

Pancreatitis

References:

- Davenport DJ, Remillard RL, Simpson KW, Pidgeon GL, Chapter 22, "Gastrointestinal and Exocrine Pancreatic Disease," in Hand Thatcher Remillard Roudebush *Small Animal Clinical Nutrition, 4th Edition*.
- Remillard RL, Armstrong PJ, Davenport DJ, Chapter 12, "Assisted Feeding in Hospitalized Patients: Enteral and Parenteral Nutrition," in Hand Thatcher Remillard Roudebush *Small Animal Clinical Nutrition, 4th Edition*.
- Simpson KW, Chapter 10, "Diseases of the Pancreas," in Todd R Tams *Small Animal Gastroenterology, 2nd Edition*.
- Steiner JM and Williams DA, "Feline Exocrine Pancreatic Disease," in Bonagura *Kirk's Current Veterinary Therapy XIII Small Animal Practice*.
- Williams DA, Chapter 146, "Exocrine Pancreatic Disease," in Stephen J Ettinger and Edward C. Feldman *Textbook of Veterinary Internal Medicine, 5th Edition*.
- Williams DA and Steiner JM, "Canine Pancreatitis," in Bonagura *Kirk's Current Veterinary Therapy XIII Small Animal Practice*.

I. Etiopathogenesis

A. Clinical categories of pancreatitis

1. Acute
 - a. Mild – no multisystem failure, uncomplicated and complete recovery
 - b. Severe – multisystem failure, complication by infected necrosis, pseudocyst or abscess
2. Recurrent acute – complete recovery between episodes
3. Chronic – fibrosis and reduction of acinar cell mass
 - a. Mild – minimal morphologic change, subclinical loss of endocrine or exocrine function. Chronic mild interstitial pancreatitis is the most common but least diagnosed form of pancreatitis in cats.
 - b. Severe – severe morphologic change, EPI or DM
4. Chronic with acute flare-ups

B. Etiologies – see DDx

C. Pathogenesis

1. Digestive enzymes are activated prematurely within the pancreas
 - a. Normally, enteropeptidases secreted by the duodenum activates trypsin, which in turn activates the pro-enzymes secreted by the pancreas.
 - i. Chymotrypsinogen activated to chymotrypsin
 - ii. Proelastase activated to elastase
 - iii. Procarboxypeptidase activated to carboxypeptidase
 - iv. Prophospholipase A2 activated to phospholipase A2
 - v. Procolipase activated to colipase
 - vi. Amylase and lipase do not need to be activated
 - b. Overstimulation of the pancreas by
 - i. CCK – normally released by the duodenal cells in response to intraluminal fats and amino acids; stimulates pancreatic and gall bladder secretion
 - ii. cerulein
 - iii. excessive dietary methionine
 - iv. pancreatic duct obstruction – IBD, duodenal foreign body, cyst, abscess, granuloma, neoplasia, duct hyperplasia
 - c. exocytosis of zymogens is uncoupled

