Pancreatitis

Functions of the Pancreas

- Endocrine Islet Cells - (learn about this more in 433C)
- Exocrine (acinar cells and ducts)
    - Digestive enzymes
        - Produced by acinar cells
    - Bicarbonate ions (counteract stomach acid)
        - Produced by ductal and ductal epithelial cells
    - Intrinsic Factor
        - Sole source in cats
        - Dogs also produce some in the stomach
        - Bactericidal peptides

Anatomy of the Pancreas

- Dogs
    - Common bile duct and pancreatic duct enter close but are not merged at the duodenal papilla
    - Most dogs have an accessory pancreatic duct opening at the minor duodenal papilla
- Cats
    - Common bile duct and pancreatic duct merge before opening at the major duodenal papilla
    - Only ~ 20% of cats have an accessory pancreatic duct

Forms of Pancreatitis *Can be clinically indistinguishable

Acute Pancreatitis	Chronic Pancreatitis
Fully reversible inflammation Neutrophilic inflammation Edema Necrosis	Irreversible histopathologic changes Lymphoplasmacytic inflammation Fibrosis
Interstitial edema Neutrophilic infiltration Possible mesenteric fat necrosis	Lymphocytic infiltration Fibrosis Cystic acinar degeneration
	Complication of acute pancreatitis Immune-mediated? Cats > Dogs Subclinical to recurrent acute-on-chronic episodes

Protective Mechanisms of the Pancreas

The pancreas keeps digestive enzymes in an inactive form (zymogen) inside of acidic lysosomes until they are needed in the duodenum. Once they arrive, they are activated in the duodenum with the help of enteropeptidase converting trypsin to trypsinogen. SPINK1 also plays a key role in pancreatic protection by inhibiting the premature activation of trypsinogen into trypsin which prevents autodigestion.

Acute pancreatitis is the result of trypsinogen activation

1. Autoactivation of cationic trypsinogen
2. Activation of zymogens by thrombin
    - Bacterial toxemia
    - Ischemia
        - Iatrogenic
        - Post-anesthesia and CKD
    - Hypoxia
3. Apical block of zymogen granule secretion > colocalization of lysosomal proteas and zymogen granules
    a. This can lead to activation of enzymes
4. Biliary-pancreatic reflux > Enterokinase entering
    a. This mechanism is used to artificially induce pancreatitis in a lab setting

Perpetuation of pancreatitis

- Increased vascular permeability
- Influx of neutrophils
- Loss of apical paracellular barriers

Vicious cycle: Zymogen activation > Cell Injury > Inflammatory response/Pancreatitis > Pain > Systemic enzyme leakage and SIRS / MODS (ARDS,AKI, DIC, Arrhythmias) > Shock, poor perfusion, hypoxia

Complications of acute pancreatitis

- Acute kidney injury
    - Increase in creatinine by 0.3 mg/dL in 24 hours
- Systemic inflammatory response syndrome (SIRS)
- Multiple organ dysfunction syndrome (MODS)
- Acute respiratory distress syndrome (ARDS)
- Pseudocysts, necrosis, abscesses
- Chronic pancreatitis
- Exocrine pancreatic insufficiency (EPI)
- Diabetes mellitus

Chronic Pancreatitis

- Can follow acute insult
- Can develop independently of trypsin activation
- CCK and oxidative stress lead to low-grade inflammation
- Activation of pancreatic stellate cells leading to fibrosis
- Primary inflammation in abdominal organs such as the liver or intestines can cause inflammation of the pancreas
- Pancreatitis is almost always sterile!

Etiopathogenesis

- Idiopathic
- Risk factors
    - Breed
        - Mini Schnauzers (Hypertriglyceridemia)
        - Yorkie
        - Boxer
        - Collie
        - CKCS
        - Cocker Spaniels
    - Hypertriglyceridemia and Obseity
        - Triglycerides > 862 mg/dL (>9.7 mmol/L) are 4.5x higher likelihood of having an increased cPLI
        - Obesity is associated with HT and marked increase in cPLI, but not with clinical signs
    - Dietary indiscretion
        - Access to trash and table scraps
        - High-fat diet?
    - Endocrine disorders
        - Cushing's
        - Hypothyroidism
        - Diabetes mellitus (DKA)
    - Other concurrent diseases
        - Chronic enteropathy
    - Drugs
        - Dogs: Potassium bromide, phenobarbital, calcium, and L-asparaginase

Diagnosis of Pancreatitis

Clinical Signs	Physical Exam Findings
• Lethargy • Hyporexia • Vomiting • Diarrhea • Weight loss • Dyspnea • Praying posture	• Dehydration • Hypotherima or hyperthermia/pyrexia • Abdominal pain • Icterus • Abdominal mass/cranial abdominal organomegaly

*Clinical signs and physical exam signs can be unspecific and usually include some GI signs

Abdominal Ultrasound

Acute	Chronic
Pancreatic enlargement Hypoechoic pancreas Hyperechoic surrounding mesentery Abdominal effusion Cysts or abscesses Sensitivity 11-67% (you won't find it 33-89% of the time, even if it's there)	Hyperechoic or mixed echogenicity Dilated common bile duct Enlarged pancreas Irregular margins Pancreatic nodular hyperplasia can be normal in older cats and dogs Very unspecific

*Never make a diagnosis of pancreatitis based on imaging findings alone!

