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Clinical Gastroenterology of Dogs and Cats

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Omaha, NE
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Overview of Diagnosis and Management of Vomiting in Dogs and Cats (Tams)

A Clinical Approach to Those Troublesome Chronic Diarrhea Cases in Dogs and Cats (Twedt)

Updates in GI Surgery (Seim)

Putting It All Together: GI Cases Discussion (Seim, Tams, Twedt)

Diagnosis of Acute and Chronic Vomiting in Dogs and Cats

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Vomiting is among the most common reasons that dogs and cats are presented for evaluation. Because there are a multitude of causes of vomiting, ranging from simple to complex, this can be a challenging problem for clinicians to accurately diagnose and manage. The problem also causes significant concern for pet owners, especially when there is an onset of frequent severe vomiting or when the occurrence becomes more chronic and intermittent without adequate control. However, by following a systematic approach beginning with an accurate history, a thorough physical exam, and appropriate baseline testing (Stage 1), then performing tests more specific for certain conditions or organ systems (e.g., bile acids assay, leptospirosis serology, baseline cortisol or ACTH stimulation, ultrasonography) (Stage 2), and finally where indicated performing advanced procedures for more thorough examination and biopsy or definitive therapy (endoscopy, exploratory laparotomy), most cases can be diagnosed successfully and managed judiciously. Vomiting does not constitute a diagnosis in itself. It is emphasized that vomiting is simply a *clinical sign* of any of a number of disorders that can involve any organ system in the body. In fact, one diagnostic registry service listed over 400 potential causes of vomiting in dogs! These notes summarize diagnostic approach and various treatment options for managing dogs and cats with vomiting.

Vomiting refers to a forceful ejection of gastric and occasionally proximal small intestinal contents through the mouth. The vomiting act involves three stages: nausea, retching, and vomiting. Serious consequences of vomiting include volume and electrolyte depletion, acid-base imbalance, and aspiration pneumonia.

It is essential that the clinician make a clear differentiation between <u>regurgitation</u> and <u>vomiting</u> at the outset. Regurgitation is defined as passive, retrograde movement of ingested material, usually before it has reached the stomach. Failure to recognize the difference between regurgitation and vomiting often leads to misdiagnosis. Regurgitation may occur immediately after uptake of food or fluids or may be delayed for several hours or more.

A Detailed, Accurate History is ESSENTIAL

One of the most important early considerations is to determine if any toxins or foreign objects may have been ingested. Some compounds can cause life threatening sequelae. The earlier a toxicity is identified, the greater the chance for successful management. Currently, xylitol toxicity is being recognized more frequently, and sago palm plants, which can cause severe hepatotoxicity in dogs and cats, are found in more homes and yards than in previous years. Cocoa mulch toxicity (theobromine) is also

occasionally seen. Many animals that have ingested toxins are presented with vomiting as a prominent sign.

History and Clinical Assessment: Clinical Features Of Vomiting

Because of the wide variety of disorders and stimuli that can cause it, vomiting may present the clinician with a major diagnostic challenge. A complete historical review with emphasis on all body systems is essential for determining a realistic and effective initial work-up plan and treatment protocol. All too often concentration on only the gastrointestinal tract leads to an incorrect diagnosis and inappropriate treatment. Consideration of the following features is useful in assessing and diagnosing a patient with vomiting:

(1) duration of signs
(2) signalment and past pertinent history
(3) environment and diet
(4) systems review (e.g., history of PU/PD, coughing and sneezing, dysuria or dyschezia, etc.)
(5) time relation to eating (vomiting of undigested or partially digested food more than 8-10 hours after eating often indicates a gastric motility disorder [more common] or gastric outlet obstruction [less common])
(6) content of the vomitus (food, clear fluid, bile, blood, material with fecal odor), and
(7) type and frequency of vomiting (projectile?, chronic intermittent?, cyclic?, morning vomiting only?).

Most Common Causes of Acute or Chronic Vomiting in Dogs

First need to Rule-Out:

Dietary/ingestive problem (always investigate for any potential environmental materials that the patient may have been chewing on (plants [toxins], debris carpet, etc)

- Indiscretion (e.g., table scraps, sudden diet change, garbage ingestion; toxins, foreign body, ingesting plants in home or yard)
- Food adverse reaction (dietary sensitivity)
- True food allergy

Parasites

- Intestinal (including *Giardia*)
- Gastric (*Physaloptera*)

Drug related problems

- NSAIDS must always be considered
- Other drugs (e.g., cardiac glycosides, antibiotics, chemotherapeutic agents)
- *Any* drug can potentially cause vomiting, always ask about any supplements that are being given to a pet

Metabolic disorders

- Renal disease
- Liver disease

- Electrolyte abnormalities
- Addison's disease (some are glucocorticoid and mineralocorticoid deficient and will demonstrate typical electrolyte abnormalities; others are only glucocorticoid deficient and require ACTH stim for diagnosis (JAVMA April 15, 2007, p. 1190-1194)

Rule-Outs for Chronic Vomiting, Once the Causes Listed Above are Ruled Out:
Main Categories:

Motility Disorders
- Gastric hypomotility (an underappreciated disorder)

Inflammatory Disorders
- Chronic gastritis (with or without *Helicobacter*)
- Inflammatory bowel disease

Obstructive Disorders
- Foreign body not already diagnosed (including cases with a partial small bowel obstruction that has eluded early diagnosis)
- Hypertrophic gastropathy (uncommon)

Neoplasia

Most Common Causes of Chronic Vomiting in Cats

Dietary problem
- Food adverse reaction (dietary sensitivity), up to 25% of cases

IBD
Hyperthyroidism
Liver disease
Renal disease
GI lymphoma (intestinal is more common)
Chronic pancreatitis
Heartworm disease

Intermittent Chronic Vomiting

Chronic intermittent vomiting is a common presenting complaint in veterinary medicine. Often there is no specific time relation to eating, the content of the vomitus varies, and the occurrence of vomiting may be very cyclic in nature. Depending on the disorder, other signs such as diarrhea, lethargy, inappetence, and salivation (nausea) may occur as well. When presented with this pattern of clinical signs, the clinician should strongly consider chronic gastritis, inflammatory bowel disease, irritable bowel syndrome, and gastric motility disorders as leading differential diagnoses. A detailed work-up including gastric and intestinal biopsies is often required for definitive diagnosis in these cases. It is important to note that chronic intermittent vomiting is a common clinical sign of inflammatory bowel disease in both dogs and cats.

Vomiting from systemic or metabolic causes may be an acute or chronic sign and generally there is no direct correlation with eating and no predictable vomitus content.

Diagnostic Plan

If reasonable concern is established based on the history (e.g., patient is inappetent, ingested a toxin, is vomiting frequently) or physical assessment (e.g., patient is listless, dehydrated, in pain), then a minimum data base of **CBC**, **complete biochemical profile** (or specific tests for evaluation of liver, kidney, pancreas, electrolytes), complete **urinalysis** (pre-treatment urine specific gravity extremely important for diagnosis of renal failure), and **fecal examination** is essential. The best way to screen for GI parasites on a single fecal sample is to run *both* a centrifugal flotation test and a *Giardia* antigen test. If only a single zinc sulfate centrifugal flotation is run, 25-30% of *Giardia* cases will be missed. **T4 and both a heartworm antibody test and heartworm antigen test** are considered routine baseline tests for vomiting cats (approximately 40% of cats with adult heartworms will have vomiting as a clinical manifestation of the disease). **Survey abdominal radiographs** are indicated if thorough abdominal palpation is not possible or suggests an abnormality (e.g., foreign body, pancreatitis, pyometra). Some institutions now routinely order 3 view abdomen films on patients presented for vomiting (both laterals and a VD). Unfortunately these tests are often not done early enough. Even if baseline results are unremarkable they are more than justified because they help to rule out serious problems at the outset (e.g., vomiting due to renal failure, diabetes mellitus, liver disease). Alternatively, any abnormalities provide direction for initial treatment and further diagnostics.

The decision for performing more in-depth diagnostic tests is based on ongoing clinical signs, response to therapy, and initial test results. These tests include **baseline cortisol** or **ACTH stimulation** to confirm hypoadrenocorticism in a patient with an abnormal Na:K ratio or to investigate for this disorder if electrolytes are normal, **complete barium series** or **BIPS study** (for gastric or intestinal foreign body, gastric hypomotility, gastric outflow obstruction, partial or complete intestinal obstruction), **cPLI* or fPLI***(canine and feline lipase immunoreactivity, respectively, for diagnosis of pancreatitis in dogs and cats), and **serum bile acids assay** (to assess for significant hepatic disease). **Barium swallow with fluoroscopy** is often necessary for diagnosis of hiatal hernia disorders and gastroesophageal reflux disease. **Serum gastrin levels** are run if a gastrinoma (Zollinger-Ellison Syndrome) is suspected.

Pancreatitis: Pancreatitis continues to be a challenging disorder to accurately diagnose, short of thorough direct examination and biopsy. Assays for amylase and lipase are of very limited value, especially in cats. In general, the following can be stated regarding the various diagnostic tests for pancreatitis:

Value of the Various Diagnostic Tests for Pancreatitis

Amylase/Lipase (sensitivity on lipase depends on which specific test is being done)
- of value as a screening test in dogs only
- need to be 3x or > above normal reference range in order to suggest pancreatitis
- normal does *not* rule-out pancreatitis
- ****new lipase assay from Antech (2 DGGR) approximates sensitivity of PLI for diagnosis of pancreatitis**
- Antech has discontinued the somewhat less sensitive 1,2-diglyceride assay as of October 4, 2015. The new assay is 2 DGGR and is on every biochemical profile for dogs and cats (where lipase is normally included)

Abdominal Ultrasound
- highly specific, but not very sensitive, especially in cats

Serum PLI
- highly sensitive for pancreatitis

Pancreatic Lipase Immunoreactivity (cPLI and fPLI)
- Exocrine Pancreatic Insufficiency (EPI)
  - cPLI is reliably significantly decreased
  - cPLI is specific for EPI
- Chronic Renal Failure
  - Increased, but usually still within reference range
- Dogs with Biopsy Proven Pancreatitis
  - cPLI sensitivity is > 80%
  - currently recommended cutoff value for *dogs* is >200 ug/L
  - results are also promising for cats

Negative contrast gastrography.
An excellent technique to quickly evaluate the stomach for presence of a nonradiopaque foreign body.
Technique:
Gastric tube, tranquilize as needed
(definitely tranq cats)
Dogs: 8-10 ml/lb air or stop if the animal shows discomfort
Cats: 5 ml/lb air
Remove tube, take rads immediately
(left lateral, VD first)
Can also use 60 ml carbonated beverage (e.g., Mountain Dew)

BIPS are barium impregnated polyethylene spheres. Traditionally, veterinarians have relied on barium liquid as the contrast agent of choice for gastrointestinal studies. However, recognized limitations of barium liquid have led to the development of barium-

impregnated solid radiopaque markers for the diagnosis of motility disorders and bowel obstructions. Barium liquid contrast studies are of limited value in detecting hypomotility. Radiopaque markers can be used to investigate a number of common gastroenteric problems. These spheres have been specifically validated for use in dogs and cats and are the only radiopaque markers with which there is extensive clinical experience in veterinary medicine. BIPS are manufactured in New Zealand and are now available in many countries. Information on availability of this product, including instructions on use and interpretation of radiographic studies, can be found at (www.medid.com; 800-262-2399).

Ultrasonography can be useful in the diagnostic work-up of a number of disorders that can cause vomiting. Among the problems that may be detected with ultrasonography are certain disorders of the liver (e.g., inflammatory disease, abscessation, cirrhosis, neoplasia, vascular problems), gall bladder (cholecystitis, choleliths, gallbladder mucocele), GI foreign bodies, intestinal and gastric wall thickening, intestinal masses, intussusception, kidney disorders, and others. Needle aspirations and/or biopsies can be done at many sites under ultrasound guidance.

One of the most reliable and cost efficient diagnostic tools currently available for evaluation of vomiting is **flexible GI endoscopy**. Endoscopy allows for direct gastric and duodenal examination, mucosal biopsy from these areas, and in many cases gastric foreign body retrieval. Endoscopy is considerably more reliable than barium series for diagnosis of gastric erosions, chronic gastritis, gastric neoplasia, and inflammatory bowel disease (a common cause of chronic intermittent vomiting in dogs and cats). It is stressed that biopsy samples should always be obtained from stomach and whenever possible small intestine regardless of gross mucosal appearance. Normal gastric biopsies may support gastric motility abnormalities, psychogenic vomiting, irritable bowel syndrome, or may be noncontributory (i.e., look elsewhere for diagnosis). Many dogs with vomiting due to inflammatory bowel disease have no abnormalities on gastric examination or biopsy. If only gastric biopsies are obtained, the diagnosis may be missed.

Abdominal exploratory is indicated for a variety of problems including foreign body removal, intussusception, gastric mucosal hypertrophy syndromes, procurement of biopsies, and for resection of neoplasia.

***fPLI** is available at Texas A&M University. Serum samples can either be sent directly to the GI Laboratory at Texas A&M University, or they can be forwarded to Texas A&M by a commercial laboratory.

The address is:
GI Lab at Texas A&M University
College of Veterinary Medicine
TAMU 4474
College Station, TX 77843-4474
979-862-2861
www.cvm.tamu.edu/gilab

Diagnosis of Vomiting

Stage 1—Baseline Assessment

- History and physical examination
- Conservative vs. more aggressive diagnostic plan based on patient's condition and clinician's concern

Conservative Approach

Fecal examination[a]
Selected diagnostics
Specific/symptomatic therapy

Serious or Systemic Clinical Signs

Complete blood count
Complete biochemical profile
Urinalysis
Fecal examination[a]
Parvovirus test if indicated
Survey abdominal radiographs (3 views)
T4 (cats)
Heartworm antibody and antigen test (cats)
Appropriate specific/supportive therapy

Stage 2—Further assessment (if vomiting persists or initial tests indicate further investigation should be performed promptly):

- **Special Blood Tests**
  - —Corticotropin baseline or ACTH stimulation
  - —cPLI or fPLI (pancreatitis)
  - —Leptospirosis serology and/or lepto PCR
  - —Bile acids assay (to asses liver function)
  - —Coagulation tests (consider in patients with hematemesis/melena)

- **Contrast Radiography**
  - —Barium contrast
  - —Air contrast gastrogram (to further assess for gastric foreign body)
  - —BIPS (barium-impregnated polyethylene spheres; with food to assess GI motility)

- **Ultrasonography**
  - —Evidence of GI or non-GI disease
  - —Aspirates or biopsy
  - —Abdominocentesis

- **Nuclear Scintigraphy**
  - —Transcolonic portal angiography for detection of portosystemic anomaly
  - —GI motility study

Stage 3—Invasive Procedures

- **Flexible GI endoscopy**[b] (minimally invasive)
  - —Examination, biopsy, foreign body retrieval
- **Laparoscopy**
  - —Biopsies (e.g., liver, pancreas)
  - —Aspirates (e.g., gall bladder, lymph nodes, mass lesion)
  - —Intestinal biopsy
- **Surgical intervention**
  - — Therapeutic or exploratory with multiple biopsies

[a]GI parasites, including *Giardia*, should always be considered in dogs with acute or intermittent vomiting. Best baseline testing on a single fecal sample includes centrifugal flotation and *Giardia* antigen test.

[b]Endoscopy is a diagnostic or therapeutic tool that can be used in Stage 1, Stage 2, or Stage 3, depending on the clinical situation.

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Drug Therapy for Vomiting in Dogs and Cats

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Pharmacologic Control of Acute Vomiting

Initial nonspecific management of vomiting includes NPO (in minor cases a 4-12 hour period of nothing per os may be all that is required), fluid support, and antiemetics. Initial feeding includes small portions of a low fat, single source protein diet starting 6-12 hours after vomiting has ceased. Drugs used to control vomiting will be discussed here.

The most effective antiemetics are those that act at both the vomiting center and the chemoreceptor trigger zone. Vomiting is a protective reflex and when it occurs only occasionally treatment is not generally required. However, patients that continue to vomit should be given antiemetics to help reduce fluid loss, pain and discomfort.

For many years I strongly favored **chlorpromazine (Thorazine),** a phenothiazine drug, as the first choice for pharmacologic control of vomiting in most cases. The HT-3 receptor antagonists **ondansetron (Zofran)** and **dolasetron (Anzemet)** have also been effective antiemetic drugs for a variety of causes of vomiting. **Metoclopramide (Reglan)** is a reasonably good central antiemetic drug for dogs but not for cats. **Maropitant (Cerenia)** is a superior broad spectrum antiemetic drug and is now recognized as an excellent first choice for control of vomiting in dogs and cats. In addition to antiemetic effect, maropitant also provides visceral analgesic effect. Maropitant is also the first choice for prevention of motion sickness vomiting in both dogs and cats.

Metoclopramide (Reglan) is a gastric prokinetic drug that also has central antiemetic effect. Metoclopramide increases gastric and proximal small intestinal motility and emptying without causing acid secretion, decreases enterogastric reflux, and provides inhibition of the chemoreceptor trigger zone. The central antiemetic effect is mediated through antagonism of dopaminergic D2 receptors in the chemoreceptor trigger zone of the medulla to inhibit vomiting induced by drugs, toxins, metabolic disease, and acid-base imbalances. Metoclopramide is a less effective central antiemetic drug in cats than in dogs because serotonin receptors, rather than dopaminergic receptors, predominate in the CTZ of cats. For vomiting in cats, I generally usually use metoclopramide only if a prokinetic effect is desired. Chlorpromazine, dolasetron, ondansetron, or maropitant should be used as a first or second choice to control acute frequent vomiting in cats. Parvovirus can cause gastric hypomotility and therefore the promotility effects of metoclopramide may prove beneficial. However, maropitant, dolasetron, or ondansetron are more effective drugs than metoclopramide for managing vomiting caused by parvovirus. Further, maropitant also helps provide visceral analgesia and is the best single drug choice in parvo cases.