- i. lysosomal vesicles fuse with zymogens to form pathologic “large vacuoles”
 - ii. lysosomal enzymes (proteases such as cathepsin B) activate trypsin within the cytosol of the acinar cell
 - d. digestive pre-enzymes in the zymogens are activated within the acinar cells, and leak into systemic circulation
 - i. trypsin activates coagulation and fibrinolysis (promotes DIC) in addition to activating pancreatic enzymes
 - ii. phospholipase A hydrolyses cell membrane phospholipids, degrades pulmonary surfactant, and demyelinates neurons; this in turn liberates myocardial depressant factor
 - iii. collagenase and elastase degrade blood vessel walls, causing hemorrhage and edema in various organs
 - iv. chymotrypsin damages cell membranes and generates free radicals
 - v. lipase causes fat hydrolysis, resulting in local fat necrosis and hypocalcemia
 - vi. kinins cause vasodilation, pancreatic edema, hypotension and shock
 - vii. complement causes cell membrane damage and aggregation of WBC
- 2. acinar cells and other tissues are damaged
 - i. edema first
 - ii. then may progress to hemorrhage, necrosis and thrombosis
 - iii. fluid is lost into the pancreatic tissue and abdomen
 - iv. large numbers of leukocytes migrate to the pancreas and release inflammatory factors into the pancreas and leak into circulation
 - i. TNF-alpha
 - ii. Interleukins
 - iii. PAF
 - iv. Free radicals
 - v. blood supply to the pancreas is reduced, which can exacerbate the process
- 3. the normal mechanisms for limiting pancreatic protease activity are depleted
 - i. PTSI (pancreatic secretory trypsin inhibitor) – secreted by the pancreas with trypsin
 - there is a genetic defect in this enzyme in people that can predispose to pancreatitis
 - ii. alpha-antitrypsin - plasma serine protease
 - iii. alpha-macroglobulins – plasma protease
- 4. hyperlipidemia
 - a. spontaneous or due to a high fat, low protein meal
 - i. >20% DMB, >50% calories as fat
 - b. Hydrolysis of triglycerides by lipase within the pancreatic microvasculature releases free fatty acids
 - c. Free fatty acids cause microthrombi or bind with calcium to cause further capillary damage, and release lecithin
 - d. Microthrombi in turn release more lipase, in a positive feedback loop
 - e. Lecithin causes marked necrosis of acinar cells when converted to lysolecithin by phospholipase A2. high fat
 - f. high fat and high arginine stimulate release of CCK, gastrin and secretin
 - g. be careful of U/D in schnauzers with calcium oxalate stones
- 5. Cholestasis.
 - a. bile refluxes into the pancreas
 - b. Especially a problem in cats because the bile and pancreatic duct(s) merge.
 - c. Protracted severe vomiting can cause bile reflux into the pancreatic duct, especially in the cat.

6. corticosteroids (most common drug to cause pancreatitis in dogs)
 - a. inhibit clearance of enzyme-alpha macroglobulin complexes by the macrophage system
 - b. Sensitize the pancreas to CCK stimulation.
 - c. stimulate proliferation of pancreatic duct epithelium
7. organophosphates – anticholinesterase stimulates the pancreas – especially cats
8. Pathophysiology of vomiting – central and peripheral.
 - a. Inflammatory factors released from the pancreas that stimulate the CRTZ.
 - b. GI local release of substance P and serotonin from enterochromaffin cells.
 - i. Substance P stimulates NK1 receptors in GI tract, CRTZ and VC.
 - ii. Serotonin stimulates 5HT3 receptors in GI tract, VC and CRTZ.
 - iii. Serotonin and substance P bind to vagal afferents, which stimulates VC.

II. Epidemiology/Signalment

A. Dogs

1. Breed – miniature schnauzer, miniature poodle, Yorkshire terrier, Silky Terrier, Briard, sheltie (shelties, schnauzers, Briard also prone to hyperlipidemia)
2. Age – middle aged to older
3. Sex – no predilection

B. Cats

1. Breed – Siamese, Himalayan
2. Age – no predilection
3. Sex – no predilection

III. History

A. Dogs

1. vomiting most common
2. can assume the “prayer position” due to abdominal discomfort (elbows on ground, standing on rear legs)

B. Cats – anorexia (97%) and weight loss most common

1. dehydration (92%)
2. Constipation
3. rarely polyphagia
4. rarely adipsia

C. Both Dogs and Cats

1. Lethargy
2. Anorexia
3. Vomiting – with or without hematemesis, cats vomit less often than dogs; 35% of cats with pancreatitis vomit
4. Diarrhea – with or without blood (15% of cats); can be large bowel due to proximity of the transverse colon to the left limb of the pancreas.
5. Fever
6. icterus
7. hunched stance
8. elevated respiratory rate

D. Common concurrent diseases, especially in cats:

1. Cholangiohepatitis
2. Inflammatory bowel disease
3. Triaditis (both a and b above)
4. Nephritis
5. Hepatic lipidosis – cats only

IV. Physical Exam

A. Dogs

1. Ascites
2. Acute abdomen
3. Petechiation
4. Necrotic skin lesions (due to elevated lipase)

B. Cats - Hypothermia or fever (hypothermia more common-68%)

C. Both Dogs and Cats

1. Lethargy
2. dehydration
3. Icterus and pale (acholic) stools
4. Increased respiratory rate (20% of cats)
5. Pain on abdominal palpation (25% of cats)
6. Palpable abdominal mass (23% of cats)

