1 Pancreatic nodular hyperplasia

• common incidental finding in old dogs, cats and cattle

• grossly, multifocal small white nodules.

Pancreatic nodular exocrine hyperplasia, pancreas, dog. Hyperplastic nodules are white and project above the surface. Microscopically hyperplastic nodules (N) are composed of numerous small acini, most of which, in this case, lack typical zymogen granules. H&E stain.
4.2 Pancreatic adenoma

- extremely rare; well demarcated; can be single or multiple (but typically larger than, and not as numerous as, nodules of pancreatic nodular hyperplasia)
4.3 Pancreatic adenocarcinoma

- mainly in dogs and cats; single or multiple, schirrous, areas of necrosis and hemorrhage.

Pancreatic carcinoma. Stomach and pancreas (center), ventral-dorsal view, dog. Pancreatic carcinoma has invaded the mesentery, wall of the stomach, and gastrosplenic ligament. Note the lobulated appearance of the mass, which is formed by neoplastic exocrine pancreatic epithelial cells and scirrhous connective tissue. Proximal duodenum (bottom), liver (top).
Pancreatic adenocarcinoma (cont’d)

- often very aggressive → metastasis by implantation and via blood / lymph.
- invasion / obstruction of duodenum and / or bile duct (post-hepatic jaundice).

Metastases of pancreatic adenocarcinoma in the liver of dog (right) and serosal implantation in the intestine of a chicken (peritoneal carcinomatosis, left).
A little advice

If you want to avoid this:

....then moderate the consumption of:

See you tomorrow
8.2.3 Phomopsin

- *Phomopsis leptostromiformis*
- Grows on lupins
- Produces chronic liver damage
  - Small livers, finely nodular (mitotic inhibition and fibrosis)
  - Photosensitization

8.2.4 Poisonous mushrooms

- *Amanita phalloides* (“death cap”)
- Hepatocellular lipidosis, hemorrhage, and centrilobular to massive necrosis
- Toxic cyclopeptides (amatoxin & phalloidin)
  - Inhibition of RNA polymerase II function

Lupins

Amanita phalloides
8.3 Blue-green algae

- *Microcystis aeruginosa*, a cyanobacteria (often called blue-green microalga)
- Grows as bloom on lakes and ponds
- Blooms usually occur in late summer or early fall
- **Microcystin** is the main preformed toxin
- **Lesions**
  - Acute hemorrhagic gastro-enteritis
  - Acute *centrilobular to massive hepatic necrosis*
  - Chronic liver disease in survivors
8.4 Hepatotoxic chemicals

- **Phosphorus**
  - Vermin control
  - Rodenticide
  - Lipidosis and periportal necrosis (does not require metabolic transformation)

- **Carbon tetrachloride (CCl₄)**
  - Fire extinguishers
  - Refrigerants
  - Dry cleaning solvent
  - Pesticide
  - Anthelmintic
  - Scientific research - model of hepatic lipidosis and necrosis

- **Cresols**
  - Massive hepatic hemorrhage and necrosis in pigs

- **Metals (Iron, copper)**
  - Iron-dextran injection in piglets – massive hepatic necrosis
8.5 Hepatotoxic therapeutic drugs

- Many drugs may cause hepatic injury in some animals
- Species and individual variation
  - Trimethoprim-sulfonamide - Doberman pinschers
  - Carprofen - especially Labrador retrievers
  - Ivermectin - collies and shelties
  - Acetaminophen - cats are more sensitive than dogs (relative deficiency of glucuronyltransferase activity)
  - Anticonvulsants (primidone, phenytoin and phenobarbital) – end-stage liver in some dogs
  - Diazepam – acute hepatic failure in some cats
- Usually centrilobular hepatocytes are affected but mechanisms are unknown
Drug-induced chronic liver damage, dog treated with phenobarbital

Hepatocellular necrosis, centrilobular, acetaminophen toxicosis

Drug-induced cirrhotic liver, dog (left) and cat (right). Prolonged primidone therapy