The recommended injectable dose of metoclopramide is 0.2 to 0.5 mg/kg IM or SC given TID to QID as needed. Metoclopramide can also be given IV as a constant rate infusion (1 - 2 mg/kg over 24 hours). Metoclopramide should not be used if gastric outlet obstruction or GI perforation is suspected, or in patients with a seizure disorder.

Metoclopramide - Clinical Applications for Chronic Vomiting

Several clinical applications for use of metoclopramide in dogs with chronic vomiting have been identified. These include gastric motility disorders, gastroesophageal reflux disease (GERD), primary or adjunctive therapy for antral and pyloric mucosal hypertrophy, and as treatment for nausea and vomiting caused by various other disorders. While cisapride is a superior prokinetic drug, metoclopramide is an effective drug and is often the first choice for prokinetic effect, with cisapride used as a second choice if metoclopramide is not effective. Other drugs that are sometimes used for prokinesis are low dose erythromycin and the H2-receptor blocker ranitidine (Zantac).

Gastric motility disorders have been recognized with increased frequency in veterinary medicine, but are still overlooked. Gastric stasis, characterized by abdominal discomfort, periodic bloating, borborhygmus, nausea and vomiting may be associated with a number of clinical states that include inflammatory disorders (e.g., chronic gastritis, IBD), gastric ulcers, gastroesophageal reflux, infiltrative lesions (e.g., neoplasia), and chronic gastric dilatation. Metabolic disturbances that may cause gastric stasis include hypokalemia, hypercalcemia, acidosis, anemia, and hepatic encephalopathy. Short-term continued vomiting that is observed in some cases after apparent recovery from viral enteritis may be due to abnormal gastric motility. Transient (3 to 14 days) gastric hypomotility may also occur after gastric or abdominal surgery. Motility disorders with no organic cause may be best classified as idiopathic. For any of the disorders listed, the primary cause should be treated, and metoclopramide may be a valuable short-term adjunct to therapy in these cases, along with feeding low fat foods in divided amounts. Metoclopramide alternatively may be used as the primary treatment on a long-term basis for idiopathic hypomotility disorders. Metoclopramide has also been useful in treatment of dogs that have chronic vomiting characterized by episodes occurring routinely in the early morning and containing bilious fluid.

In general, patients less than 4.5 kg (10 lb) receive 2.5 mg per dose), 4.5 to 18 kg (11-40 lb) 5 mg per dose, and greater than 18 kg (40 lb) 10 mg per dose. Metoclopramide is given 30 to 45 minutes before meals and again at bedtime. Animals that require chronic medication may need only 1 to 2 doses daily. Because of its short half-life, the drug is not effective when given by intravenous or intramuscular bolus injection for purposes other than when only one treatment would be administered (i.e., to aid in evacuating the stomach if an anesthetic procedure in a non-fasted patient becomes necessary, pre-radiologic contrast study). Subcutaneous administration into fat may be of benefit when oral therapy is contraindicated and an intravenous line is not available.

Metoclopramide is less effective as a promotility drug than cisapride (see later discussion). While many animals with gastric hypomotility respond well to metoclopramide, some have a less than desired response. If a patient with a suspected gastric hypomotility disorder has an inadequate response to metoclopramide, cisapride should be tried next.

Side Effects

Some adverse effects may occur if metoclopramide is given in the usual therapeutic doses. Clients should be apprised of these before the medication is prescribed. These effects are uncommon in animals, and somewhat more common in humans.

Motor restlessness and hyperactivity may occur; and when observed, these signs usually begin 20 to 30 minutes after a dose and last 4 to 5 hours. The reaction can range from mild

to quite dramatic. Alternatively, drowsiness and depression occasionally occur. Side effects are infrequent in cats, but clients have reported disorientation, frenzied behavior, and hiding tendencies associated with the medication. Hospitalized animals may chew excessively at catheter sites or be more aggressive toward hospital staff. Sometimes these effects are subtle and nursing staff need to be observant. These side effects are reversible (diphenhydramine [Benadryl 2.2 mg/kg IV] or discontinuing the drug) but generally do not subside when lower doses are given. Unless side effects are infrequent, the use of metoclopramide should be discontinued if adverse reactions are seen. Cisapride does NOT cause these same type of adverse reactions. Metoclopramide crosses the blood brain barrier, cisapride does not.

In general, metoclopramide should not be given to epileptic patients. Other contraindications include evidence of significant mechanical obstruction, simultaneous use of anticholinergic agents (antagonism of metoclopramide's effects), and pheochromocytoma.

Ondansetron - Clinical Applications for Acute Vomiting

Ondansetron (Zofran) is a potent antiemetic drug that has proven to be effective in both humans and animals for control of severe vomiting. It has been used in human cancer patients undergoing cisplatin therapy, a drug that frequently causes nausea and severe vomiting, with very good results. Ondansetron acts as a selective antagonist of serotonin S3 receptors (a principal mediator of the emetic reflex). S3 receptors are found primarily in the CTZ, on vagal nerve terminals, and in the gut in enteric neurons. The principal site of action of ondansetron is in the area postrema, but it also has some peripheral gastric prokinetic activity.

In my experience, ondansetron has produced very good results in either controlling or at least significantly decreasing the frequency of vomiting in dogs and cats with frequent or severe vomiting, including in dogs with severe parvovirus enteritis, in pancreatitis patients, and cats with hepatic lipidosis. The recommended dose is 0.5 to 1 mg/kg IV given as a slow push every 6 to 12 hours (based on patient response). Frequently dogs that appear quite distressed due to nausea and vomiting look much more relaxed and comfortable within 15 minutes of receiving ondansetron. There are no reports of any significant side effects such as diarrhea, sedation, or extrapyramidal signs in human and animal trials. While Zofran was quite expensive for many years, it came off patent in 2007 and is now more affordable for use at any small animal hospital. *Currently, however, my top antiemetic drug of choice is maropitant (Cerenia), because it is a highly effective antiemetic drug but also because it provides visceral analgesic effects as well.* Animals with significant liver disease may be best managed with ondansetron or dolasetron, as maropitant should be used with caution in animals with significant hepatic dysfunction (although it is not contraindicated – some clinicians have used maropitant successfully and safely in animals with liver disease).

Dolasetron

Dolasetron (Anzemet) is also a 5-HT3 receptor antagonist antiemetic drug, with action similar to ondansetron. It is a slightly less expensive alternative to ondansetron and only needs to be administered once daily. Indications are the same as for ondansetron, namely, for control of frequent vomiting that is poorly responsive to lesser expensive front-line antiemetic drugs. The dose is 0.5-1 mg/kg IV once daily. Dolasetron is generally well tolerated in animals.

A NEWER ANTIEMETIC DRUG FOR DOGS

Most drugs used to control vomiting in animals have been developed for use in humans. There has been a need for a broad-spectrum antiemetic drug for use in animals that is effective in a variety of situations, has a rapid onset of action, is safe and affordable, and is available in both injectable and oral preparations. **Maropitant citrate (Cerenia)** is a newer broad-spectrum antiemetic drug that is indicated for the treatment of acute vomiting in dogs. Maropitant is a neurokinin receptor antagonist that blocks the pharmacologic action of the neuropeptide substance P in the central nervous system. Substance P is found in significant concentrations in the nuclei comprising the emetic center and is considered a key neurotransmitter involved in emesis. By inhibiting the binding of substance P within the emetic center, maropitant provides broad-spectrum effectiveness against both neural and humoral causes of vomiting.

Clinical trials and recent clinical experience, since August 2007 when the drug was released for use in the U.S., have shown maropitant to be very effective for control of a variety of causes of acute vomiting in dogs. It is administered as a once-daily injection (0.45 mg/lb [1 mg/kg] SC for dogs), which is a significant advantage over many other antiemetic drugs, and has a rapid onset of action. Maropitant is also available in tablet form for outpatient use, which makes it a very attractive choice for use in small animal practice. It is the drug of choice for dogs with motion sickness.

CAUTION: We generally advise that Cerenia be used at a reduced dose (50%) for animals with significant hepatic dysfunction, OR select an alternative antiemetic for animals with liver disease – e.g., ondansetron or dolasetron.

The issue of stinging on injection: Information from clinical experience and studies indicates that there is less likelihood for stinging to occur with maropitant injections when the product is kept refrigerated. The current guidance is that the solution should be kept refrigerated and drawn up and injected right away at refrigerated temp. In practice a sting can still be expected in some patients even when the product is kept refrigerated.

CATS: Studies have now been done using maropitant in cats and some clinicians in general practice have been using it since 2008. In May 2012 Cerenia was approved for use in cats and also in puppies as young as 8 weeks of age.

Recommended dose of maropitant for cats:
Injectable: 0.5-1 mg/kg SC or IV (give SLOWLY over 60-90 seconds if administering IV)
Oral: (1 to 2 mg/kg). This is the starting dose recommended for prevention of motion sickness in cats as well; i.e., somewhat lower than the canine dose for motion sickness.

Note: On January 14, 2016, Zoetis announced a new label claim for IV use of Cerenia. In two separate bioequivalence studies conducted in 2015 by Zoetis in dogs and cats, when delivered intravenously, CERENIA reached concentration and absorption levels as quickly as with subcutaneous injection. Additionally, two separate safety studies in dogs and cats indicated no related effects on survival or clinical findings, and there were no reports of pain on intravenous injection.

Consider Using Cerenia More Routinely Administered PRE-Operatively

Some practices have now instituted the practice of including an injection of Cerenia administered routinely in the pre-operative period. I am a strong proponent. Reasons for doing this include:

- Help prevent post-op vomiting and nausea and decrease chances of aspiration
- Adjunctive visceral analgesia
- Improved patient comfort in the post-op period
- Earlier return to eating, with improved appetite and volume of food consumption

In this setting, Cerenia can be administered anytime in the pre-op period. If morphine or hydromorphone are going to be given as part of the pre-anesthesia sedation and preemptive analgesia plan, and the clinician desires to *prevent* vomiting secondary to these emetogenic drugs, Cerenia is administered 45 minutes prior to the emetogenic drugs. In one study when Cerenia was administered 45 minutes prior to morphine at 0.5 mg/kg, 0/15 dogs vomited, while 15/16 dogs who received saline instead of Cerenia vomited at least once (and 4 of the dogs vomited 4 times). We have seen excellent post anesthesia recovery periods in dogs that have undergone a variety of procedures, including OVH/neuter as well as prolonged anesthesia for dental procedures, major abdominal procedures, etc. We are also using Cerenia more routinely prior to performing endoscopic procedures.

The uniform response is that most patients recover more smoothly, more quietly and are presumably more comfortable overall. Clients of course are very happy when their pet eats earlier than would be otherwise expected. This has represented a gratifying advance in patient care in many ways - - helping our patients be more comfortable is always good.

How long can Cerenia be used on a consecutive days schedule?

The original label guidance stated that Cerenia should not be given for more than 5 consecutive days (injectable or oral at the anti-emesis dose) and for 2 days at the motion sickness prevention dose. However, experience has shown that in some patients Cerenia has been used safely and effectively on a longer term basis (anecdotal reports, e.g., patients with neoplasia or renal disease that were experiencing ongoing nausea, vomiting, and inappetence). Many of these patients have a much better quality of life while on Cerenia, as they have less nausea and vomiting and a much better appetite. There are cats that have been treated with a daily oral dose for months to several years. Use of Cerenia in this fashion is being investigated further.

Further, in 2015 the label was changed, based on studies that evaluated the effect of maropitant when given at various doses for longer periods of time. Cerenia has a high safety profile and a longer duration of use, based on each patient's individual needs, is now well accepted.

A study was presented at the Veterinary Cancer Society (VCS) meeting in San Diego Oct. 29-November 1, 2010, and then subsequently at the ACVIM Forum in Denver in June 2011: **Pharmacokinetics of maropitant citrate dosed orally to dogs at 2 mg/kg and 8 mg/kg once daily for 14 consecutive days.** Two groups of eight healthy beagle dogs were administered maropitant citrate at 2 or 8 mg/kg orally once daily for 14 days. Concentrations of maropitant and its metabolite were measured in plasma using a LC-MS/MS assay.

Pharmacokinetic parameters were estimated using non-compartmental pharmacokinetic techniques and a modeling approach was used to estimate steady-state.

Results: The model estimate for the number of doses required to reach 90% of steady-state was 4.30 for 2 mg/kg and 8.09 for 8 mg/kg. Four dogs experienced a single dose of vomiting.

Conclusions: Dosing maropitant citrate beyond the original label duration of 5 days was well tolerated by healthy dogs. During the 14 days of dosing there was accumulation, however, steady-state was reached after approximately 4 doses for daily 2 mg/kg dosing and 8 doses for daily 8 mg/kg oral dosing.

Use of Oral Maropitant (Cerenia)

- ❑ Confident there is no GI foreign body (i.e., do not use ongoing antiemetic therapy if there could be a foreign body ledged in the GI tract)
- ❑ Prevent vomiting during cyclosporine, azithromycin, or other drug induction period (use for 3-5 days in conjunction with the start of a drug that might cause vomiting)
- ❑ Vomiting flare-ups in IBD patients (or other chronic disorders)
- ❑ Pancreatitis, parvovirus, etc for a few days after vomiting is fairly well controlled with injectable maropitant. Excellent control of nausea may help improve appetite and earlier food intake
- ❑ Prevention of vomiting in chemotherapy patients
- ❑ Prevention of motion ("car") sickness
- ❑ Renal disease patients – and perhaps chronic use (these patients may benefit tremendously and we have observed many patients that eat better, do not vomit or exhibit nausea, and feel better overall. Studies are ongoing).

Cisapride

Cisapride is a potent GI prokinetic drug and is superior in action to metoclopramide. It is no longer on the market for use in humans, as of 2000, because of an association with fatal arrhythmias. There are no reports of similar complications existing in dogs and cats, however, and cisapride continues to be readily available to veterinarians through compounding pharmacies.

Cisapride has broader promotility effects than metoclopramide (e.g., cisapride has demonstrated excellent efficacy in management of colonic inertia and small intestinal ileus). In contrast to metoclopramide, which has central effect at the CRTZ in addition to its peripheral effects, cisapride has no known direct antiemetic properties. Another contrast is that metoclopramide's prokinetic effect is most significantly on the stomach. It is NOT a reasonable choice for treatment of small intestinal ileus.

The most relevant uses of cisapride in animal patients include treatment of gastroparesis, especially in patients that experience significant side effects from metoclopramide (e.g., hyperactivity and other dystonic reactions) or where metoclopramide is not sufficiently effective, idiopathic constipation, gastroesophageal reflux disease (if H2-receptor antagonists or proton pump inhibitors and dietary management alone are not effective), and postoperative ileus.

Cisapride is extremely well tolerated by animal patients. I have used cisapride in dogs and cats that have experienced neurologic side effects from metoclopramide. I have observed no adverse reactions to cisapride in any of these patients, even in those whose side effects to metoclopramide included very bizarre behavior changes. The suggested dose of cisapride is similar to what has been recommended for metoclopramide (see earlier discussion).

INFLAMMATORY BOWEL DISEASE (IBD) IN DOGS – DIAGNOSIS AND THERAPY

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Introduction

Inflammatory bowel disease (IBD) is not a specific diagnosis, rather it is a histological description of a syndrome resulting from a host hypersensitivity response to antigenic stimuli. In IBD there is an increase in the inflammatory cell population in the intestinal mucosa. The predominant inflammatory component can be lymphocytic-plasmacytic (most common type), eosinophilic, neutrophilic, or granulomatous. Primary causes of intestinal inflammation that should be considered include parasites, bacteria (specific agents or bacterial overgrowth), fungal disorders (e.g., *Histoplasma,* pythiosis), immune-mediated diseases, and food sensitivities. Many cases of IBD are likely idiopathic in nature. A presumptive diagnosis of IBD is made on the basis of history, physical exam and elimination of other disorders by laboratory tests and other studies such as radiography and ultrasonography. A definitive diagnosis can be made only by intestinal biopsy.

Clinical Course

The clinical course of inflammatory bowel disease can be characterized by diarrhea only, vomiting only, or both vomiting and diarrhea. Associated clinical signs that may also be seen, either singly or in combination, include weight loss, listlessness, borborygmus, flatulence, and abdominal pain. In some patients, inappetance may be the only sign, although this is more common in cats than dogs.

Inflammatory bowel disease is a *common* cause of chronic vomiting in dogs. Vomiting may be reported as a problem of recent onset or it can be an intermittent problem occurring over a period of several months or years before it becomes more frequent and severe. It is important for the clinician to recognize that vomiting may be the only major sign that occurs in a patient with inflammatory bowel disease. Gastric hypomotility can occur secondary to an infiltrative bowel disease such as IBD.

In some dogs with IBD, chronic intermittent or chronic intractable diarrhea is the major clinical sign. In these cases, the clinician must determine if the diarrhea is resulting primarily from small bowel or large bowel involvement, or is a mixed component of both large and small bowel.

Although inflammatory bowel disease is not breed specific, the Sharpei breed requires special consideration because they can develop a severe type of IBD. Most Sharpei dogs with IBD will present with a ravenous appetite, chronic diarrhea and weight loss. They often have intestinal dysbiosis (bacterial overgrowth) and other intestinal problems as well. Sharpeis with diarrhea, even for short durations of 3 to 4 weeks, due to IBD seem to be at increased risk of developing hypoproteinemia.

Early clinical investigation in these patients should always include a complete blood count and complete biochemical profile.

If clinical investigation of a patient with chronic vomiting and/or diarrhea shows decreased albumin and globulin levels (panhypoproteinemia), IBD of a moderate to severe degree should be one of the leading differentials. Lymphangiectasia, intestinal lymphoma, histoplasmosis, and pythiosis should also be considered. There is a regional geographic distribution with the latter two conditions. IBD is by far the most common cause of protein losing enteropathy in dogs. The presence of panhypoproteinemia indicates that the degree of disease is significant and likely chronic in nature. Many dogs with IBD will not develop hypoproteinemia, but for those that do, hypoproteinemia heralds severity and indicates that the disease is advancing. Steps to establish a definitive diagnosis should be expedited and an aggressive treatment regimen will likely be necessary.