V. Diagnosis

A. CBC

1. Dogs
 - a. neutrophilia with or without a left shift
 - b. increased hematocrit if dehydrated or septic
 - c. anemia is possible
 - d. if thrombocytopenic, do coag panel to check for DIC
2. Cats
 - a. mild anemia
 - b. leukocytosis (usually no left shift)

B. Serology

1. Dogs
 - a. lipemia – high triglycerides, cholesterol even after prolonged fasting
 - i. can be a cause or an effect
 - ii. can present for opaque eyes.
 - b. hypocalcemia – calcium may be consumed by saponification of fat
 - c. hypoalbuminemia
 - d. amylase – may be elevated (amylase normal in 47% of dogs with pancreatitis)
 - e. lipase – may be elevated (lipase normal in 61% of dogs with pancreatitis)
--dexamethasone may increase lipase up to 5-fold
2. Cats
 - a. hypercalcemia

- b. elevated cholesterol
- c. amylase and lipase not useful

3. Both Dogs and Cats

- a. BUN, creatinine, phosphorus – may show pre-renal azotemia
- b. elevated bilirubin – post hepatic and/or hepatic
- c. elevated liver enzymes
 - i. pre-existing or caused by pancreatitis
 - ii. toxic substances carried from the pancreas to the liver by portal venous system
- d. hyperglycemia.
 - i. may be a result of high glucagon levels, which will subside with time
 - ii. may be contributed to by high cortisol/epinephrine levels, especially in cats
 - iii. or a result of DM (low insulin) , which can be transient or long term diabetic
 - iv. blood glucose may be erratic
 - v. might be exquisitely sensitive to insulin – give only as needed (may not need it BID or even every day)
- e. PLI – species specific tests (cPLI, fPLI) – high
 - 1) <200 normal.
 - 2) 200-400 – equivocal
 - 3) >400 pancreatitis.
- f. TLI – species specific tests – high (TLI not as specific as PLI)
 - renal disease and corticosteroids can increase TLI in dogs and cats
 - IBD and intestinal LSA can increase TLI in cats
 - ii. TLI spikes quickly at onset of disease, then goes back to normal
 - iii. some dogs and cats with pancreatitis will have normal or low TLI
 - may have missed the spike if checked too late
 - stored enzymes may be depleted
 - synthesis of new enzymes may be disrupted
- g. vitamin B12 may be low, since intrinsic factor from the pancreas is needed to absorb this vitamin
- h. folate might be low if concurrent inflammatory bowel disease
- i. TAP (trypsinogen activation peptides) will be high. TAP is labile, and sample submission requires special handling.

C. Urinalysis

- 1. Dogs – may have transient proteinuria due to enzyme mediated glomerular damage
- 2. Cats
- 3. Both
 - a. diabetics may have UTI
 - b. ketonuria and glucosuria suggest diabetes mellitus

D. Coags – abnormal if DIC

- 1. prolonged PT, PTT, ACT
- 2. low AT3
- 3 high FDP or d-dimers

E. Blood Gases/electrolytes

- 1. Dogs may have metabolic acidosis
- 2. Dogs have variable alterations in electrolytes
- 3. cats usually hypokalemic
- 4. diabetic dogs and cats often hypokalemic

F. Radiographs

- 1. thorax
 - a. pleural effusion

- b. pulmonary edema (especially if hypoalbuminemic)
 - c. pneumonia
- 2. abdomen – may be normal (rule out many other causes of abdominal pain)
 - a. ascites, general or localized to the right cranial abdomen
 - b. loss of abdominal detail (“ground glass sign”) – peritonitis
 - c. displacement of stomach to the left, gastric distension
 - d. displacement of duodenum ventrally and right (“reverse seven sign”)
 - e. dilated, thickened, corrugated duodenum
 - f. caudal displacement of transverse colon
 - g. calcification (saponification) of fat
- 3. barium series
 - a. delayed emptying of stomach and duodenum
 - b. corrugation of duodenal wall
- 4. 25-50% of cats with pancreatitis have pleural and/or abdominal effusion