Clinical Pathology

CBC	Chemistry
Nonregenerative anemia • GI hemorrhage • Anemia of inflammatory disease Increased PCV • Dehydration Leukocytosis/leukopenia • +/- toxic change/left shift Thrombocytopenia • Consumption	Hypocalcemia • Pancreatic lipase reacts with mesenteric fat to generate free fatty acids. These FFA chelate calcium slats leading to the precipitation of calcium soaps (saponification) Hypoalbuminemia Hypovitaminosis D (Concurrent enteropathy) Amylase and Lipase • No diagnostic utility • Produced by extra-pancreatic sources • Reflect renal clearance Trypsin-like immunoreactivity • Relatively insensitive • Test of choice for EPI

Canine Pancreatic Lipase Immunoreactivity

- Quantitative and qualitative test SNAP

- Sensitivity ranges from 64-93%
- Specificity 74%
    - Need clinical signs because 26% of cases that test positive won't have pancreatitis
- No correlation with disease severity
- Increases reported with other diseases such as Cushing's, IVDD, IMHA

Precision PSL

- Sensitivity 93%
- Specificity 53% (basically a coin toss)
- Moderate correlation with spec cPL
- Severe outliers noted with Boxers

Overview on Diagnostics

- A single test cannot rule pancreatitis in or out
- A diagnosis of pancreatitis is based on the combination of signalment, clinical signs, laboratory and imaging findings
- The presence or imaging findings or laboratory findings alone in an otherwise healthy patient should not prompt a diagnosis of pancreatitis

Treatment of Acute Severe Pancreatitis

- Fluid therapy
    - Balanced isotonic crystalloids
        - LRS, Plasmalyte 148
    - Colloidal support
        - Hetastarch
- Analgesics
    - Partial and full mu-agonists
    - Buprenorphine 0.005-0.01 mg/kg SQ q 4-6h
    - Methadone 0.1-0.5 mg/kg SQ q 2-4 hours
- Antiemetics
    - Ondansetron 02-0.5 mg/kg IV q 12-24h
        - 5-HT3 antagonist
    - Maropitant 1mg/kg SQ q 24h
        - NK1 antagonist
- Nutrition
    - Enteral feeding should be prioritized
    - Oral, NG/NE tube, E tube
    - Appetitie stimulants

        - Capromorelin (Entyce) – ghrelin receptor agonist
        - Mirtazapine
    - Combine with an anti-emetic

Treatment of Chronic Pancreatitis

- Treatment of concurrent/underlying conditions
    - Hypertriglyceridemia
        - Low-fat diet
        - Omega-3 fatty acids
        - Gemfibrozil, benzafibrate, etc.
    - Chronic enteropathy
        - History, chemistry panel
        - Cobalamin, folate

Controversial or Not Recommended Treatments

Antimicrobials	Not recommended since pancreatitis is usually sterile
Steroids	No benefits in humans with acute pancreatitis
NSAIDS	May potentially cause pancreatitis
Acid Suppressants	Not indicated unless evidence of ulceration is present (melena)
Plasma Transfusion	Controversial but usually not indicated unless patient is actively bleeding from DIC
Surgical Intervention	Not indicated unless pancreatic abscess is present

Similarities and Differences Between Feline and Canine Pancreatitis

Feline Pancreatitis

- Chronic > Acute
- Comorbidities
    - Chronic Enteropathy
    - Cholangiohepatitis
    - Triaditis
- Complications
    - Exocrine pancreatic insufficiency
    - Diabetes mellitus
    - Hepatic lipidosis
        - Variable/cholestatic enzyme pattern (Increased ALP and Bilirubin)
        - ALT, AST variable
        - GGT normal or mildly increased
        - Early enteral feeding is crucial
- Treatment

    - Directed at comorbidities

Canine Pancreatitis

- Acute or chronic
- Predisposing factors
    - Breed
    - Diet
    - Hypertriglyceridemia
    - Ischemia, hypoxia, toxemia
    - Endocrine diseases
- Diagnosis
    - Combination of clinical signs, laboratory and imaging findings
- Treatment
    - No specific treatment available, supportive and correction of predisposing factors
- Compilations
    - Diabetes mellitus
    - EPI