Diagnosis

A presumptive diagnosis of canine inflammatory bowel disease is made on the basis of history, physical examination and the elimination of other disorders through laboratory tests and radiographic studies. The most important diagnostic procedure for a definitive diagnosis of IBD, however, is biopsy.

Baseline laboratory tests in dogs with chronic vomiting or diarrhea should always include a *complete blood count*, *biochemical profile*, *urinalysis* (as a means of assessing renal function and to evaluate for proteinuria), and *fecal examination for parasites*. Baseline tests are frequently normal or negative, but abnormalities that may be identified include mild nonregenerative anemia (anemia of chronic inflammatory disease); leukocytosis (20,000 to 50,000 cells/ul) without a left shift (suggests active chronic inflammatory disease); eosinophilia (mild to dramatic increase) in some dogs with eosinophilic enteritis; and hypoproteinemia. Any abnormalities of liver enzymes should also be noted.

Testing for parasites in dogs with diarrhea is best accomplished using zinc sulfate flotation with centrifugation. This is an excellent test medium for detection of nematode parasites as well as *Giardia*. *Zinc sulfate flotation with centrifugation* is superior to flotation with sodium nitrate, or flotation with zinc sulfate without centrifugation. Testing for *Giardia*-specific antigen in feces is also an excellent means of diagnosing giardiasis. In fact, *Giardia* antigen testing is very sensitive and can identify infections that may be missed on one or two zinc sulfate centrifugation tests with centrifugation or where there is incorrect interpretation of the identity of cyst structures (a common error in clinical practice). A fecal assay for *Clostridium perfringens* enterotoxin should also be done.

Although exocrine pancreatic insufficiency (EPI) is uncommon in dogs, it is always a good idea to do a *trypsin like immunoreactivity (TLI)* test on dogs with chronic diarrhea to definitively rule out (EPI). *Serum cobalamin (B12) and folate assays* may be useful in evaluating dogs with chronic diarrhea, especially for intestinal dysbiosis

(formerly referred to as intestinal bacterial overgrowth) and clinical hypocobalaminemia. Subnormal serum cobalamin concentrations may occur in association with small intestinal disease, EPI, dysbiosis, and inherited selective defects in cobalamin absorption. Serum folate concentrations may be increased in dogs with dysbiosis and decreased with infiltrative small bowel diseases.

A definitive diagnosis can be made only by biopsy, the single most important diagnostic procedure in the evaluation of chronic intestinal disease. Biopsy should be done to confirm diagnosis and determine type and extent of involvement. It is especially useful in determining treatment and prognosis. Endoscopic and surgical biopsies are discussed in a subsequent section.

Diagnostic Imaging of the Intestinal Tract
(Diagnostic Imaging section contributed by Dr. David S. Biller, DACVR, Kansas State University)

Normal Radiographic Anatomy of the Small Intestine
The small intestine should be evaluated for margination (serosal surface definition). The margin should be smooth. It will normally be visible due to fat in the serosa except when the animal is young (< 6 months) or emaciated or if abdominal fluid or cellular infiltrates are present. The normal diameter of the small intestine in dogs is < 2–3 rib widths, or less than the dorsoventral dimension of the second lumbar vertebral body.

The small bowel should be evenly distributed throughout the abdomen, occupying space not taken up by other organs. As organomegaly occurs, whether normal (distended stomach or urinary bladder) or abnormal (e.g., mesenteric lymphadenopathy, pancreatic enlargement, splenic mass), the intestine will be displaced. The direction helps to determine the differentials for the mass causing the displacement. In obese cats, it is common for the intestines to be localized in the ventral abdomen to the right of midline. The small bowel should have a smooth, continuous, curved appearance.

It is often necessary to have contrast studies (upper GI series) to identify normal or abnormal shape or diameter of small bowel. The radiopacity of the bowel loop is dependent on whether it is fluid-filled, gas-filled, or filled with a combination of fluid and gas. Fluid-filled loops of bowel appear as white rope-like structures. Gas-filled loops appear as black, thin-walled tubes. A small amount of gas above fluid appears as a narrow, radiolucent band with an apparent thickening of the bowel wall. A larger volume of gas reflects wall thickness more accurately and therefore bowel wall thickness should never be evaluated on survey films but only with use of contrast (whether negative or positive).

In dogs, barium should enter the duodenum in 13–20 minutes, the jejunum in 30 minutes, the jejunum and ileum in 60 minutes, and the ileocolic junction in 90–120 minutes. Barium should clear the upper GI tract and enter the ileum and colon in 3–5

hours.

The appearance of the mucosa or wall of the small bowel is best evaluated using positive contrast material. The mucosa should appear as a smooth, even surface or as a finely fimbriated edge. This fimbriation is due to barium dissecting between groups of aggregated villi. In normal young dogs, the mesenteric border of the duodenum has numerous or single, usually square or conical depressions, in the bowel overlying lymphoid follicles. These are pseudoulcers and considered normal. They are not seen in cats.

Abnormal Anatomy of the Small Intestine on Survey Radiographs
Ileus is an obstructive condition of the intestine and is either mechanical or functional. Mechanical ileus is also referred to as "dynamic" (or obstructive) ileus. It is usually simple and nonstrangulating. The radiographic signs may be influenced by the degree, location, and duration of obstruction. Dilatation of small intestine secondary to mechanical obstruction results from swallowed air and saliva and accumulation of mucosal secretions in the digestive tract.

Functional ileus, also referred to as paralytic or adynamic ileus, can be localized or generalized and may be a sequelae to mechanical ileus. The stages of development of functional ileus include muscle fatigue allowing stretching of the intestine, muscle ischemia secondary to stretching, and muscle necrosis. Functional ileus has numerous causes, such as extrinsic (which tend to be more generalized) that include spinal cord injury, reflex to pain, peritoneal trauma or irritation, or vascular compromise, and intrinsic (which is most often regional). Intrinsic causes include edema, amyloidosis, and acute inflammation or enteritis.

Survey radiographs of inflammatory bowel disease are usually normal or luminal fluid maybe increased.

Abnormal Anatomy of the Intestinal Tract on Contrast Radiographs
Intraluminal disorders usually appear as radiolucent areas surrounded by positive contrast medium. They often delay intestinal transit time and cause ileus proximal to their location. Intramural disorders should be evaluated with an upper GI series (positive contrast/barium).

The following questions should be answered while evaluating the upper GI series:

1. whether the lesion projects into the lumen, causes a narrowing or constriction;
2. whether the lesion projects away from the lumen, causing an enlargement of the diameter of the lumen as a result of a defect in the bowel wall;
3. whether thickening and rigidity of the bowel wall, irregularity at the serosal or mucosal surfaces, or a combination of these changes has occurred.

Radiographically, intramural disorders of the bowel may appear pedunculated, broad-based, smooth or irregular, and may expand the width of the bowel. Benign tumors tend to be smooth; malignant tumors tend to be irregular. The causes of

intramural lesions include neoplasia, granuloma, abscess, scar, and hematoma. Inflammatory diseases of the small intestine (enteritis) tend to increase the rate of intestinal motility (i.e., reduced transit time). Chronicity and severe enteritis may cause irregularity of the mucosal surface; chronic enteritis may also decrease the width of the bowel lumen. Chronic and very severe enteritis can cause alterations or erosion of the mucosa.

Barium studies of patients with severe/chronic inflammatory bowel disease may be characterized by the appearance of thumbprinting. Thumbprinting is described as irregularly arranged mural based indentations into the contrast column.

Ultrasonography of the Normal Gastrointestinal Tract

Until recently, ultrasonography was considered to be a poor choice for evaluation of the GI tract because of the ultrasonographic barrier caused by luminal gas. Over the past 5 years, however, it has been applied successfully in diagnosis of a number of GI disorders, including gastric and intestinal foreign bodies, intussusception, uremic gastropathy, chronic pyloric hypertrophic gastropathy, enteric duplication, and GI neoplasia. It has proven useful not only in the diagnosis of morphologic GI disease but also in the evaluation of GI function. Maximizing resolution by using a high-frequency transducer is critical in the examination of the GI tract. Fasting the animal before ultrasonography also improves the results of the examination.

Normal Wall Thickness in Dogs

Stomach	**3-6 mm**
Duodenum	**3-5 mm**
Jejunum	**2-4 mm**
Ileum	**2-4 mm**
Colon	**2-3 mm**

**Larger dogs have thicker walls.*

Ultrasonography enables differentiation of the layers of the stomach, which alternate in echogenicity. Under optimal conditions, five separate layers can be identified. They are the luminal–mucosal interface (hyperechoic), mucosa (hypoechoic), submucosa (hyperechoic), muscularis (hypoechoic), and subserosa–serosa (hyperechoic). The submucosa and subserosa–serosa are hyperechoic because of the presence of relatively more fibrous connective tissue. The mean number of peristaltic contractions in the stomach is 4–5 per minute.

The ultrasonographic appearance of the GI lumen depends on its contents. In a collapsed, state the bowel lumen appears as a hyperechoic core ("mucosal stripe") surrounded by a hypoechoic halo of bowel wall. This core represents mucus and small air bubbles trapped at the mucosal–luminal interface. When fluid is present in the bowel lumen, an anechoic area is present between the walls of the bowel that appears tubular in long-axis views and circular in short-axis views. Gas in the GI lumen causes a highly echogenic interface with reverberation artifact. The presence of fluid in the bowel lumen improves the sonographer's ability to evaluate the

mucosal and submucosal layers of the GI tract, whereas the presence of luminal gas hinders it.

As with the stomach, the layers of the intestine alternate in echogenicity. Under optimal conditions, five separate layers can be identified: the luminal–mucosal interface (hyperechoic), mucosa (hypoechoic), submucosa (hyperechoic), muscularis (hypoechoic), and subserosa–serosa (hyperechoic).

Real-time ultrasonography should be included in the examination of enteric motility. The mean number of peristaltic contractions in the intestine is 4–5 per minute. Contractions are not seen in the colon.

Ultrasonography of the Abnormal Gastrointestinal Tract
Ileus
Both mechanical and paralytic ileus have been described as ultrasonographic findings. Mechanical ileus occurs proximal to an area of obstruction; paralytic ileus can be generalized (e.g., viral enteritis, hypokalemia) or focal (e.g., duodenitis secondary to pancreatitis). When ileus is present, the bowel appears dilated and fluid-filled and GI motility is decreased or absent.

Inflammatory Disease
With inflammatory bowel disease, the intestine may be normal on ultrasound examination. The measurement of the intestinal wall thickness by ultrasound is neither specific or sensitive for diagnosing IBD. Changes, especially those of severe or chronic disease, have been reported as focal to diffuse thickening, altered echogenicity, poor intestinal wall layer definition, and mild enlargement of adjacent lymph nodes. Mucosal echogenicity may remain hypoechoic, appear hyperechoic with striations or hyperechoic with speckles and be associated with but nonspecific for IBD. Jejunal lymph node thickness of > 6 mm maybe consistent with IBD but nonspecific for the type of disease. Round, enlarged, hypoechoic LNs maybe more consistent with neoplasia, while inflammatory lymph nodes may be enlarged but tend to maintain their normal shape.
The most common finding with inflammation is extensive and symmetric wall thickening with the layering retained. In comparison, neoplasia is usually localized with greater wall thickness and loss of normal layering. These categories can overlap, and therefore cytology or histopathology is required for definitive diagnosis. Acute enteritis or inflammatory bowel disease may demonstrate corrugation of the intestine on ultrasound examination.

Intestinal Biopsy Techniques
Endoscopic Biopsy: Endoscopy is a minimally invasive procedure in which multiple biopsies can be obtained and this procedure generally has greater client compliance than with surgery because it is less invasive and less expensive than exploratory abdominal surgical procedures. Endoscopy offers a means of examining the upper and lower small intestine, stomach, and colon. It is especially advantageous because biopsies can be obtained early in the course of the disorder,

at a stage when a client will likely be reluctant to agree to an exploratory surgery for their pet. Endoscopy also offers significantly reduced risk to the patient with hypoproteinemia. The degree of intestinal changes noted on biopsy also provides useful guidelines for both type and duration of therapy that will be needed to control the specific disorder.

Clinicians need to make sure they are taking an adequate number of endoscopic biopsy samples for accurate diagnosis. Even expert endoscopists report that in some cases one-fourth to one-third of the biopsies they take from a patient will have some degree of damage to the tissue that may preclude the samples from being useful or representative. Therefore, it is recommended that clinicians take 8 to 12 biopsy samples from the upper small intestine so that the pathologist will have enough tissue to work with. Also, it is recommended that both upper and lower GI endoscopy be done in dogs with chronic diarrhea. In this way biopsies from the ileum can be obtained by passing the endoscope along the full length of the colon and through the ileocolic orifice and into the ileum. When a pediatric diameter endoscope is used this is possible in most dogs over 4 to 5 kg. If the ileum can not be entered, it may be possible to obtain at least blind biopsies of the ileum by passing the endoscopic biopsy instrument through the ileocolic orifice with the endoscope tip positioned at the ileocolic sphincter area. Colon biopsies are always obtained as well during colonoscopy in order to evaluate for inflammation in the colon.

Organ Biopsy Via Laparoscopy or Laparotomy

Organ biopsy is required to confirm canine IBD, and full-thickness samples procure tissue samples that will help the pathologist make the most accurate diagnosis. Full thickness intestinal biopsies can be accomplished by laparoscopic techniques or open abdominal surgery. Laparoscopic techniques have been well described for visceral organ biopsy. They are minimally invasive and well-suited for tissue procurement; however, laparoscopy is not yet readily available as a tool in most small animal general practice hospitals. Surgery on the other hand is an excellent way to obtain liver, pancreatic, and full thickness intestinal biopsies. In addition to biopsy, liver, pancreas and bile aspirates can be obtained for culture and cytology.

TREATMENT OF INFLAMMATORY BOWEL DISEASE

Successful treatment of canine inflammatory bowel disease depends on accurate diagnosis. The presumed pathogenesis of IBD involves antigenic stimulation and an inflammatory response mediated by the mucosal immune system. Therefore, therapy should include the suppression of the inflammatory response which requires the use of pharmacologic therapy. Removal of any antigenic source of inflammation is also necessary, and that is where dietary therapy is important. Food allergens can be a causative factor in some animals with IBD. The goal of dietary management is to reduce the antigenic stimulation of the intestinal immune system.

Drug Therapy

For patients with mild IBD, diet alone may be the only treatment needed. If, however, pharmaceutical therapy is also indicated, steroids may be used at a range of 0.5 - 1 mg/kg, divided BID for two to four weeks. The dose is then gradually decreased at two to four week intervals, and an attempt is made to achieve alternate or every third day therapy by two to three months or so. Some patients with mild IBD will respond well to metronidazole therapy, without concurrent use of corticosteroids (see below).

In moderate cases (based on biopsy changes and the patient's overall condition), the steroid dosage should be higher (1.1 to 2.2 mg/kg per day for two to four weeks before an attempt to decrease the dosage is initiated). Moderate to severe and severe IBD cases are managed initially with prednisone at 2.2 to 3.3 mg/kg per day. Combination therapy is often used for dogs with moderate to severe IBD. Combination therapy includes prednisone and metronidazole, or in dogs with severe IBD and concurrent panhypoproteinemia (with a total protein level of 4.5 g/dl or lower) prednisone, metronidazole, and azathioprine are used concurrently.

Some dogs do not tolerate corticosteroids very well. For example, Arctic breeds and Rottweillers frequently cannot tolerate very high doses for an appreciable period of time. In these breeds I generally start with conservative doses of steroids, usually no higher than 0.5 to 1 mg/kg total per day. This may still be too high for some dogs. Metronidazole is sometimes used concurrently from the outset. For patients exhibiting severe steroid hepatopathy (panting, severe PU/PD, lethargy, weakness, and sometimes a decreased appetite) steroids should be stopped completely for 36 hours to allow for adequate metabolism and clearance. Steroids can then be resumed at approximately 25 percent of the initial dose. If prednisone is still poorly tolerated at this lower level, try oral dexamethasone next (0.01 to 0.02 mg/kg per day initially).

Some larger canine breeds do not tolerate prednisone well, but will often tolerate dexamethasone at 0.25 to 0.5 mg total, one to two times per day. Very large breeds such as Great Danes and others weighing 68 kg (150 lb) or more, will sometimes do well even on as low as 0.5 mg of dexamethasone, BID when there was initial difficulty in tolerating prednisone. In some cases, steroids simply cannot be used due to severe drug reactions in the patient and other drugs must be used.

When a patient is either poorly responsive to corticosteroids when used as outlined above, or if there is poor tolerance, the next best options are to try either budesonide or cyclosporine. Cyclosporine is described further below. Budesonide is a newer corticosteroid for use in humans. Budesonide is a glucocorticoid that also represents an alternative for management of IBD in dogs, especially in severe cases that have proven to be refractory to prednisone, metronidazole, azathioprine, and dietary management; or that are intolerant of the corticosteroids discussed above. It is one of a group of novel corticosteroids that have been in development for use in humans in an attempt to make available alternative preparations that will help limit

toxicity associated with corticosteroid use. Others include fluticasone propionate, tixocortol pivalate, and beclomethasone dipropionate.

Budesonide undergoes high first pass metabolism in the liver and 90% is converted into metabolites with low corticosteroid activity. It has minimal systemic availability. The potential for typical corticosteroid side effects is significantly reduced as a result of decreased bioavailability and the resulting limited systemic exposure, which makes this a particularly attractive drug for use in humans and animals that are poorly tolerant of other corticosteroids. Budesonide also has a high receptor-binding affinity in the mucosa. It has been referred to as a "locally acting" corticosteroid.