G. Ultrasound – abdomen

- 1. Prior to PLI, used to be the next best test to pancreatic biopsy
- 2. Highly specific, but not as sensitive.
 - a. 60% of cats with pancreatitis can have normal abdominal ultrasound.
- 3. pancreas
 - a. enlarged.
 - b. mixed echogenicity, or hypoechoic.
 - 1) pancreatic edema can also be caused by portal hypertension or hypoalbuminemia
 - d. hypoechoic, cavitory lesions if abscess or pseudocyst
 - 1) aspirates of cavitory lesions can distinguish
 - e. dilated pancreatic duct
- 4. duodenum
 - a. dilated
 - b. hypomotile (normal motility 5 waves per minute)
 - c. corrugated
 - d. edematous
- 5. common bile duct – dilated and tortuous
- 6. gall bladder
 - a. enlarged
 - b. maybe secondary wall edema if cholecystitis
 - c. may have sludge
- 7. ascites – localized around the pancreas or generalized
- 8. peripancreatic fat and omentum
 - a. may be hyperechoic if saponification and fibrosis.
 - b. maybe hypoechoic if edema.

H. Abdominocentesis - suppurative inflammation, usually sterile.

I. Exploratory Laparotomy

- 1. pancreas
 - a. usually grossly abnormal in the dog
 - b. may or may not be grossly abnormal in the cat, even with severe disease

J. Histopathology – by surgical or laparoscopic biopsy

- 1. pancreas - biopsy to differentiate neoplasia from inflammation in dogs, to document pancreatitis in cats – DEFINITIVE DIAGNOSIS
 - a. acute pancreatitis – edema, hemorrhage, necrosis, mononuclear cell to neutrophilic infiltrates
 - b. chronic pancreatitis – fibrosis, mononuclear cell infiltrate, nodular hyperplasia
 - c. pancreas biopsy is not dangerous in cats

2. peripancreatic tissues – fat necrosis, thrombosis

VI. Treatment

A. Dogs

1. Glucocorticoids contraindicated in dogs in general. The exception would be immune mediated pancreatitis, which is rare in the dog. Theoretically, glucocorticoids do stabilize lysosomal membranes and could potentially limit zymogen exocytosis uncoupling
2. Nutrition:
 - a. NPO until no vomiting for 12 hours
 - i. to decrease stimulation of the pancreas. This is not thought to be as important as it was in the past.
 - ii. keep in mind that adequate nutrition intake significantly improves survival.
 - iii. Each must be weighed against the other.
 - iv. TPN or PPN should be considered if vomiting is severe.
 - v. If feeding causes vomiting or abdominal pain, start NPO period again.
 - vi. Use antiemetics to feed sooner.
 - vii. Enteral feeding is preferred to parenteral.
 - i. Supports GI integrity.
 - ii. Decreases bacterial translocation across the gut.
 - iii. Improves immune function.
 - iv. Less expensive, by a long way.
 - v. TPN and PPN have many associated potential complications.
 - b. then water only for 12 hours
 - c. then 3 very small low fat low protein meals for 24 hours – protein and fat are potent stimulators of the pancreas
 - i. use low fat low protein foods such as rice, pasta, potatoes, non-fat cottage cheese
 - ii. turkey should probably be avoided, as it is high in tryptophan, one of the amino acids which is more potent at stimulating the pancreas (also valine and phenylalanine)
 - iii. keep protein 15-30% DMB (13-23% of calories)
 - iv. keep fat <10% DMB (<17% of calories) for dogs with lipemia
 - Waltham/Pedigree Canine Low Fat dry (canned protein 34%)
 - No Hill's Diets with less than 10% DMB fat
 - v. Keep fat 10-15% DMB (17-23%) in non-lipemic patients
 - Hill's I/D canned and dry
 - Medi-Cal Canine Gastro Formula canned and dry
 - Leo Specific Digest (CIW canned, CID dry)
 - Purina CNM EN canned and dry
 - Select Care Canine Sensitive Formula canned and dry
 - vi. low fiber (low residue) is preferred at first, as fiber slows gastric emptying, prolonging duodenal stimulation
 - d. monomeric (elemental) food has also been recommended, as first food, and then move to solid food if monomeric food is well tolerated for 1-2 days
 - i. water soluble liquid foods containing nutrients in their simplest absorbable form
 - ii. should minimally stimulate pancreatic secretion