Therapeutic results with budesonide have been promising in humans with Crohn's disease, collagenous colitis and lymphocytic colitis, ulcerative colitis, either when administered as a retention enema or in oral form, and primary biliary cirrhosis. Budesonide has been used by some veterinary clinicians in recent years to treat IBD in dogs and cats. Dose recommendations vary. In humans, a range of 6 mg to 9 mg per day has been used during initial therapy. The following general recommendations have been made for dogs. In general, budesonide is administered to small dogs at 1 mg administered once per day. Medium size dogs receive 2 mg once daily. Large dogs receive a maximum of 3 mg once daily initially. Budesonide is available as a 3 mg capsule preparation and lower dosage forms are prepared by compounding pharmacists.

Budesonide can be used in combination with other drugs. Potential adverse effects include PU/PD, when budesonide is used at the high end of the dose range, and GI ulceration. These reactions have been observed in some human patients. These problems would be more likely to occur in dogs than in cats. It appears to be very safe when used at the levels listed above.

Metronidazole has both antibacterial and anti-inflammatory effects. It is very useful in treatment of IBD in dogs. In mild to moderate cases metronidazole alone may be sufficient to help control the intestinal inflammation. When used in combination with steroids metronidazole often allows for earlier reduction of the steroid doses. The dose of metronidazole for antibacterial and anti-inflammatory effect is 11 to 22 mg/kg BID. It is sometimes administered once daily to once every other day for maintenance therapy once the patient is deemed to be well under control but not yet able to be entirely without some form of drug therapy.

Use of azathioprine is generally reserved for severe IBD cases. Azathioprine has a potent immunosuppressive effect. Although azathioprine can cause bone marrow suppression, marrow suppression is rare when azathioprine is dosed accurately. The canine dose is 2 mg/kg SID, orally. Azathioprine also has the potential to induce pancreatitis.

Azathioprine has a lag phase of 3 to 4 weeks, so it should be instituted *early* once a diagnosis of *severe* IBD is made. Azathioprine is usually used for 3 to 9 months in

dogs. Once adequate control is achieved, the daily dose is decreased by 50%, and subsequently alternate-day therapy is used. A complete blood count and platelet count should be run to monitor for evidence of anemia, leukopenia, or thrombocytopenia at 3 week intervals for the first 2 months of therapy and then once every several months.

Many canine IBD patients are thought to have intestinal bacterial overgrowth as well, and they can often be helped with the use of antibiotics. The antimicrobial drugs used most commonly include metronidazole or tylosin. In some cases cephalosporins or enrofloxacin are used (not usually the first choice, however). Combination therapy with metronidazole plus enrofloxacin or metronidazole with tylosin is used in some cases, e.g., those with longer duration of signs or where there may be more significant patient compromise. In mild cases two to four weeks of antimicrobial therapy is frequently sufficient. If crypt abscesses are reported on the histopathologic exam antimicrobial therapy is used for a longer time in conjunction with appropriate anti-inflammatory therapy.

Tylosin is a macrolide, bacteriostatic antibiotic that has activity against most gram-positive and gram-negative cocci, gram-positive rods, and *Mycoplasma.* However, the gram-negative bacteria *E. coli* and *Salmonella* spp. are intrinsically tylosin resistant. Studies (Westermarck) have revealed that administration of tylosin leads to significant but transient changes in the composition of the small intestinal flora. It may be that tylosin promotes the growth of commensal bacteria whole suppressing deleterious bacteria. In addition to antimicrobial properties tylosin may also have anti-inflammatory The term "tylosin responsive diarrhea" has been coined as a result of observations that dogs with nonspecific diarrhea will often respond to tylosin therapy. Some cases are intermittent or chronic in nature. Dose range is 7 to 20 mg/kg orally every 12 to 24 hours (administer BID initially).

Use of other drugs may be indicated in some dogs with IBD. If large intestinal inflammation is present either metronidazole or 5-amino salicylic acid derivatives (sulfasalazine, osalazine, mesalazine) or both in combination will usually control large bowel diarrhea due to colitis. Corticosteroids are usually ineffective for controlling signs of large intestinal inflammation in dogs (although steroids are very effective for this purpose in cats). Other alternative therapies may include cyclophosphamide, chlorambucil, and cyclosporin. Omega 3 fatty acids (antiinflammatory effects) or vitamin E (antioxidant) may also be beneficial in some chronic cases.

Cyclosporine: Cyclosporine A (cyA) has been shown to be effective in steroid-resistant IBD in humans and also perianal fistula management in both humans and dogs. Other uses in dogs have included management of atopic dermatitis and sebaceous adenitis. A study was undertaken to evaluate the pharmacokinetics and clinical efficacy of oral cyA treatment in 14 dogs with steroid-refractory IBD (Allenspach K, et al). Patient assessment included determination of a clinical activity score to assess severity of clinical signs before and after treatment. The total

number of infiltrating lymphocytes and T cells in duodenal biopsies obtained via endoscopy were also assessed before and after treatment. Improvement was noted in 12/14 dogs. There was a significant improvement in clinical activity score and a decrease in T cell numbers, implying that T cell lysis is a possible mechanism of action. Results from this study suggest that cyA is an effective option for managing some dogs with steroid refractory IBD.

The anti-inflammatory effect of cyA in human IBD is believed to be due to suppression of activated T cells infiltrating the mucosa, thereby decreasing the amount of proinflammatory cytokines, and ultimately, the clinical signs of disease. The cyA dose used in the study of 14 dogs was 5 mg/kg SID. The sole therapy was cyA. Previous therapy had included immunosuppressive doses of steroids in all dogs (starting dose of prednisolone was 2.2 mg/kg/day, administered for a range of 6 to 14 weeks before the dose was decreased). Other drugs tried in most of the dogs included metronidazole (range of 2 to 38 weeks).

There were transient adverse effects observed in 5 dogs, most of which occurred in the first 1 to 2 weeks of therapy, after which time they abated. Adverse reactions included vomiting and inappetence (4/14 dogs), and gingival ulceration and alopecia followed by hypertrichosis in 1 dog. A lag phase of 7 to 10 days has been seen in humans before there are obvious signs of clinical improvement, and a similar finding was observed in the dogs in the study reported here.

The clinical efficacy study showed that cyA was effective in 11/14 of the dogs (78%). Nine dogs were considered complete responders after 10 weeks of treatment, 3 were partial responders, and 2 were nonresponders that had to be euthanized during the study because no clinical improvement was observed. Eight out of the 9 dogs that responded well initially were still doing well after 6 months to 2 years follow-up. One dog responded well for 14 weeks but then relapsed and declined with severe vomiting and was euthanized. Eight dogs were discontinued from cyA after 10 weeks of therapy. Three dogs were kept on therapy for 4, 6, and 36 months. These dogs had all shown significant improvement in clinical score but the owners elected to keep their dogs on therapy.

Duration of Pharmacotherapy

The duration of therapy that is required in dogs with IBD is quite variable. Patients with milder forms of IBD may need medical management for as little as 2 to 4 months. IBD in middle age to older dogs that is initially graded as moderate to severe can usually be managed quite successfully and can be maintained in remission but not often cured. However, in the author's (T. Tams) experience young dogs that are diagnosed and managed early enough rarely require long-term therapy (more than 1 to 2 years). In some young dogs (3 to 4 years of age or less) with severe lymphocytic-plasmacytic enteropathy and marked hypoproteinemia, therapy can be successfully discontinued as early as 9 months to 1 year. As a general clinical rule of thumb, an attempt can be made to discontinue therapy after 2 to 3 months of successful control on twice-weekly medication. If signs recur, medication

is resumed on a daily basis for 7 to 14 days before a gradual reduction program is started.

Dietary Therapy

As was mentioned earlier, the goal of dietary therapy in IBD is to reduce the antigenic stimulation of the intestinal immune system. Many pet food companies today provide myriad information on adverse food reactions and offer many good diets from which to choose. Dogs with IBD should be fed divided feedings, two or three times per day. The two main categories of foods used in dietary trials are novel protein diets and hydrolyzed protein diets.

A diet that is hypoallergenic is one that contains no additives or preservatives and has a single source of protein that is easily digestible. The protein source must be one that is "novel," meaning one that the dog has not eaten before. Examples of novel proteins now being used by pet food manufacturers include white fish, venison, rabbit, duck, salmon, catfish, and lamb. Manufacturers have been using lamb in their diets for many years now, so many dogs have eaten lamb containing diets. Dogs that have eaten lamb before should be tried on some other protein. It may be helpful to consider switching the initial novel protein to another source at six to eight weeks into the treatment course. When there is considerable inflammation and damage to the intestinal mucosa, the antigens that are in the new protein source can get absorbed and the animal may acquire an allergy to this protein. Switching them periodically could potentially alleviate this situation. The primary carbohydrate source used in hypoallergenic diets is either potato or rice.

Treatment Failure

An inadequate response to therapy is most frequently due to either incomplete diagnosis (i.e., the patient has more problems that have been diagnosed), the diagnosis is incorrect, or inadequate therapy is being administered (e.g., wrong drugs, or right drugs but incorrect doses). Veterinarians need to stress the importance of GI biopsy for dogs with disorders that do not resolve fairly early on therapeutic regimens which include dietary trials, antimicrobials, and management for any GI parasites that have been identified. In chronic cases, too often the empirical therapy route is tried for too long and ultimately the patient suffers for this approach. A thorough diagnostic approach will significantly increase the chances that therapeutic intervention will be successful. In dogs with IBD that are vomiting, a secondary gastric hypomotility problem should be considered, and gastric prokinetic therapy may prove beneficial. Sometimes anti-inflammatory medication doses are reduced too rapidly. It is better to use aggressive therapy, while carefully monitoring the patient, rather than be too conservative.

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INFLAMMATORY BOWEL DISEASE AND INTESTINAL LYMPHOMA IN CATS

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Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is not a specific diagnosis, rather it is a histological description of a syndrome resulting from a host hypersensitivity response to antigenic stimuli. In IBD there is an increase in the inflammatory cell population in the intestinal mucosa. The predominant inflammatory component in cats with IBD can be lymphocytic-plasmacytic (most common type), eosinophilic, or neutrophilic. Changes in mucosal architecture and cell morphology should also be noted (crypt lesions including abscesses, villus atrophy or fusion, edema, epithelial erosions or ulceration, fibrosis). The etiology of IBD is poorly understood. Primary causes of initiation and perpetuation of intestinal inflammation that should be considered include parasites, bacteria (specific agents including normal luminal bacteria or bacterial overgrowth), immune-mediated diseases, and food sensitivities. Many cases of IBD are likely idiopathic in nature.

Clinical Course

Inflammatory bowel disease (IBD) currently is recognized as a common and important medical problem in cats. Three general types of clinical presentations have been identified in cats with idiopathic IBD: (1) a clinical course characterized primarily by vomiting, (2) a clinical course characterized primarily by diarrhea, and (3) a clinical course that includes both vomiting and diarrhea as primary signs. Associated clinical signs can include change in appetite (anorexia, inappetence, or ravenousness), weight loss, and lethargy. In some cats, the clinical signs are cyclic; they seem to flare up and then abate in a predictable pattern.

Vomiting, one of the most frequent clinical signs of IBD in cats, is most often recognized as an intermittent occurrence for weeks, months, or years. As the disorder progresses, an increased frequency of vomiting often leads the owner to seek veterinary attention. In addition to vomiting, diarrhea is a common sign observed in feline IBD and most likely is due to derangement of normal mechanisms of absorption and motility caused by mucosal inflammation. In most cases, diarrhea is intermittent early in the course of the disorder, and there may be a transient response (weeks to several months) to dietary manipulation or any of a variety of medications (in some

cases, however, dietary manipulation can effect excellent control and drug therapy may ultimately not be necessary). Later, the diarrhea becomes persistent and usually responds only to specific treatment, which is determined after a definitive diagnosis is made. Signs of small bowel diarrhea predominate, but signs of large bowel diarrhea may be evident as well if there is generalized intestinal tract involvement.

Appetite changes in cats with idiopathic IBD vary from decreased appetite to complete anorexia to ravenousness. Inappetence seems to occur more commonly in cats that have vomiting as the primary clinical sign and usually occurs during exacerbation of clinical signs, and vomiting or diarrhea is not observed until later or not at all. The three leading differential diagnoses for a cat with a ravenous appetite, diarrhea, and weight loss are IBD, hyperthyroidism, and exocrine pancreatic insufficiency (uncommon).

Diagnosis

A definitive diagnosis of IBD can be made based only on intestinal biopsy (performed either at endoscopy or exploratory laparotomy, and ensuring that both upper and lower [ileum] biopsies are obtained). A definitive diagnosis of IBD *cannot* be made based on barium series radiography or ultrasonography. Diagnostic work-up prior to performing biopsies includes baseline testing to evaluate the overall health status of the patient and to rule out other disorders. Recommended baseline tests include a complete blood count, complete biochemical profile, urinalysis, fecal exams for parasites, serum thyroxine test, serum cobalamin level, and FeLV/FIV. Cats with chronic vomiting should be screened for heartworm disease. fTLI is done to rule-out exocrine pancreatic insufficiency. Ultrasonography is useful for assessing the abdominal organs, intestinal wall thickness, searching for any masses, and examining for lymphadenopathy. Dietary sensitivity is a common problem in cats with vomiting and/or diarrhea and food trials are an important part of the diagnostic work-up, especially early in the clinical course. Hydrolyzed protein and novel protein foods should be fed for 2-3 weeks at a time to determine if dietary therapy will either reduce or resolve the problem entirely.

Abdominal Imaging in Cats – IBD vs. Lymphoma

Radiology

Radiography is important for diagnosing intestinal diseases. During evaluation of the small bowel on survey radiographs, important factors that should be evaluated include location of small intestine (normally fills the abdomen where nothing else is present, not unusual to be mostly right-sided in cats), appearance of bowel contents (gas, fluid, or mottled material), contour of small bowel, and diameter of the small intestine. The normal diameter in cats is up to 12 mm.

In normal animals, intestinal luminal contents should appear as a homogeneous fluid opacity. Disease of the small intestine may be missed on survey films unless there is a change in bowel opacity (mineralized mass or foreign material), luminal diameter (functional ileus or complete or partial mechanical obstruction), or changes in contour of the small bowel (linear foreign body).

Contrast studies (upper GI series) are often necessary to identify normal or abnormal shape, diameter, or continuity of small bowel. The transit time of barium varies greatly in cats. It usually travels from the stomach through to the ileum in about 60 minutes, although it can take as long as

4 hours. The range of transit times for organic iodides through the small bowel is approximately 15–90 minutes. The organic iodide usually reaches the ileum and colon in less than 60 minutes.

Small Intestinal IBD

Diagnostic radiographs are recommended in the work-up of cats with gastrointestinal signs. Although survey and contrast radiographs are usually not specific/diagnostic for IBD, abdominal radiography is most helpful in defining extra-alimentary tract disorders causing gastroenteritis. Survey radiography might detect organomegaly (liver, kidney) unrelated to IBD or intestinal obstruction that might cause similar GI signs. Survey radiographs of inflammatory bowel disease are usually normal. There is no consistent radiological finding in cats with inflammatory bowel disease. The intestines may appear thickened (intestinal thickness *cannot* adequately be determined on survey radiographs), or luminal fluid maybe increased and there may be more gas than normal in the intestines, but these signs can occur in many conditions. Contrast examinations (upper GI series) are helpful in identifying a mass or obstruction. With contrast, assessment of the location and extent of the intestinal lesion may be more accurate than on survey images. Changes associated with IBD on barium study are often not present. With severe inflammatory however; changes may include: irregular mucosal lining abnormalities and thickened intestinal walls. In most cases contrast radiography is unrewarding.

Intestinal Lymphoma

Survey radiography might detect organomegaly (liver, kidney, lymph nodes) associated with lymphoma. Radiographic findings may reveal a mid-abdominal mass associated with the GI tract and/or mesentery, or localized or diffuse decrease, or loss, of serosal detail suggestive of peritoneal effusion. If a mass is suspected radiographically or historically, or a mass has been palpated, then compression radiography may be helpful to isolate and visualize the mass. Obstruction occurs more often with adenocarcinoma of the small intestine than with small intestinal lymphoma. Contrast examinations (upper GI series) are helpful in identifying the mass or the obstruction. With contrast, the location, bowel wall thickening, mucosal irregularity and extent of the intestinal lesion may be more accurate than on survey images.

Ultrasonography of the Feline Small Intestines

The small intestines can be seen throughout the abdomen, both end-on and longitudinally oriented. The duodenum has a slightly larger diameter than the rest of the small intestinal loops, and is the most lateral and ventral bowel loop in the right cranial abdomen. It can be located usually just ventral and lateral to the right kidney and followed cranially into the pylorus. The ileum has a distinct cross-sectional appearance (resembling spokes on a wheel) and can be visualized as it enters the colon, just medial to the right kidney. The colon typically is gas-filled, with poor visualization of the lumen.

The following five layers are present in the intestinal wall, from outside to inside:
Serosa: Thin hyperechoic layer
Muscularis: Thin hypoechoic layer
Submucosa: Thin hyperechoic layer
Mucosa: Prominent hypoechoic layer (typically the thickest layer)
Mucosal surface–lumen interface: Hyperechoic layer in the center of the bowel

These individual layers are best visualized with higher-frequency transducers.

Normal wall thicknesses have been established in the cat for various segments of the GI tract:
Duodenum: 2.0–2.4 mm (mean of 2.2 mm)
Jejunum: 2.1–2.5 mm (mean of 2.3 mm)
Ileum: 2.5–3.2 mm (mean of 2.8 mm)
Colon: 1.4–1.7 mm (mean of 1.5 mm)

One to three contractions per minute should be seen with normal small intestinal peristaltic activity.

Ultrasonographic features of intestinal disease include bowel wall thickening, loss of wall layers, loss of motility, and regional lymph node involvement.

Intestinal Ultrasound: IBD versus Lymphoma
An abdominal ultrasound examination may be helpful in cases of suspected small intestinal disease. Abdominal ultrasound is superior to radiology in defining focal versus diffuse disease, loss of layering, intestinal thickening and mesenteric lymphadenopathy seen with IBD and lymphoma. Ultrasonography also allows for precise guidance of fine needle aspiration or biopsy for cytologic or histopathologic sampling of small intestinal disease and associated lymphadenopathy.

Ultrasonography can also be used to assess response to therapy noninvasively. A limitation of ultrasonography would be the difficulty in assessing the exact anatomic location (duodenum and ilium should be more easily identified by an experienced operator). Findings may be normal, especially in cases of low-grade small cell lymphoma or mild IBD

Changes of the small intestine may or may not be present dependent upon chronicity and/or severity. The changes may be diffuse or focal. The intestine may appear normal. Biopsy is indicated to confirm disease.

The most common finding with inflammation is normal to symmetric wall thickening with the layering retained. In comparison, neoplasia is usually localized with greater wall thickness and loss of normal layering. These categories can overlap, and therefore cytology or histopathology is required for definitive diagnosis. Acute enteritis or inflammatory bowel disease may demonstrate corrugation of the intestine on ultrasound examination.

Ultrasound of IBD
With inflammatory bowel disease, the intestine may be normal on ultrasound. The measurement of the intestinal wall thickness by ultrasound is neither specific or sensitive for diagnosing IBD. Changes, especially those of severe or chronic disease, have been reported as focal to diffuse thickening, altered echogenicity, poor intestinal wall layer definition, and mild enlargement of adjacent lymph nodes. Mucosal echogenicity may remain hypoechoic. Round, enlarged, hypoechoic lymph nodes may be more consistent with neoplasia, while inflammatory lymph

nodes may be enlarged but tend to maintain their normal shape.

Ultrasonographic Measurements of Feline Abdominal Lymph Nodes

	US Length (mm)	US Diameter (mm)	Frequency of detection
Jejunal	20.2 (11.4-39.0)	5.0 (2.8-7.2)	90%
Colic	9.0 (4.6-12.1)	3.1 (1.9-5.2)	50%

Ultrasound of Intestinal Lymphoma

Perform abdominal ultrasonography to evaluate the extraintestinal organs in addition to GI tract wall thickness, layering, and motility. Lymphoma most commonly presents as transmural, circumferential, homogenous, hypoechoic thickening with loss of normal wall layering. Lymphoma tends to involve a long bowel segment or multiple bowel segments. Regional moderate, hypoechoic lymphadenopathy is generally present. Lymphoma is less likely to cause obstruction of the lumen.

Six major patterns of ultrasonographic features in feline lymphoma include: transmural-circumferential, symmetrical and asymmetrical, transmural-bulky, transmural-nodular, transmural-segmental, and mucosal infiltration. The transmural-circumferential pattern is most common. The transmural-bulky pattern has been described as a space occupying mass representing the thickened wall with areas of increased and decreased echogenicity. The transmural-segmental pattern has been described as wall thickening involving only a portion of the wall. The transmural-nodular pattern appeared as nodular wall infiltration and local nodular spread into the mesentery. Mucosal infiltration pattern demonstrated mild thickening of the intestinal wall associated with faint hyperechoic foci throughout thickened mucosal layer. In cats GI lymphoma can affect the intestinal tract without disrupting the wall layering.

Ultrasonographic Evaluation of Muscularis Propria in Cats with Diffuse Small Intestinal Lymphoma or IBD

It is difficult to detect small intestinal lymphoma or IBD in cats without a mass lesion, loss of layering or thickened bowel wall. Thickening of the muscularis propria is associated with diffuse infiltrative bowel disease such as lymphoma or IBD in cats. This has also been seen in normal cats as well. The most common ultrasound descriptions of GI lymphoma in cats are as mass lesions previously discussed.

Intestinal Biopsy Techniques

Endoscopic Biopsy: Endoscopy is a minimally invasive procedure in which multiple biopsies can be obtained and this procedure generally has greater client compliance than with surgery because it is less invasive and less expensive than exploratory abdominal surgical procedures. Endoscopy is considered a gold standard procedure for tissue collection. Operator experience and the quality and number of biopsy samples obtained are very important. Endoscopy offers a means of examining the upper and lower small intestine, stomach, and colon. It is especially

advantageous because biopsies can be obtained early in the course of the disorder, at a stage when a client will likely be reluctant to agree to an exploratory surgery for their pet. The degree of intestinal changes noted on biopsy also provides useful guidelines for both type and duration of therapy that will be needed to control the specific disorder.

Clinicians need to make sure they are taking an adequate number of endoscopic biopsy samples for accurate diagnosis. Even expert endoscopists report that in some cases one-fourth to one-third of the biopsy samples they take from a patient will have some degree of damage to the tissue that may preclude the samples from being useful or representative. Therefore, it is recommended that clinicians take 8 to 12 biopsy samples from the upper small intestine so that the pathologist will have enough tissue to work with. Also, it is recommended that both upper and lower GI endoscopy be done on cats with chronic GI signs (vomiting and/or diarrhea, weight loss). In this way biopsies from the ileum can be obtained by passing the endoscope along the full length of the colon up to the level of the ileocolic orifice. **It is very important that the effort be made to obtain ileum samples, since some cats with small cell lymphoma have disease in the ileum but not in the upper small intestine.** The diagnosis can be missed in these cats if only upper small intestinal biopsies are obtained.

When a pediatric diameter endoscope is used it is possible in most *dogs* over 4 to 5 kg to advance the endoscope through the ileocolic orifice and into the ileum, where it can then be advanced along the terminal ileum for exam and biopsies. However, in *cats* the ileocolic orifice is very small and in most cats it is not possible to advance the endoscope through this junction and into the ileum. In cats ileum biopsies are obtained blindly by advancing the endoscopic biopsy instrument through the ileocolic orifice with the endoscope tip positioned at the ileocolic sphincter area. Usually 3 – 4 samples are procured in this way. Colon biopsies are always obtained as well during colonoscopy in order to evaluate for inflammation in the colon.

Surgical Biopsy Techniques for Abdominal organs

Biopsy. Organ biopsy is usually required to confirm feline IBD and Lymphoma. This can be accomplished using either laparoscopic techniques or open abdominal surgery. Laparoscopic techniques have been well described for organ biopsy. These techniques are minimally invasive and well suited for tissue procurement, however, laparoscopy is not yet readily available as a diagnostic tool in most small animal clinics. Surgery on the other hand is an excellent way to obtain liver, pancreatic and intestinal biopsies. In addition to biopsy the liver should be cultured as well as bile aspirates for culture and cytology. We also currently culture the pancreas as well during laparotomy.

Intestinal Biopsy: One can obtain intestine using several techniques. A full thickness biopsy allows the pathologist to porovide the most accurate diagnosis. When taking an intestinal biopsy, the easiest way to guarantee you will get an adequate size, full thickness piece of intestine is to use a brand new 4mm or 6mm skin punch biopsy instrument. The skin punch is placed on the antimesenteric border of the proposed segment of intestine and 'drilled' through all layers of intestine until the biopsy punch can be felt to enter the lumen of the intestine. The skin punch is removed and the biopsy retrieved from the shaft of the skin punch biopsy. This technique is particularly useful for ileal biopsy as it is easy to biopsy between the mesenteric and

antimesenteric vessels. Transverse closure of the biopsy site is recommended to eliminate the possibility of lumen compromise. The biopsy site is closed using a simple interrupted or simple continuous suture pattern. 3-0 or 4-0 monofilament absorbable suture with a swaged-on sharp taper or taper-cut (penetrating point) needle is recommended. Care is taken to ensure that at least 3 mm bites are taken into the intestine and the sutures are no more that 2-3 mm apart. This is Dr. Seim's preferred technique for intestinal biopsy.

An alternate technique for intestinal biopsy is to make a 2-3 mm long incision on the antimesenteric border of the intestinal segment. A #11 or #15 BP scalpel blade is used to penetrate the intestinal wall. The blade is withdrawn to create a 2-3 mm long incision. A second parallel incision is made 1 – 2 mm from the original incision. A DeBakey forcep is used to grasp one end of the parallel incisions, a Metzenbaum scissor is used to cut out the piece of intestine. The surgeon should be careful not to crush the specimen with forceps. Only handle one end of the specimen while excising the biopsy specimen. If excessive trauma is created during biopsy, the pathologist may not be able to determine if the pathology is real or surgically created. The excised piece of intestine is examined closely to ensure that all layers have been included in the specimen. The biopsy site is closed using a simple interrupted or simple continuous suture pattern. 3-0 or 4-0 monofilament absorbable suture with a swaged-on sharp taper or taper-cut (penetrating point) needle is recommended. Care is taken to ensure that at least 3 mm bites are taken into the intestine and the sutures are no more that 2-3 mm apart. Complications associated with multiple intestinal biopsies are rare. Complications in patients undergoing intestinal surgical procedures are generally related to the surgeon's technical ability and not the patient's preoperative status.

Lymph node biopsy: All lymph nodes are encased in a layer of peritoneum. When performing a lymph node biopsy it is best to tent the peritoneal covering with forceps and incise it with metzenbaum scissors. The peritoneum is then gently dissected off the lymph node. The exposed lymph node is biopsied using a #15 or #11 scalpel blade. Generally, a thin section of lymph node is 'filleted' off and placed in a moistened gauze sponge. The peritoneum covering the remaining lymph node is sutured to create suture pressure to help control surface hemorrhage.

Liver Biopsy: Surgical biopsies obtained during exploratory laparotomy are described here. The simplest method is performed by cutting a strip of liver parenchyma 5 to 6 mm thick along the border of the liver lobe. Excessive bleeding is rarely a problem with this technique; hemorrhage is controlled via cautery or direct pressure. Diffuse liver disease must be present if this method is to be diagnostic.

A second technique involves placing an encircling ligature around a pedicle of liver tissue. As the ligature is tightened, it cuts through the hepatic parenchyma, ligating hepatic vessels and bile ducts. This technique, widely known as the Guillotine technique, has been criticized for leaving excessive amounts of devitalized parenchyma. This can be avoided by inserting scissors through the cut parenchyma and cutting hepatic vessels and bile ducts just distal to the ligature. This method requires the presence of diffuse liver disease to obtain a diagnostic biopsy unless the lesion is present in the distal aspect of the liver lobe.

More localized abnormalities can be biopsied by wedge resections or partial lobectomy. Wedge resections may be performed by placing a row of overlapping, full-thickness, interrupted mattress sutures of 0 or 2-0 Maxon or Biosyn along each side of the wedge to be removed; these sutures should commence at the edge of the liver lobe and meet proximally to form a "V". The sutures should be tied so as to compress the liver slightly but not cut into liver parenchyma. The wedge of tissue to be removed is incised about 5 mm from the suture line. Alternatively, the wedge may be removed prior to tightening the mattress sutures; preplaced mattress sutures are then gently tied with enough tension to control bleeding.

An alternate technique for use in patients with diffuse fibrotic liver disorders is performed by penetrating the affected liver lobe with a straight mosquito hemostat. The hemostat tip is placed on the surface of the liver lobe to be biopsied and gently plunged through the liver lobe until the tip of the hemostat is seen penetrating through the opposite side of the liver. The jaws of the hemostat are opened just wide enough to accept a piece of 2-0 or 3-0 Maxon or Biosyn suture. The suture is doubled on itself, the loop is passed into the jaws of the hemostats, and the loop pulled through the liver lobe. The exiting loop is cut leaving two strands of suture coursing through the liver lobe. Each strand is tied individually to "cut" through the liver. A "V" wedge is cut through the liver when both strands of suture have been tied. A number 15 BP scalpel blade is used to cut the V-shaped liver biopsy wedge from the sutures.

Pancreatic Biopsy: Samples from the pancreas should be obtained in all suspected triaditis cases. The old wive's tale stating "don't touch the pancreas" needs to be put to rest in veterinary medicine. Gentle manipulation and biopsy of the pancreas is a predictably successful procedure with almost no incidence of postoperative pancreatitis. Biopsy of the pancreas is performed in a similar manner as biopsy of the liver. In patients that have diffuse pancreatic disease, a segment of the right or left limb of the pancreas is identified. An encircling ligature of 3-0 Biosyn is placed around the pedicle. As the ligature is tightened, it cuts through the pancreatic parenchyma, ligating vessels and pancreatic ducts. The distal pedicle of pancreas is carefully removed with a number 15 BP scalpel blade or metzenbaum scissors. Care is taken to avoid cutting the suture.

Treatment of IBD

It is important that the clinician formulate a treatment plan based on a correlation of clinical course, laboratory and gross findings, and histologic findings (considering both cellular infiltrate and morphology) rather than relying on histologic changes alone. Since food sensitivities can be a cause of IBD, dietary trials are an essential part of both the diagnostic and therapeutic strategy, utilizing hydrolyzed protein diets and novel protein diets and treating each patient as an individual (i.e., there can be variable responses to specific diets varying from patient to patient). Regarding pharmacotherapy, while corticosteroids have long been considered the cornerstone of treatment for idiopathic inflammatory bowel disorders, antimicrobial agents may play a role as well. Bacteria have been implicated in the pathogenesis of IBD.

Guidelines for corticosteroids in cats with IBD are as follows. Mild to moderate cases of IBD often respond to prednisolone (preferred over prednisone in cats) at a starting dose of 1 to 2.2 mg/kg divided twice daily for two to four weeks followed by a gradual decline in 50% increments at two week intervals. Cats with inflammatory changes graded as mild usually

respond quite well to the lower dose and alternate day or every third day treatment can often be achieved by two to three months. Occasionally treatment can be discontinued altogether by three to six months.

If biopsies reveal disease that is moderate to severe a prednisolone dose of 2 to 4 mg/kg divided twice daily is used in cats for the first 2 to 8 weeks or until clinical signs resolve. This dose of corticosteroid is usually well tolerated in cats. In some cases a dose of 1 to 2 mg/kg per day may be necessary long term (months to years) to maintain clinical remission. Use of combination drug therapy may also be required at the outset to control clinical signs and prevent progression of the disease (e.g., metronidazole or tylosin plus prednisolone). Cats with hypoproteinemia and histologic changes graded as severe often respond quite well when an aggressive therapeutic course is undertaken.

Budesonide is a glucocorticoid that represents an alternative for management of IBD in dogs and cats, especially in severe cases that have proven to be refractory to prednisolone, metronidazole, azathioprine, chlorambucil, tylosin, and dietary management; or that are intolerant of the corticosteroids discussed above. Budesonide is one of a group of novel corticosteroids that have been in development for use in humans in an attempt to make available alternative preparations that will help limit toxicity associated with corticosteroid use.

Budesonide undergoes high first pass metabolism in the liver and 90% is converted into metabolites with low corticosteroid activity. It has minimal systemic availability. The potential for typical corticosteroid side effects is significantly reduced as a result of decreased bioavailability and the resulting limited systemic exposure, which makes this a particularly attractive drug for use in humans and animals that are poorly tolerant of other corticosteroids. Budesonide also has a high receptor-binding affinity in the mucosa. It has been referred to as a "locally acting" corticosteroid.

Therapeutic results with budesonide have been promising in humans with Crohn's disease, collagenous colitis and lymphocytic colitis, ulcerative colitis, either when administered as a retention enema or in oral form, and primary biliary cirrhosis.

Budesonide has been used by some veterinary clinicians in recent years to treat IBD in dogs and cats. Dose recommendations vary. In humans, a range of 6 mg to 9 mg per day has been used during initial therapy. In general, budesonide is administered to cats at 1 mg administered once per day (this dose level is prepared at a compounding pharmacy).

Budesonide can be used in combination with other drugs. Since cats tolerate corticosteroids very well, there is little indication to use budesonide as initial therapy for IBD. However, this may be a very attractive option for use in diabetic cats that also have IBD, or in patients where conventional therapies have not been sufficiently effective.

Potential adverse effects include PU/PD, when budesonide is used at the high end of the dose range, and GI ulceration. These reactions have been observed in some human patients. These

problems would be more likely to occur in dogs than in cats. It appears to be very safe when used at the levels listed above.

When combination therapy is indicated metronidazole is usually the first choice to be used in conjunction with prednisolone. Metronidazole's mechanism of action includes an antiprotozoal effect, inhibition of cell-mediated immune responses, and anaerobic antibacterial activity. A dosage of 10 to 20 mg/kg two times daily is used for IBD. Ideally, at least several months of metronidazole therapy is given once it is started. In some cats with severe disease long term consecutive use or one to two month cycles of treatment may be required. Side effects to metronidazole at this low dose are uncommon in cats. Occasionally nausea or vomiting may be seen.

If a client is unable to successfully administer oral medications, methylprednisolone acetate (Depo-Medrol) can be used as sole treatment for cats with mild to moderate IBD or as adjunctive therapy when oral prednisolone and/or metronidazole are used as the primary treatment and flare-ups of clinical signs occur. Consistent control of clinical signs in cats with moderate to severe IBD is more difficult to maintain when methylprednisolone acetate is used alone, however. It is recommended that sole use of methylprednisolone acetate be reserved for situations in which the owner is unable to consistently administer tablet or liquid prednisolone preparations. Initially 20 mg is given subcutaneously or intramuscularly and is repeated at 2-week intervals for 2 to 3 doses. Injections are then given every 2 to 4 weeks or as needed for control.

If remission cannot be maintained with use of corticosteroids and metronidazole then chlorambucil (Leukeran) should be used. Azathioprine was used more in the past but it has been largely supplanted now by chlorambucil. Chlorambucil is an alkylating agent. Alkylating agents alter DNA synthesis and inhibit rapidly proliferating cells. Chlorambucil is administered initially at 0.1 to 0.2 mg/kg/day in conjunction with prednisolone at 2.2 mg/kg/day. The small pill size of chlorambucil (2 mg) allows for easy dosing. Most cats receive one-half tablet (1 mg) per day. Various dosage schedules for cats have been published. An alternate schedule is 0.15 to 0.3 mg/kg every 72 hours. Toxicities are uncommon in cats but may include anorexia, vomiting, and diarrhea, but these problems generally resolve rapidly when chlorambucil is reduced from daily to every other day administration. Bone marrow suppression is possible but uncommon, and is mild and rapidly reversible when it does occur. Once the desired clinical response is achieved, chlorambucil is gradually tapered over several months while prednisolone is continued as the primary maintenance drug.