- iii. some contain added glutamine to stimulate enterocyte hyperplasia after mucosal atrophy that may have occurred due to prolonged NPO
- e. then slowly build up to full feed of low fat low protein food over 3-5 days
- f. If any vomiting, start over at the beginning, with NPO for 12 hours.
- g. Consider low fat and low protein TPN if no food intake for 5 days
 - i. TPN administered prior to 5 days after onset of pancreatitis can exacerbate pancreatitis
 - ii. Monitor carefully blood glucose and for lipemia
 - iii. to have TPN formulated, see appendix 8
- h. weeks after complete recovery (minimum 10 days), can attempt to switch back gradually to regular diet
- i. low fat/high fiber diets can be used long term after complete recovery from the acute episode, to avoid recurrence. Indicated especially for dogs with persistently high triglycerides and/or obesity.
 - i. Hill's R/D and W/D canned and dry
 - ii. Leo Specific CRW (canned) and CRD (dry)
 - iii. Medi-Cal Canine Fibre Formula canned and dry
 - iv. Medi-cal Canine Weight Control/Geriatric canned and dry
 - v. Purina CNM OM canned and dry
 - vi. Purina CNM DCO dry
 - vii. Purina CNM GL dry
 - viii. Select Care Canine Hifactor Formula canned and dry
 - ix. Waltham/Pedigree Canine High Fiber canned and dry

B. Cats

1. Glucocorticoids are indicated in cats with inflammatory bowel disease or triaditis
 - a. controlling concurrent immune mediated hepatitis and IBD will remove predispositions to pancreatitis
 - b. pancreatitis can be immune mediated per se in cats
 - c. prednisone 1 mg/lb/day or dexamethasone 1 mg/kg every other day
 - d. wean to lowest effective dose after clinical response
2. Nutrition
 - a. place feeding tube ASAP
 - b. E-tube first – safer than G-tube (see Chapter 3 – Feeding Tube Placement)
 - c. G-tube if e-tube can not be maintained due to vomiting (see Chapter 3 – Feeding Tube Placement)
 - d. drip liquid diet CRI into E-tube or G-tube if bolus feeding is not tolerated
 - e. consider jejunostomy tube if vomiting can not be controlled with drip feeding and anti-emetics – jejunostomy is distal to the segment of small intestine that secretes CCK in response to fat in the lumen
 - f. anecdotal evidence supports that we need not be as concerned about protein and fat content in cats, when compared to dogs