Cyclosporine is another immunosuppressive drug that can be used in management of IBD. Cyclosporin inactivates calcineurin phosphorylase in T cells, preventing transcription of interleukin-2 (IL-2) as well as other cytokines. Cyclosporin inhibits activation of T cells, natural killer cells, and Langerhans (i.e., antigen-presenting) cells. Suppression of the Th_1 or Th_2 response induces antigen tolerance. The dose is 5 mk/kg once daily. Once sufficient response is achieved the dosage interval can be reduced to administration of a full dose every 48 hours and subsequently even further, on an individual patient basis.

Cobalamin therapy in cats: Significant tissue level cobalamin deficiency is present in some animals with GI disease. This is usually secondary to reduced cobalamin absorptive capacity. It is essential that all cats with any form of GI disease (including involvement of liver, stomach, pancreas, intestines) have a serum cobalamin level run to determine if the patient is hypocobalaminemic. Response to therapy will be limited if low cobalamin levels are not resolved. The reference range for cobalamin in cats is 290-1500 ng/L. Therapy is given if the value is less than 500 ng/L (i.e., in the low part of the reference interval; don't wait until the level drops below the low end point of the reference range).

Therapy involves administering injectable cobalamin at the following schedule for cats: 250 ug subcutaneously once a week for 6 weeks, then every 2 weeks for the next 6 doses, then dose monthly. Most generic cobalamin preparations contain 1 mg/ml (1000 ug/ml). It is important to note that multi-vitamin and B-complex injectable formulations contain significantly lower concentrations of cobalamin and they also cause pain when injected. Therefore, it is recommended that these preparations not be used for cobalamin supplementation. Unless the intestinal disease is totally resolved, long-term and perhaps lifelong supplementation with cobalamin may be necessary. The frequency of injections on a long-term basis is determined by regular measurement of serum cobalamin concentration.

Because dietary allergens may play a role in the cause if IBD, specific dietary therapy may be beneficial. Often, moderate to severe degrees of IBD are either temporarily responsive or only minimally responsive to careful dietary manipulations. However, long term control of IBD with as minimal a drug administration schedule as possible may be aided by specific dietary management. This should be started as soon as a diagnosis is made and continued as drug therapy is decreased later. Feed elimination (novel protein) or hydrolyzed protein diets. Chicken, duck, lamb, fish, or venison based diets are often tried initially. Elimination diets have been found to be very beneficial in cats.

Poor responses to treatment of cats with IBD usually result from:

1. Inadequate initial or long-term maintenance corticosteroid dosage in cats with more severe forms of IBD (moderate t severe disease).
2. Failure to use ancillary medications (metronidazole, chlorambucil, cyclosprinetylosin) in cases where disease is moderate to severe.
3. Failure to recognize and treat a concurrent condition (e.g., gastric hypomotility disorder that may either be secondary to IBD or idiopathic in nature, hyperthyroidism, parasitism [e.g., *Giardia*, *Cryptosporidium*], *Clostridium perfringens* enterotoxicosis, cholangitis/cholangiohepatitis, chronic pancreatitis).
4. Treatment for only small intestinal inflammatory disease when colitis is present as well. Some cats with concurrent IBD and colitis may show minimal or no clinical signs of colitis.
5. Failure to recognize and treat low body cobalamin levels (measure serum cobalamin).
6. Failure to identify an effective diet.
7. Poor client compliance

What If Biopsies are Not Definitive for Either IBD or Small Cell Lymphoma?
It can be difficult to definitively differentiate benign IBD from small cell intestinal lymphoma, even when full thickness intestinal biopsies are obtained. If the biopsies were obtained via endoscopy, one option is to proceed to exploratory laparotomy to obtain full thickness samples. However, this is not practical in some cases and involves a more invasive procedure and more expense. Further, there is no guarantee that the differentiation can be made even when full thickness samples are obtained. Another option that is employed more commonly now is to perform special tests to help differentiate benign IBD from low-grade, small cell lymphocytic malignant lymphoma. Specific immunohistochemical techniques can be done to identify populations of malignant B and T lymphocytes (i.e., phenotyping) and molecular (PCR) testing is done for clonality. Clients should be given the option of ordering these additional tests if the pathologist indicates on the initial histopathology interpretation that the differentiation can't be made definitively between IBD and lymphoma. If the client declines to have the additional tests performed, the clinician then needs to decide whether or not to just go ahead and treat for the disease that poses greater concern, i.e., lymphoma. Low grade small cell lymphoma is often treated with the combination of prednisolone and chlorambucil (see later discussion on treatment details in the next section).

Treatment of Intestinal Lymphoma in Cats

Lymphoma is the most common feline neoplasm. It is also the most common form of gastrointestinal neoplasia in cats. Gastrointestinal lymphoma is often referred to as either well differentiated (low grade or lymphocytic), poorly differentiated (high grade, lymphoblastic, or immunoblastic), and intermediate (or mixed). Endoscopy has been shown to be a very useful modality for diagnosis of intestinal lymphoma in cats, especially when multiple biopsies are obtained using proper technique and instruments that can procure adequate size tissue samples. Immunohistochemical stains are beneficial for differentiating IBD from intestinal lymphoma in cases where it is difficult for the pathologist to distinguish between the two. Full thickness intestinal biopsies may be required in a very limited number of cases in order to establish the correct diagnosis.

Many cats respond favorably to treatment for intestinal lymphoma, especially with the low grade or chronic lymphocytic type. Clinical signs can be very similar to cats with IBD. Therefore, it is strongly recommended that cats with chronic GI signs undergo a biopsy procedure as early as possible, so that the correct diagnosis can be established and the best course of therapy be made available for each individual cat. Biopsies should be obtained from *both* the upper and lower (ileum) small bowel.

Multi-agent chemotherapy is recommended for all cats with GI lymphoma. Surgery is done only if there is an isolated mass that is causing some degree of luminal obstruction. Survival times in excess of 12 to 18 months are not unusual. In some cats the response is somewhat shorter (three to six months). The prognosis for longer survival time is much better if the diagnosis is made before clinical signs become chronic and debilitation results.

One study has reported excellent results in cats with chronic lymphocytic lymphoma using a protocol of prednisone (10 mg PO per cat per day) and chlorambucil (Leukeran) at a dosage of 15 mg/m2 PO, once every day for 4 days, repeated every 3 weeks (Note: prednisolone is used routinely at this time, rather than prednisone, in cats). Sixty-nine percent of the cats with lymphocytic lymphoma treated with this regimen achieved a complete remission. The median disease free interval for cats that achieved complete remission was 20.5 months (range, 5.8-49 months). The median survival for all cats with lymphocytic lymphoma treated with chemotherapy was 17 months (range, 0.33-50 months). Cyclophosphamide (Cytoxan) was used for rescue in some of the cats that were entered in this protocol (225 mg/m2, PO, every 3 weeks). For further reference on this protocol, see Richter,K: Feline gastrointestinal lymphoma, ACVIM Proceedings 2001, p. 547-549.

The protocol that Dr. Tams has used most often for cats with the more aggressive lymphoblastic form of GI lymphoma was originally published by Cotter in 1983. Dosage levels have been modified slightly since that time. This protocol utilizes cyclophosphamide, oncovin, and prednisolone (COP). This protocol can be easily managed in any practice setting. Vincristine is administered intravenously at a dose of 0.5-0.75 mg/m^2 once weekly for 4 consecutive weeks and then once every 3 weeks. The initial doses are often decreased by approximately 25 percent for cats that are inappetent or debilitated. If well tolerated the dose can then be gradually increased. Care is taken to ensure that none of the vincristine is given extravascularly. The average volume that is administered is quite low (0.1 to 0.15 ml for many cats, using a vincristine concentration of 1 mg/ml). Cyclophosphamide is given orally at a single dose of 225 mg/m2 every 3 weeks (50 mg tablets are used with dosage adjusted to the nearest 25 mg on the low side of the calculated dose). Prednisolone is given orally at 10 mg per cat per day. Although cyclophosphamide and vincristine can be given on the same day I often prefer to have the owner administer the cyclophosphamide 2 to 3 days after the oncovin. A CBC is done several times during the first month and then every 3 weeks to be sure that adequate granulocytes are present before treatment. At least 3,000 granulocytes/ul must be present before cyclophosphamide is given. If the granulocyte count drops to less than 1,000/ul 5 to 7 days after cyclophosphamide, the dose for subsequent treatments is reduced by 25 percent. The highest non-toxic dose is most likely to result in the greatest tumor cell kill.

The COP protocol is generally well tolerated, although side effects may occur and dosage or interval adjustments may be necessary. Side effects of COP in cats may include anorexia, vomiting, lethargy, and severe tissue irritation if any vincristine is given extravascularly. Also, the haircoat may become thinner, but complete hair loss does not occur. Cats do tend to lose whiskers. Cats should be carefully observed for sepsis especially during the induction phase. Prophylactic antibiotics are not indicated, but any infections that occur should be treated aggressively. Advantages of this protocol include hospital visits at only 3 week intervals after the first 4 weeks, lower cost to the owner, and a treatment interval that allows recovery of normal cells between treatments. I would like to emphasize that with careful monitoring and use of a dosage schedule that is tailored to each individual cat few problems are encountered It is our general practice to encourage owners of most cats with GI lymphoma to pursue treatment that includes chemotherapy.

Nutritional and metabolic support are also important. If inappetence is a problem cyproheptadine can be administered as an appetite stimulant (1 to 2 mg orally every 12 to 24 hours) on an as needed basis

(long-term if necessary). Mirtazapine is another appetite stimulant that can be used (one-fourth of a 15 mg tablet every three days). Intermittent vomiting, nausea, and inappetence is managed with maropitant (Cerenia) administered at 4 mg for most cats once orally daily as long as it is needed. If there is concurrent renal disease with azotemia or if dehydration is a problem owners are taught how to administer subcutaneous fluids at home (e.g., lactated Ringer's 100 to 150 ml every 24 hours to 48 hours, based on each individual cat's needs). Special attention is given to ensuring that low cobalamin levels are addressed, if serum tests indicate that hypocobalaminemia is present.

Rarely chemotherapy can be discontinued after one year. This is done only if follow-up endoscopic intestinal biopsies indicate that there is no remaining lymphoma. Most cats remain on treatment for the remainder of their lives. If chemotherapy is poorly tolerated and reduced dosages and increased intervals between treatment times are unsuccessful in adequately decreasing side effects chemotherapy should be suspended. Prednisolone should be continued however because it may help maintain remission for a period of time. Doxorubicin (Adriamycin) can also be used in cats.

For clinicians inexperienced in administering chemotherapy, or who have not treated many cats with intestinal lymphoma, it is recommended that a veterinary oncologist or internist be consulted for guidance on protocol selection and ongoing management. Many cats with intestinal lymphoma can be managed successfully for some period of time!

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THOSE TROUBLSOME CHRONIC DIARRHEA CASES; SOME PRACTICAL TIPS

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Diarrhea is a common clinical complaint but most resolve within several days most likely due to a dietary indiscretion. Diarrhea that lasts longer than several weeks is considered to be chronic and requires a systematic work-up to determine the cause and appropriate therapy (Figure 1). GI parasites, dietary intolerances, metabolic disease, pancreatic disease, bacterial causes, and inflammatory bowel disease are but a few etiologies of chronic diarrhea. Inflammatory bowel disease (IBD) is a common condition diagnosed in dogs and cats; however, it is not a specific disease but rather a term that describes animals having gastrointestinal (GI) signs with histologic evidence of inflammation within the intestine. IBD does not however describe the etiology, nor does the extent of inflammatory cells parallel the severity of clinical signs. Before beginning extensive diagnostics or obtaining an intestinal biopsy specimen from a patient with chronic diarrhea, there are a few diagnostic tests or trial therapies to consider. Obviously the course of action is predicated in part on a good clinical evaluation and based on the severity of the clinical disease.

THE APPROACH

Every patient with chronic GI signs should have a thorough history, physical examination, complete blood count, biochemical profile, urinalysis, and fecal examination. In many cases, this initial evaluation will determine if the etiology of the diarrhea is primary GI disease or secondary to other systemic or metabolic disease or if the diarrhea is predominately of small bowel or large bowel origin. For example, Addison's disease, liver disease, pancreatic disease and renal disease can all be associated with secondary GI involvement. If the initial workup fails to provide a clue as to the etiology, then I will begin a specific GI evaluation. The fecal sample should be fresh and include standard fecal flotation, wet mount preparation, and stained cytology. Fecal centrifugation technique is recommended for the most accurate means of detecting GI parasites. A stained Diff-Quick cytology may reveal such things as neutrophils, eosinophils, fungal organisms, or characteristic bacteria (spiral bacteria or spores) and may provide clues about the etiology. With large bowel signs I will also perform a mucosal scraping with cytology. Cytology may identify fungal, neoplastic or inflammatory disease. Next I will classify the patient based on the severity of disease: either having minimal signs and no debilitation or those cases that fail conservative therapy or those having severe disease obviously requiring an in-depth GI workup. For the animal with relatively mild diarrhea without weight loss or debilitation, I prefer to use trial therapy as part of the clinical evaluation. Trial therapy involves antiparasitic therapy, dietary food trials, and antibiotic therapy. If these trial therapies fail to resolve the diarrhea, further GI evaluation is indicated. Additional diagnostic testing may include imaging studies (ultrasonography is preferred as barium studies are rarely helpful), trypsin-like immunoreactivity (TLI), serum folate and cobalamin, and endoscopy or surgery for intestinal biopsies.

ALWAYS RULE OUT PARASITES

Parasites must always be considered in any dog experiencing chronic GI signs. *Giardia* and common nematodes are usually diagnosed using proper fecal examination techniques. Often it is difficult to find *Giardia* cysts on flotation, and hence a more accurate ways to diagnose *Giardia* are by fecal ELISA or IFA staining of spores, both of which are highly sensitive and specific.[1] It is important to know that *Giardia* can display antimicrobial sensitivity patterns similar to bacteria and therefore it is impossible to predict which anti-*Giardia* drug will be most effective in an individual dog or cat. The treatment of choice for years has been metronidazole. Currently, metronidazole at a dose of 25 mg/kg orally twice daily for seven days is preferred; however, there are many different doses and durations of therapy reported (*Table 1*). Other suggested *Giardia* therapies include febendazole or febantel for five days.[1] High-fiber diets may help lessen re-

infection when given during the therapy. With treatment failure, one should make sure that *Giardia* is truly the problem and also that subsequent recontamination is not occurring. Infection with *Giardia* does not confer immunity. In resistant cases, combined febendazole and metronidazole therapy has been suggested. In difficult cases, bathing the animal before therapy and decontaminating the environment using quaternary ammonium compounds is also recommended. Other considerations include diets, probiotics, silybin (milk thistle) or GI antibiotics.

It is controversial whether to treat healthy dogs and cats that test positive for *Giardia* because *Giardia* is generally not considered a significant human health risk. I recommend treating the asymptomatic, positive dog and if on recheck evaluation the patient is still positive but subclinical, I will repeat therapy using a different agent. If the animal remains positive after two therapies, I simply recheck the patient again at the next yearly health evaluation. Some animals are chronic asymptomatic carriers and are very difficult to clear. I have observed some animals spontaneously clear when they reach maturity. It is a more significant concern when infected dogs live with immunocompromised individuals or young children.

The organism *Tritrichomonas foetus* (TTF) has been identified as a cause of chronic diarrhea in young cats.[2] Most of the affected cats are under 1 year of age and are reported to have a watery to sometimes mucoid diarrhea. It is most often observed in cats from humane shelters or catteries, and Abyssinians and Bengal cats appear to be over-represented or to have a more resistant disease. There are several ways to diagnose TTF. The diagnosis can sometimes be made by performing a wet mount fecal prep. A small amount of stool is thinned with warm saline solution, a coverslip applied, and the feces examined at 40X. It is important that the stool is fresh for examination. A colonic flush of saline can also be used to obtain fecal material for cytology and culture. TTF is identified by its progressive forward motion (*Giardia* has a falling leaf motion). Feces can also be cultured using the bovine TTF culture technique employing an In Pouch TF™ culture method (Biomed Diagnostic Labs). With these pouches, a very small amount of stool is placed in the broth and cultured at room temperature. The bag is then examined under a microscope from 24 and up to 72 hours later for evidence of motile organisms. Fecal PCR for TTF is offered by many commercial labs and is considered the test of choice for confirming the infection.

Ronidazole is the only antimicrobial so far shown to have efficacy in treating TTF infection.[3] Ronidazole is given at 30 mg/kg q24h PO for up to 14 days. It appears to have a very narrow therapeutic range; higher doses or a longer duration can result in neurotoxicity. Ronidazole must be obtained through a reliable compounding pharmacy. It is very bitter and therefore should be given via capsule; liquid solutions are not recommended. Treatment failure can occur, and a fecal PCR should be performed if a cat fails to respond to therapy because a negative PCR result means TTF is a less likely cause of the diarrhea. When left untreated many cats eventually become normal, especially young cats under 1 year of age. In one study, 88% cats with TTF infection were reported to undergo spontaneous resolution of diarrhea within two years of a diagnosis; however, most remained infected based on PCR results when retested as long as two to five years after the initial diagnosis.[4] The role of these asymptomatic carriers in disease transmission remains unclear.