C. Both Dogs and Cats

1. PRIMARY THERAPIES

- a. IV/SQ fluids – supporting pancreatic perfusion is crucial

- i. add potassium if hypokalemic (different sliding scales for diabetics and non-diabetics – see appendix 12)
 - ii. Add glucose if hypoglycemic
 - iii. Add bicarb if severely acidotic (see appendix 9)
 - iv. LRS if acidotic, acetated ringers if severe liver disease
 - v. 35-40 ml/lb/day until drinking water without vomiting for 24 hours (more conservative if hypoalbuminemic, until colloids are restored)
- b. colloids if albumin <2.0 g/dl
 - i. hetastarch 5-10 ml/lb/day
 - added benefit of antithrombotic effects to promote pancreatic microcirculation
 - reduces trypsinogen activation to prevent acinar necrosis
 - ii. plasma 10 ml/lb/day over 2-3 hours – premed with benadryl; can repeat daily until the patient is improving
 - also treats DIC when incubated with heparin 35-75 units/kg for 30 minutes prior to administration
 - provides antiproteases to inactivate trypsin, which are likely depleted (alpha-macroglobulin) can give whole blood if PCV low enough
 - dextran 70
- c. Nutrition for both dogs and cats
 - i. see also sections above for issues specific for dogs and cats
 - ii. Water – keep patients with pancreatitis slightly over-hydrated (give at least 30-35 ml/lb/day after off IV fluids)
- d. Analgesia
 - i. IMPORTANT – THIS IS A PAINFUL DISEASE!!
 - ii. Butorphanol 0.2-0.4 mg/kg IV, IM, SQ QID
 - iii. Buprenorphine 0.01 mg/kg IV, IM, SQ BID-QID
 - iv. Oxymorphone 0.025-0.05 mg/kg in cats and 0.05-0.1 mg/lb in dogs IM or SQ every 1-3 hours
 - v. Morphine 0.05-0.2 mg/lb in cats and 0.2-0.5 mg/lb in dogs SQ or IM QID
 - vi. Hydromorphone 0.05-0.2 mg/kg IV, IM, SC q2-4h
 - vii. Meperidine 5-10 mg/kg every 2-4 hrs IM SQ for dogs; 1-2 mg/kg every 2-4 hrs IM SQ in cats
 - viii. Fentanyl
 - i. patch
 - i. at least 12-24 hours to take effect in dogs and 6-12 hours to take effect in cats
 - ii. 25 ug/hr patch for cats and dogs 5-30 lbs q72hrs for dogs and q118hrs for cats
 - iii. 50 ug/hr patch for dogs 30-60 lbs q72hrs
 - iv. 75 ug/hr patch for dogs 60-120 lbs q72hrs
 - ii. CRI – 2-4 ug/kg/hr
 - ix. Administer low dose acepromazine (0.005 mg/lb SQ IM or IV) acepromazine with opioid if patient becomes dysphoric due to opioid.
 - x. Buprenorphine is a mixed agonist-antagonist and can antagonize the other pure agonists on the list.
 - xi. NSAIDs are generally not used due to concerns about GI ulceration, kidney side effects and potential hepatotoxicity
- e. Antioxidants – free radicals contribute considerably to progression of disease.
 - perfusion of the pancreas with free radical scavengers ameliorated the severity of experimentally induced pancreatitis

--people with recurring pancreatitis have fewer episodes if they take daily antioxidants

- i. Milk thistle
 - dried whole herb 15-20 mg/lb PO SID
 - 80% silymarin extract capsules 2-5 mg/lb PO BID-TID
 - Alcohol extract 2-5 mg/lb PO BID-TID (cats hate it)
- ii. SAMe – on empty stomach 1 hour before feeding
 - 90 mg PO SID if less than 12 lbs
 - 90 mg PO BID if 12-25 lbs
 - 225 mg PO SID if 25-35 lbs
 - 225 mg PO BID if 35-65 lbs
 - 675 mg PO divided BID if 65-90 lbs
 - 450 mg PO BID if over 90 lbs
- iii. VetriScience Cell Advance – according to the label
- iv. zinc (dose)
- v. Vitamin E is also an inexpensive option that has been shown to help people with relapsing pancreatitis to have fewer episodes.
- vi. Selenium (0.1 mg/kg selenium IV SID, 0.3 mg/kg selenious acid or sodium selenite)
 - selenium lowered the death rate significantly in one study of canine pancreatitis (54% to 18%)

2. SECONDARY THERAPIES – AS INDICATED

- a. heparin 35-75 u/kg SQ TID – questionable efficacy in cats
 - i. definitely indicated in dog with DIC
 - ii. many think indicated in all cases of severe canine pancreatitis, as these dogs are hypercoagulable and prone to thromboembolic disease
 - iii. may promote adequate microcirculation in the pancreas, slowing progression of disease
- b. anti-emetics –
 - i. not all patients need them; some consider this primary therapy.
 - ii. Sometimes analgesia precludes need for anti-emetics.
 - iii. first choice probably 5HT3 blocker or NK1 blocker
 - i. these work peripherally and centrally
 - ii. Maropitant (Cerenia).
 - iii. Ondansetron (Zofran) 0.05-0.15 mg/lb PO or slowly IV SID-TID.
 - iv. Dolasetron (Anzemet) 0.4-0.6 mg IV SID-BID.
 - iv. then try metoclopramide CRI (1-2 mg/kg/day IV)
 - i. also peripheral and central.
 - ii. Reduce dose by 50% if renal failure.
 - iii. Metoclopramide doses not likely to work well.
 - v. then try cisapride (0.2-0.5 mg/kg BID-TID)
 - vi. careful of chlorpromazine and prochlorperazine, as they can cause hypotension which might compromise pancreatic circulation
 - vii. suctioning of gastric secretions is often tried, but has not shown to be of benefit in one study on dogs with pancreatitis
 - viii. anticholinergics contraindicated.
- c. antibiotics -- some authors think antibiotics are unnecessary, but I use them
 - i. increased survival in people with pancreatitis if treated with antibiotics
 - i. infection in dogs and cats with pancreatitis are rare
 - ii. penicillin or cephalosporin
 - i. to limit sequellae of bacterial translocation if severe GI signs or shock

- ii. if fever or toxic changes in WBC
 - iii. if diabetes mellitus (to treat/avoid infection in immunosuppressed patients)
avoid Clavamox, as it often causes vomiting
 - iii. some like enrofloxacin, but I don't use it
 - i. no activity against anaerobes, one of the likely causes of infection due to bacterial translocation
 - ii. 5 mg/kg/day, SID or divided BID
 - iv. if concurrent cholangiohepatitis
 - i. metronidazole 10-15 mg/kg PO or IV BID
 - ii. amoxicillin or ampicillin 10 mg/lb SQ IM or IV BID-QID
- d. B vitamins
 - i. B complex can be added to the fluids at 1 cc per liter
 - ii. B12 250-500 ug SQ once a week, or 1 mg every 14 days.
 - iii. Folate 200 ug per day for cats and dogs less than 40 pounds, and 400 ug per day in dogs larger than 40 lbs.
- e. H2 blockers – some think they help when vomiting is severe. May prevent esophagitis from protracted vomiting. Controversial.
 - i. Famotidine 0.25 mg/lb IV BID
 - ii. Cimetidine and ranitidine probably should be avoided, as there is some evidence that cimetidine may cause pancreatitis in some people
- f. vitamin K may be necessary if concurrent liver failure and evidence of coagulopathy related to vitamin K deficiency – 2.5 mg/kg/day PO or SQ
- g. bicarbonate –
 - i. acute acidosis due to sepsis, hypovolemia, etc (see appendix 9 for rules of bicarbonate supplementation)
 - ii. chronic acidosis - some cats with chronic fibrosing pancreatitis can develop chronic acidosis due to inability of the pancreas to secrete adequate amounts of bicarbonate
--start at 5 grains (1 tablet) sodium bicarbonate daily, and adjust according to mentoring of venous blood gases.
--baking soda can also be added to the water.
- h. treat lipemia if persistent (see appendix 10) – more common in dogs than cats
- i. calcium
 - i. only if clinical signs
 - ii. only if calcium falls below 6.5 mg/dl
- j. surgery/laparoscopy:
 - i. biopsy to differentiate pancreatic neoplasia from chronic pancreatitis in recurring or severe cases, and cases with very large pancreas.
 - ii. debridement of infected pancreatic abscesses (distinguish from sterile by cytology) and necrotic tissue
 - iii. restore bile flow
 - iv. strongly consider surgery in cats, to get biopsies (liver, intestinal, pancreas, lymph node) to evaluate for other inflammatory disease which will need to be treated if the patient is to do well long term
 - v. pseudocysts are collections of pancreatic sterile juice, enclosed by fibrous or granulation tissue
--not necessarily an indication for surgery

--can resolve spontaneously or after US guided percutaneous drainage
--surgery is an option if they do not resolve with time or after aspiration

- k. anthelmintics:
 - i. fenbendazole – if pancreatic flukes in cats – 30 mg/kg PO SID x 6 days
 - ii. praziquantel – if liver flukes in cats – 40 mg/kg PO SID x 3 days (high dose)