THE POWER OF DIETS

Over the years I have become more and more impressed with resolution of GI signs by simply changing the diet. My impression and also supported by clinical studies that would suggest that up to 50% of dogs and cats with non-specific GI disease may respond to diet alone.[5,6] Dogs with food responsive diarrhea (FRD) tended to be younger and more have large bowel signs and normal protein concentrations. However, I have recently observed a debilitated and hypoproteinemic patient respond to only a diet change. Consequently, a dietary trial should be the first step in evaluating a patient that has chronic diarrhea after systemic, metabolic and GI parasitic disease is eliminated as a potential cause. Severely debilitated or anorexic patients with GI disease would obviously require more specific and aggressive evaluation. The remainder of patients having chronic diarrhea a dietary trial is justified. A positive response to a diet trial is referred to as a food responsive diarrhea.[6] FRD include both true dietary allergies and dietary intolerances. Allergies result to a reaction with a protein antigen while intolerances occur in

response to some substance in the diet such as a preservative or food coloring as examples. Dietary trials using a test diet generally requires a 2-weeks or even less to appreciate a response; the GI seems to respond much faster than dermatologic conditions that may take as long as 8 weeks or more to improve. There is no ideal diet that will consistently resolve diarrhea. The main options for diets include diets that optimize assimilation of nutrients (e.g. highly digestible, fat restricted or low fiber) or diets that favors antigenic modification (e.g. a novel protein source or a protein hydrosylate).[7,8] My personal favorite is the use of the hydrolyzed diets such as Purina HA™. The hydrolyzed diets are single protein sources (usually soy, rice or potato based) and have undergone digestion producing low molecular-weight protein derivatives that are thought to be highly digestible with low antigenic potential. Perhaps their benefit might actually be due to the fact that they are very pure and contain very little else that might contribute to a dietary intolerance. The hydrolyzed diets have now become my primary trial diet. If I observe a positive response then I know I can control the patient's GI signs with a diet and either continue on that test diet or attempt to find for another long-term diet that works well for both the client and patient. Only a small percentage of dogs with GI signs relapse on challenge and are therefore likely truly food allergic.[6] Novel protein diets containing a single protein antigen would be an alternative approach. If using the novel antigen diets one should only prescribe the veterinary diets as many of the over the counter novel protein diets are not all that novel and have been shown many other antigens not listed on the label.[9] Highly digestible gastrointestinal diets such as Purina EN™ may improve assimilation, promote gastrointestinal health and modify the microbiota. Diets containing highly fermentable fibers such as those containing fructooligosaccharides (also referred to as prebiotics diets) are often useful for colonic disease because fermentation products are shown to have beneficial effects on mucosal function and modify enteric microbiota promoting "good" bacteria and inhibiting certain pathogenic bacteria.[10] If a diet trial is unsuccessful, no improvement in clinical signs after 10-14 days, the next step is to institute an antibiotic trial.

ANTIBIOTICS; SOMETIMES AN EASY CURE

There are many dogs with chronic large or small bowel disease that have an antibiotic-responsive diarrhea (ARD).[11] An old term for ARD is *small intestinal bacterial overgrowth (SIBO).* However, SIBO is a poorly defined syndrome in dogs, and we currently have no way to adequately and convincingly diagnose bacterial overgrowth or to know in which cases antibiotics would be beneficial short of a therapeutic trial. More recently the term *gastrointestinal dysbiosis* has been given to conditions associated with an abnormal GI bacterial ecosystem.[11] In simple terms, GI dysbiosis refers to an imbalance in GI bacteria with the loss of the more "good bacteria" coupled with an increase in the so-called "bad bacteria." For chronic diarrhea cases that do respond to antibiotic therapy, it is likely the antibiotics have not eliminated a specific pathogen but rather changed the overall bacterial ecosystem, promoting a more normal bacterial makeup. Some cats and dogs with gastrointestinal dysbiosis have decreased serum cobalamin (vitamin B_{12}) concentrations.[12] The cobalamin deficiency can be due to lack of intrinsic factor production, abnormal increased intestinal bacterial utilization, or ileal disease causing inadequate cobalamin absorption. Serum folate concentrations are usually variable in cases having dysbiosis.

Metronidazole is frequently used in GI cases but long-term administration and potential side effects make it less desirable than other options. Further, metronidazole has been shown to cause DNA damage to feline lymphocytes in vitro. There is also evidence in laboratory animals that it has carcinogenic potential.[13] A suggested GI dosage for metronidazole in cats and dogs is 7.5 to 10 mg/kg given orally twice daily. A commonly used alternative, and my first GI antibiotic choice, is tylosin. Tylosin was first reported to be useful for chronic diarrhea in the early 1970s and there has been a recent resurgence in interest and use of the antibiotic. Tylosin is a macrolide, bacteriostatic antibiotic that is currently marketed over the counter for the treatment of respiratory disease in chickens. Tylosin has activity against most gram-positive and gram-negative cocci, gram-positive rods, and *Mycoplasma*; however, the gram-negative bacteria *Escherichia coli* and *Salmonella* species are intrinsically tylosin-resistant.[14] Tylosin works by transiently changing the GI enteric bacterial population, probably by promoting the growth of beneficial commensal bacteria while suppressing deleterious bacteria or preventing their sporulation. Once tylosin is discontinued, the original bacterial population often returns to its pretreatment state. There is also a suggestion that tylosin may exhibit anti-inflammatory

properties.[14] Tylosin appears to have almost no systemic or toxic side effects. The initial dose recommendation for tylosin in both dogs and cats is 15 mg/kg orally, twice a day, mixed with the food (has a bitter taste) or given via gelatin capsule. (Note: it comes as a powder and a #3 gelatin capsule holds 130 mg, a #1 capsule holds 240 mg, a #0 capsule holds 345 mg, and a #00 capsules hold 430 mg.) For cases that respond, the long-term dose can be reduced to as low as 5 mg/kg/day.[14] Tylosin is effective for most *Clostridium perfringes* and is considered by many to be the treatment of choice for suspected clostridial diarrhea.[15]

ANTIBIOTIC ALTERNATIVE

Probiotics are live microorganisms that, when given in adequate amounts, confer a health benefit to the host. The microorganisms most frequently used are lactic acid bacteria (i.e. *Lactobacillus*, *Enterococcus*, *Streptococcus*, and *Bifidobacterium* species). They are believed to impart a beneficial effect, but the mechanism remains poorly understood. Some probiotic strains have been shown to modulate the immune system. Others help to restore or normalize the function of the mucosal barrier or protect the normal microbiota from pathogenic bacteria through the production of antimicrobial substances or from competitive exclusion of pathogens. To date, there have been very few controlled clinical studies evaluating probiotic success. However, a large double-blinded placebo control study of shelter dogs and cats developing diarrhea found significantly fewer cats that received *Enterococcus faecium* (FortiFlora®, 2.1×10^9 cfu/day) developed diarrhea for greater than a two-day duration.[16] Probiotics exert their effects as long as they are being given but once stopped the GI flora generally returns to the pretreatment state. It may seem counterintuitive to give antibiotics with probiotics, but clinical improvement is sometimes seen when they are given in combination. Probiotics are considered a safe adjunctive therapy and are commonly used for both acute and chronic diarrhea in dogs and cats as well as for the prevention of stress induced diarrhea.[17] Recommendations for the ideal probiotic, containing an adequate type and number of viable organisms for specific GI disorders, become difficult to make. Some over-the-counter preparations may not have been found not to contain the label claims.[18] My recommendation is to use a product produced by a reputable veterinary company that has done research on their product.

There has been a recent interest in veterinary medicine using fecal microbiota transplantation (FMT) for diarrhea. There are anecdotal reports of improvement in some patients having chronic diarrhea requiring antibiotic therapy. The premise is that the transplant replaces good colonic bacteria that have been suppressed or killed. It involves collecting stool from a young normal tested donor, mixing with saline, strained, and placed in the patient's colon via enema. Time will tell but FMT may become a low-cost, low-risk means of treating some chronic diarrhea cases.

UNIQUE TO GERMAN SHEPHERDS?

A clinical syndrome frequently encountered in German shepherd dogs is chronic GI signs and weight loss. Exocrine pancreatic insufficiency is common in the breed, requiring pancreatic enzyme supplementation, and it must first be ruled out. The diagnosis is made by documenting a subnormal trypsin-like immunoreactivity (TLI) concentration and is supported by improvement with pancreatic enzyme replacement. A second group of German shepherd dogs with similar clinical signs have normal TLI concentrations. Many of these dogs turn out to have an antibiotic-responsive diarrhea due to GI dysbiosis. Testing should include measurement of folate and cobalamin (serum B_{12}) concentrations. Low cobalamin and high folate levels are characteristic of both exocrine pancreatic insufficiency and GI dysbiosis. Dogs with subnormal cobalamin concentrations will require parenteral supplementation (initially, about 500 µcg subcutaneously weekly) as part of the therapy. Ancedotal reports suggests some dogs correct with oral cobalamin supplementation (1 mg/PO daily). The cause of the GI dysbiosis in German shepherds is unknown. Researchers have investigated IgA concentrations, suggesting the possibility of an inherent deficiency leading to abnormal GI immunity. More recently researchers have measured toll-like receptors (TLR) in the GI tract of these dogs with a documented abnormal expression of the receptors. Using candidate gene analysis, polymorphisms in TLR4 and TLR5 were recently shown to be significantly associated with IBD in German shepherds.[19] Furthermore, the same polymorphisms in TLR5 were also associated with IBD in a heterogeneous population of dogs

consisting of 38 different breeds.[19] These mutations could well play an important role in the pathogenesis of IBD in dogs, as a mutated receptor will lead to misrepresentation of commensal bacteria as pathogens, therefore signaling "danger" to the host and initiating the characteristic inflammatory response seen in this disease. Management of affected German shepherds involves diet, antibiotics, and cobalamin supplementation. Prebiotics and probiotics are also often given as additional adjunctive therapy. This condition tends to require life-long management.

WHEN IS IT IBD?

I generally consider IBD as the probable diagnosis when the patient fails to respond to appropriate anthelmintic, dietary and antibiotic trials or if the clinical severity is such that trial therapies should be precluded. The classification of IBD is generally based on the region of the GI tract affected and on the predominant cell type in the inflammatory infiltrate. Lymphocytic-plasmacytic enteritis is the most common type of IBD observed in dogs and cats. Other forms include eosinophilic, neutrophilic and granulomatous enteritis. There are also breed specific forms of IBD best recognized in Soft-Coated Wheaten Terriers having a protein-losing enteropathy (PLE), in Basenjis with an immunoproliferative enteropathy, in Norwegian Lundehunds with IBD and PLE and Boxers having histiocytic ulcerative colitis.

Although the exact etiology of IBD is unknown it is widely accepted that the pathogenesis involves a complex interplay among host genetics, the intestinal mucosal immune system, the environment and the intestinal microbiota. Studies using both histochemical and immunohistochemical techniques to describe immune cell populations and cytokine expression in the intestinal mucosa have had variable results precluding making a general description of abnormalities in IBD. Histopathology confirms IBD; more appropriately inflammatory changes in the intestine. However, architectural changes (such as villous atrophy) seem to be more important than solely identifying the inflammatory infiltrates present. Also the lesions can be variable throughout the GI tract so multiple biopsies from different areas are suggested.

The diagnosis of IBD requires a complete laboratory evaluation to rule out other diseases. A CBC, biochemical profile, urinalysis and fecal cytology and parasite evaluation is required in all cases. An eosinophilia or hypoproteinemia may provide clues to IBD. Abdominal radiographs or ultrasound may be helpful. However ultrasounds showing increased wall thickness is neither specific or sensitive for the diagnosis of IBD.[20] Specific testing may include measurement of fecal 1-proteinase inhibitor concentrations for documenting GI protein loss and measurement of serum folate and cobalamin concentrations. Cobalamin deficiency is a common complication of feline gastrointestinal disorders and complete improvement in GI function is not possible until cobalamin deficiency is corrected.[13]

An overall impression is that most cases of IBD can be managed but unless the underlying etiology can be identified and removed it can become a long term proposition.[21] A retrospective study demonstrated that only 26% of canine IBD cases progress to complete remission, with intermittent clinical signs remaining in approximately half of cases and 4% were completely uncontrolled with 13% being euthanized because of poor response to treatment.[22] Another study found 8% of the dogs were euthanized because of their disease.[21] Poor prognostic indicators are hypoalbuminemia and hypocobalaminemia.

It is estimated that about 30% of the dogs that fail diet and antibiotics will respond to corticosteroids. Generally oral prednisolone 1-2 mg/kg q 24h PO is given that is then tapered over an 8-week period. However, the side-effects of glucocorticoids can be marked and I never try to exceed a total of 40 mg per day in large breed dogs. Budesonide is a novel glucocorticoid that is reported to have a high first-pass hepatic metabolism and exerts a "local effect" on the intestine with minimal systemic effects. An enteric-coated formulation is used for humans with IBD but a non-enteric coated formulation made by a compounding pharmacy should be used. There is apparent efficacy using budesonide in dogs and cats but the systemic steroid effects are also present and consequently may have no benefit over traditional corticosteroid therapy in most cases. Recommended dose is 1 mg q 24h in cats and toy breeds and up to 2 mg q12h for large breed dogs.

If there is poor response to glucocorticoids after the first 3-4 weeks or if the side effects are severe then I recommend oral cyclosporine at 5-10 mg/kg q 24h, PO for at least 2 months. Many dogs with IBD that are steroid refractive are reported to respond to cyclosporine.[22] In cats,

the use of chlorambucil, 2-6 mg/m^2 q 24h, PO (alternatively 2 mg/cat given 3 times a week) with prednisolone is preferable if there is inadequate response to glucocorticoid treatment alone. Hematologic parameters should be monitored regularly if chlorambucil is used. Other novel or adjunct therapy could include omega 3 fatty acids for anti-inflammatory effects and various antioxidans. Probiotics have also been suggested to be beneficial for IBD due to multiple mechanisms described above.

WHEN PROTEIN IS LOST

Protein loss through the GI tract (PLE) generally results in a panhypoproteinemia with loss of albumin and globulins. There are many GI disorders that can cause enteric loss of proteins including primary and secondary intestinal lymphangiectasia, IBD, neoplasia or ulceration. When proteins levels get to the point of decreasing oncotic pressure thoracic or abdominal effusion, peripheral edema and thrombosis from loss of antithrombin (AT3) will occur (Figure 2). The Wheaten terrier, Lundehund and Basenji are over represented. The Yorkshire terrier appears to have a unique protein losing enteropathy associated with lymphatic dilatation, villous crypt lesions and stunting.[23] In addition to low protein, low cholesterol, decreased calcium and magnesium, and lymphopenia may occur. Endoscopic findings include large dilated lacteals over the mucosal surface (Figure 3).

Management of a PLE involves fat restriction (dietary fat increases intestinal lymphatic flow and subsequent protein loss).[24] Diets containing less than 25% fat in total calories is suggested. Hydrolyzed (Purina HA has 24% fat in calories) or special prescription diets are usually adequate. Sometimes more strict fat restriction requires home-cooked diets formulated by a veterinary nutritionist. In addition anti-inflammatory therapy, a bioflavonoid rutin, vitamin D and magnesium may also be required. With significant protein loss anticoagulants such as aspirin or clopidogrel to prevent thrombosis is indicated. When the total protein drops below 3 mg/dl the loss is significant and patients have a guarded prognosis.[25]

IS IT FELINE IBD OR LYMPHOMA

With a failure to respond traditional therapy for IBD in the cat one must consider GI lymphoma. Lymphoma is the most common neoplasia in the cat and approximately 10% of feline lymphomas involve the gastrointestinal tract. GI lymphoma has been classified histologically as B or T cell in origin. The most common is the low grade T cell lymphoma that is typically characterized by the mucosal and sub-mucosal infiltration of small well-defined lymphocytes. These lymphomas are usually FeLV negative. The low-grade lymphocytic form usually responds very well to chemotherapy. The infiltration in the bowl by the tumor generally results in malabsorption. In contrast lymphoblastic (generally B cell origin) usually present as a mass like lesion (most often stomach and colon) and generally has a poor prognosis and will not be discussed further.

Most cats with GI lymphoma (small cell) are middle aged or older DSH cats. Weight loss, vomiting, chronic small bowel diarrhea and progressive inappetance are common features of GI lymphoma. Some cats may only present with weight loss as the chief complaint. On physical examination the bowel may be normal or feel diffusely thickened. Mesenteric lymphadenopathy may also be identified. Less commonly organomegaly may occur.

Routine laboratory testing is often unremarkable or may reveal hypoalbuminemia. Anemia may also be present. Most all cats having GI lymphoma have significantly subnormal serum concentrations of cobalamin. Serum folate concentrations may also be reduced. Some cats may also have concurrent pancreatitis with increases in pancreatic lipase or cholangitis with increased liver enzymes. Ultrasound is useful for evaluating intestinal thickness or loss of normal layering and detecting mesenteric lymphadenopathy. The diagnosis can sometimes be made by demonstrating neoplastic lymphocytes in aspirates from enlarged intestinal or peripheral lymph nodes. Frequently though, lymph nodes show only reactive changes. Endoscopic visualization and biopsy can enable the accurate diagnosis of many cases of GI lymphoma. Endoscopy biopsies can however miss submucosal and serosal lesions or yield a diagnosis of lymphoplasmacytic enteritis (IBD) because of inadequate tissue. One report suggests that GI lymphoma is more common in ileum than in duodenum and so ileal biopsies are indicated in

suspected cases.[26] Because of concurrent liver and pancreatic disease and possible location of tumor in ileum a surgical exploratory may be indicated in some cases.[27]

In a study of 41 cats with low-grade lymphoma, the lymphoma was confined to the gastrointestinal tract in 68% of cats.[27] Eighty-nine percent of the lymphomas were determined to be of T-cell origin via immunohistochemistry, while 8% (3 of 36) were of B-cell origin. Fifty-five per cent of cats achieved a complete response to therapy and 37% achieved a partial response. The majority of cats (76%) received prednisolone at a dose of 5-10 mg, PO, q 12-24 hrs and most (85%) received chlorambucil at a dose of 2 mg, PO, every other day.[28] Overall median remission duration was 948 days. Partial response to therapy was associated with shorter remission duration. Overall median survival time was 704 days. No factors were significantly associated with survival time. Eight percent of the cats experienced no response. Hypocobalaminemia was found in 78% of cats tested and supplemental cobalamin (250µg SC q weekly) should be given as required. IV pulse chlorambucil or other chemotherapy may be also tried however in most cases every other day oral therapy is often easier for the client.