3. CONTROVERSIAL THERAPIES

- a. dopamine
 - i. had a protective effect when administered to cats within 12 hours of induction of experimental pancreatitis
 - ii. no beneficial effect after 12 hours
 - iii. can cause nausea, vomiting and seizures in cats
 - iv. 1-3 mcg/kg/minute CRI (constant rate IV infusion)
 - v. higher dosages of 3-10 mcg/kg/min CRI are indicated if greater cardiostimulant and BP support are indicated.
- b. peritoneal dialysis – to remove toxins that accumulate in the abdomen. Of help probably only when there is significant ascites.
- c. oral pancreatic enzymes
 - i. reported to reduce pain in humans with pancreatitis
 - ii. less likely to be effective in dogs because they do not appear to have a protease-mediated negative feedback system
 - iii. however, some have observed clinical effects in dogs with chronic pancreatitis with pain
 - iv. 0.5-2 tsp Viokase per meal
- d. drugs to inhibit pancreatic secretion – seems to work with experimental pancreatitis, but have little effect on spontaneous pancreatitis
 - i. glucagon
 - ii. gabexate mesylate
 - iii. nafamostat mesylate
 - iv. atropine
 - v. acetazolamide
 - vi. somatostatin – of help in humans with pancreatitis, but has not been evaluated in dogs or cats
 - vii. calcitonin
- e. future – antagonists to systemic inflammatory proteins such as PAF, IL-1 and TNF- alpha
 - i. lexipafant – PAF antagonist
 - ii. aprotinin – protease inhibitor
 - i. very expensive
 - ii. 250 mg (1.5 x 10⁶ kallikrein inhibitory units KIU) per dog IP TID-QID – preferred dose
 - iii. 5000 KIU/kg IV QID – another published dose

VII. Monitoring

- A. TPR BID-QID
- B. Electrolytes at least every other day until stable – K Na Cl
- C. Weight at least SID, and BID if oliguric or weight gain $\geq 10\%$
- D. HCT SID-BID if falling

- E. Albumin daily if <1.5 and every other day if <2.0
- F. Fluids in and out – not always practical in all practices; can be approximated by weighing often
- G. Glucose – every 2 hours if unstable diabetic, BID-QOD if stable; if spot checking is done, better to do it mid-way between insulin than at time of insulin injection
- H. PLI – long term, to determine resolution of pancreatitis (remember, species specific)
- I. Ultrasound – long term, to determine development/resolution of abscesses, pseudocysts after recovery from acute pancreatitis; cytologies as indicated by sonogram
- J. Monitor other abnormal values until they return to normal (azotemia, liver enzymes, etc)

VIII. Sequellae/Prognosis

A. Sequellae

1. pancreatic abscess
2. bacterial pancreatitis
3. pancreatic pseudocyst
4. chronic pancreatitis – diabetes mellitus, EPI - cats are more likely to have chronic pancreatitis as a sequella to acute pancreatitis than are dogs.
5. recurrence of acute pancreatitis in the future
9. Systemic inflammatory response can precipitate
 - a. thromboembolic disease - trypsin activates coagulation factor 12
 - b. DIC
 - c. SIRS – multiorgan failure
 - d. Respiratory distress
 - e. Pancreatic encephalopathy
 - f. Arrhythmia
 - g. Metabolic acidosis (also due to decreased production of bicarbonate by the pancreas)

B. Prognosis

1. Dogs - variable
 - a. Good if response to short term therapy is good. Many dogs with mild pancreatitis respond to NPO for 48 hours
 - b. Guarded if severe pancreatitis
 - c. less severe in lean dogs
 - d. clinical response to therapy is probably the best predictor of prognosis for the individual.
2. Cats – usually guarded, though some cats can do very well
 - a. tend to take longer than dogs to respond to therapy
 - b. worse if concurrent hepatic lipidosis or suppurative pancreatitis rather than mononuclear
 - c. cats that have pancreatitis once tend to have it again in the future
3. Both Dogs and Cats – things associated with poor prognosis
 - a. shock
 - b. oliguria
 - c. icterus
 - d. hypocalcemia in dogs
 - e. hypoglycemia
 - f. hypoproteinemia
 - g. acidosis
 - h. falling hematocrit
 - i. thrombocytopenia and DIC
 - j. elevated TNF-alpha, c-reactive protein, IL-6
 - k. elevated TAP (trypsin activation peptide) – this is the peptide that is cleaved off of trypsinogen when it is activated to trypsin.
 - l. elevated phospholipase A

m. CT is useful for prognosis in people (detects necrosis), but studies show it is of limited clinical use in dogs and cats.

IX. Public Health Significance – only in the rare case of feline pancreatitis caused by *Toxoplasma gondii*.