The differentiation of IBD and lymphoma histologically can sometimes be difficult and it is also possible IBD may progress to lymphoma over time. PCR evaluating for clonality PARR (neoplastic cells have one basic clone type) my help and is thought to be about 90% accurate for detecting lymphoma. Fresh tissue from a biopsy or an unstained histology slide is needed for this test. PARR is available at Colorado State University (http://www.cvmbs.colostate.edu/ns/departments/mip/cilab/faq_parr.aspx). More recently a blood test measuring thymidine kinase activity used to distinguishing feline IBD from GI lymphoma has become commercially available. Increased thymidine kinase activity results with proliferative neoplastic disease. As yet there is limited information on this test.

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Figure 1. A simplified approach to chronic diarrhea.

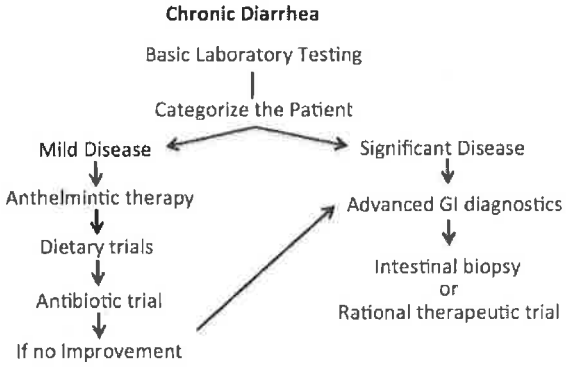

Figure 2. A young Yorkshire terrier with a protein losing enteropathy having with chronic diarrhea, panhypoprotenima, and abdominal effusion. Endoscopy showing large white dilated intestinal villi in the duodenum characteristic of lymphangiectasia and histology of intestine.

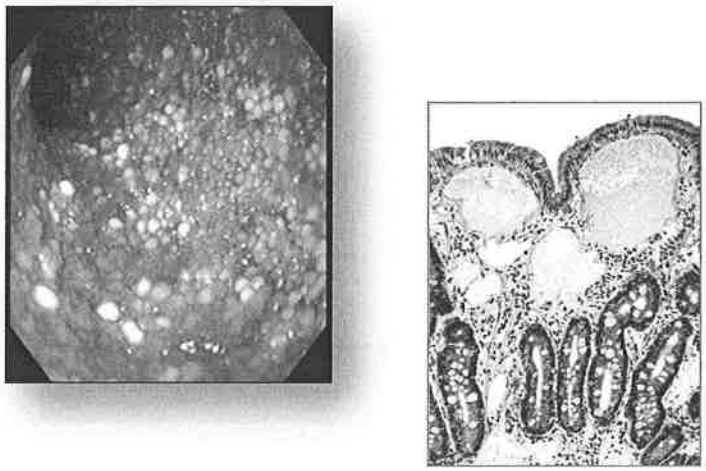

Table 1. Therapies used for treating Giardia in the dog and cat.

Drug	Dose	Comments
Metronidazole	Dogs and cats: 15-25 mg/kg q24h for 5-7 days PO	Neurotoxicity at high doses possible
Fenbendazole	Dogs and cats: 50 mg/kg q 24h for 5 days PO	Safe in dogs and cats
Febantel with pyrantel, praziquantel	Dogs: Label dose for 3-5 days	Feline dose: 56 mg/kg q24h for 5 days PO (based on the febantel dose)
Nitazoxznide (Alinia™)	10-25 mg/kg 12h PO, for 7 days	Little experience, resistant cases, frequent GI signs

A CLINICAL APPROACH TO THE DOG WITH ABNORMAL LIVER ENZYMES

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The identification of abnormal liver enzymes usually indicates liver damage but rarely provides a diagnosis or etiology. Abnormal liver enzymes are common and in a study of 1,022 blood samples taken from both healthy and sick dogs and cats, one diagnostic laboratory found 39% had ALP increases and 17% had ALT increases. When presented with a patient having abnormal liver enzymes it is important to recognize that the patient could have primary liver disease but more likely the patient has other primary non-hepatic condition resulting in secondary liver involvement. It is therefore important to perform a complete review of all other body systems.

It is also important to understand the reason for increased liver enzyme activity and the following sections will deal with liver specific tests.

Tests of Heptocellular Necrosis or degeneration

Increases in either alanine aminotransferase (ALT) or aspartate aminotransferase activity (AST) indicate hepatocellular membrane damage and leakage of the enzymes. This could be due to death of the hepatocyte or from hepatocyte degeneration where the membrane just has increased permeability. Conceptually ALT and AST should be thought of as hepatocellular "leakage" enzymes. Subsequent to an acute and diffuse injury, the magnitude of increase crudely reflects the number of affected hepatocytes. The plasma half-life of ALT activity is about 2.5 days (60 hours) in dogs however concentrations may take days to weeks to decrease following an acute insult based on models of acute hepatic injury. Persistent increased ALT and AST enzyme activity over weeks is characteristic of chronic hepatitis in the dog. As a general rule, ALT increases should be investigated when they are greater than twice normal or persistently abnormal over weeks to months. Hepatic AST is located predominately in hepatocyte mitochondria (80%) but is also soluble in the cytoplasm. Because of the mitochondrial location, AST elevations are more sensitive for liver disease than ALT and reflect more significant cell damage. On the other hand, AST is less specific than ALT because of the presence in other tissues (i.e., muscle so always check CK). Following an acute injury resulting in a moderate to marked increase in the serum ALT and AST concentrations, due to their difference in plasma half-life, the serum AST will return to normal more rapidly (hours to days) than the serum ALT (days).

Tests of Cholestasis and Drug-Induction

Alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT) show minimal activity in normal hepatic tissue but can become increased in the serum subsequent to increased enzyme production stimulated by either impaired bile flow or drug-induction. These enzymes have a membrane bound location at the canalicular surface; ALP associated more with the canalicular membrane and GGT associated more with epithelial cells comprising the bile ductular system. With cholestasis, surface tension in the canuliculi and bile ductules increases and production of these surface enzymes is then up-regulated. An increase in the serum ALP and GGT activity can be the result of induction by endogenous, topical or systemic glucocorticoids, anticonvulsant medications (ALP only) and possibly other drugs or herbs. The plasma

half-life for hepatic ALP in the dog is 66 hours in contrast to 6 hours for the cat and the magnitude of enzyme increase (presumably a reflection of the synthetic capacity) is greater for the dog than the cat. Bone source arises from osteoblastic activity and is elevated in young growing dogs before their epiphysial plates close or in some dogs with bone tumors or lytic lesions. One study identified that increased ALP concentrations in some dogs with osteogenic bone tumors tended to indicate a poorer prognosis, probably from diffuse bone metastasis. In the adult without bone disease, an increased serum ALP activity is usually of hepatobiliary origin. Hepatic GGT is located predominately on the canalicular membrane and bile ducts. Chronic elevations in GGT tend to better reflect hepatobiliary tract disease, with he most marked elevations resulting from diseases of the biliary epithelium such as bile duct obstruction, cholangiohepatitis, cholecystitis or neoplasia. In dogs, GGT has a lower sensitivity (50%) but higher specificity (87%) for hepatobiliary disease than total ALP. If ALP is elevated with a concurrent increase in serum GGT, specificity for liver disease increases to 94%. Bone does not contain GGT and the administration of anticonvulsant medications to dogs does not cause an increase in the serum GGT activity.

Evaluation of Liver Function

On a routine biochemical profile it is important to note the liver function tests (or tests that involve liver function) including bilirubin, albumin, glucose, BUN, and cholesterol. Bilirubin elevations can occur from hemolysis, hepatic dysfunction or extrahepatic cholestasis. Measuring the percent conjugated to unconjugated bilirubin to determine location is not useful in the dog. Albumin is exclusively made in the liver and if albumin is not lost, sequestered or diluted, a low concentration would suggest significant hepatic dysfunction. It may take greater than 60% hepatic dysfunction for albumin concentrations to decline. Cholesterol can be variable and increased in cholestatic conditions and decreased in portosystemic shunts. When glucose and BUN activity is low from liver dysfunction suggests significant hepatic disease and a guarded prognosis.

Bile Acids. Measurement of serum bile acids is thought to be the most sensitive function test that is readily available in small animal practice. Bile acids are synthesized from cholesterol in the liver and then conjugated and excreted into the bile. Bile acids are transported to the gallbladder and following a meal are excreted into the intestine where they emulsify fat for absorption. In the distal small intestine bile acids are actively resorbed and return to the liver where they are efficiently extracted by the hepatocytes and then re-circulated back into the bile. Only a small fraction of the total bile acid pool ever escapes into the systemic circulation. Thus, the enterohepatic circulation of bile acids occurs with a 95-98% rate of efficiency. The current suggestion for performing bile acid levels is to differentiate between congenital portal vascular anomalies and liver insufficiency, prior to the development of jaundice. The determination of total bile acids can contribute to the decision to obtain histological support for a definitive diagnosis. The fasting total serum bile acid concentration (FSBA) is a reflection of the efficiency and integrity of enterohepatic circulation. Pathology of the hepatobiliary system or the portal circulation results in an increased FSBA prior to the development of hyperbilirubinemia, therefore, bile acid measurement is not useful in the icteric patient. An increase is not specific for a particular type of pathologic process but is associated with a variety of hepatic insults or abnormalities of the portal circulation. Bile acids

should be used to screen patients with persistently abnormal liver enzymes, to determine if there could be loss of hepatic function, which adds further diagnostic support during investigation of the case. It is also helpful to measure bile acids to determine level of hepatic dysfunction in animals with PSS or portal vein hypoplasia (PVH), also known as microvascular dysplasa. When the fasting value is greater than 25 µmol/L for the dog and cat, there is a high probability that the histology findings will define a lesion.

When the total fasted bile acid concentration is normal or in the "gray zone" the FSBA should be followed by a 2-hour postprandial serum total bile acid (PPSBA) looking for an increase of greater than 25 µmol/L. The diagnostic value of determining PPSBA concentration is increased sensitivity for the detection of hepatic disease and congenital portal vascular anomalies. In dogs, the specificity of fasting and postprandial bile acids for hepatobiliary disease is 95% and 100% when cutoff values greater than 15 µmol/L and 25 µmol/L are used, respectively. When using these guidelines it is prudent to recognize that a small number of apparently healthy dogs have been reported with PPSBA values above 25 umol/L or these may actually represent dogs that have PVH. Occasionally the FSBA value is greater than the PPSBA value. The reason for this non sequitur is probably multifactorial. It has been shown that (1) the peak PPSBA concentration for individual dogs is variable, (2) fasted dogs store about 40% of the newly produced bile in the gallbladder and (3) a meal stimulates the release of only between 5 to 65% gallbladder bile. Undoubtedly these physiologic variables in addition to physiological variation in intestinal transit time and concurrent underlying intestinal disease contribute to the dichotomy.

Recently, urinary bile acids have become available as a diagnostic tool. Identifying increased urinary bile acids provides similar information to what is obtained from serum bile acids and neither test appears to be better than the other. The advantage of urinary bile acid measurements would be for the screening of litters of young puppies for suspected inherited vascular anomalies where urine collection is simpler than paired serum samples.

Coagulation Panels. Major clotting factors are synthesized in the liver (except factor 8) and therefore prolonged clotting time may suggest significant hepatic dysfunction or factor consumption. Because coagulation abilities may not be normal in patients with liver disease, it is advisable to check clotting times prior to performing liver biopsy.

Ammonia. High ammonia levels reflects abnormal hepatic portal shunting (acquired or congenital shunts) or significant hepatocellular dysfunction of greater than 70%. The liver detoxifies ammonia that primarily arises from the gastrointestinal tract by conversion to urea. Elevated fasting blood ammonia levels have been shown to be a sensitive (98%) and specific (89%) test for the detection of congenital or acquired portosystemic shunting in dogs. Due to problematic requirements for sample handling and submission, blood ammonia or the ammonia tolerance test is infrequently performed by some clinical practices. However, recent availability of blood ammonia for in-clinic analyzers, has helped make the test more feasible.

Diagnostic Strategies.

In the asymptomatic patient with an increased liver biochemical test(s) the increased value should be confirmed. If no likely explanation for the laboratory

abnormalities can be found there are two courses of action that one can take; either begin a diagnostic evaluation of the patient starting with bile acid determinations, or re-evaluate the patient's liver enzymes at a later date. The diagram below depicts a general algorithm for the work-up of dogs that have abnormal liver enzymes. The identification of abnormal liver enzymes may occur when the sick patient is presented for evaluation or during a routine health screen in the healthy patient. Abnormal liver enzymes in the sick patient could either be the result of primary liver disease/damage or secondary due to a multitude of other non-hepatic disorders. The most common cause of abnormal liver enzymes is in fact, not primary liver disease at all but rather the result of reactive hepatic changes occurring secondary to other non-hepatic causes. Generally, secondary hepatic changes are reversible once the primarily disease is treated. Successful resolution of the non-hepatic disease and continued abnormal liver enzymes would be a strong indication for further investigation of the liver for a primary disease process.

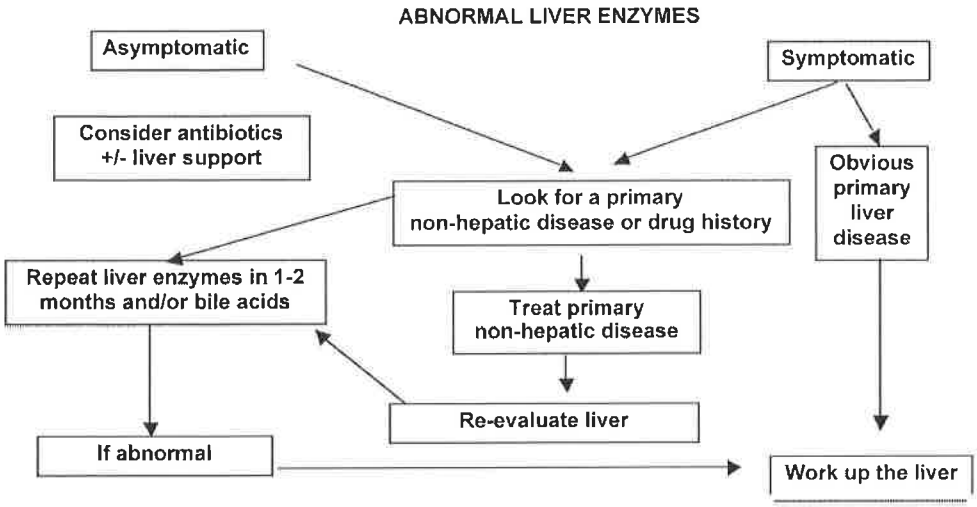
Imaging. Routine abdominal radiographs are helpful in determining liver size and shape and for detection of other intra-abdominal disorders. Ultrasonography is noninvasive, readily available and is the most informative initial imaging modality for liver disease. Ultrasound can determine parenchymal changes, mass lesions and disorders of the biliary system. Ultrasound however is not accurate in differentiation of the major parenchymal changes.

Fine needle aspiration (FNA) for cytological evaluation is safe easily performed using ultrasound direction. One should be cautious in over interpretation of those results however. FNA is best for identification of vacuolar hepatopathies and neoplasia and is poor in detecting inflammatory hepatic changes. In one study we found FNA and cytology to only correlate in about 1/3 of the cases.

Liver Biopsy. A biopsy is required for a definitive determination of the nature and extent of hepatic damage and to appropriately direct the course of treatment. The method for liver biopsy procurement may be surgery, ultrasound guided needle biopsy or laparoscopy. We believe if a needle biopsy is obtained that at least a 16g biopsy needle or larger be used and multiple liver lobes are biopsied. We generally take 3-4 biopsies with one split for culture and hepatic copper analysis and the remainder placed in formalin for histological evaluation

What You Might Find On A Liver Biopsy

When we evaluated 150 consecutive canine liver biopsies we identified the largest category to be secondary reactive hepatopathies (25%) followed then by chronic hepatitis (23%) and then neoplasia and vacuolar hepatopathies making up 69% of the biopsies performed. Smaller categories included vascular anomalies, acute liver damage and other miscellaneous conditions.



Reactive Hepatopathies, A Common Diagnosis

The so-called "non-specific reactive hepatopathies" (NSRH) that occur secondary to non-hepatic disease can result in increased serum biochemical hepatic tests and histomorphologic abnormalities. Most of the NSRH cause increases in laboratory tests that evaluate hepatocellular integrity (ALT, AST) and tests of hepatic cholestasis (ALP, GGT). In most cases there are little if any changes in tests that evaluate hepatic function (bilirubin, albumin, glucose, and BUN). Most of the animals with this type of secondary liver disease often retain normal hepatic function (albumin, serum bile acid concentrations), which again supports a concept that there is generally minimal loss of hepatocellular dysfunction. NSRH is often characterized by variable amount of hepatocellular degeneration or necrotic changes without evidence of significant chronic progressive inflammation. The reason the liver often undergoes these changes revolves from the fact that the liver is involved in so many metabolic and detoxification functions. Endogenous toxins, anoxia, metabolic changes, nutritional changes and endogenous stress related glucocorticoid release are all examples of conditions responsible for the majority of these changes. Gastrointestinal disease frequently results in secondary hepatic changes uptake of bacteria, toxins or nutrient abnormalities.

Histological findings associated with NSRH changes include descriptors such as vacuolar degeneration, hydropic degeneration, swollen hepatocytes, lipidosis, intracellular or intrahepatic cholestasis, mild multifocal hepatitis or periportal hepatitis or variable random hepatic necrosis. These changes are devoid of the typical progressive chronic inflammatory cell infiltrates characteristic of chronic hepatitis. Whenever I observe these changes on histology I always begin a search for an underlying etiology.

A good example that helps explain this concept is inflammatory bowel disease in which it is not unusual to observe mild inflammatory changes around portal triads presumed to be the result of abnormal portal uptake of gastrointestinal "toxins". Throughout the liver and closely associated with portal areas are Kupffer cells (fixed macrophages) that function to filter the blood of injurious toxins, inflammatory mediators

and bacteria. When this macrophage system is abnormally insulted Kupffer cells release their own inflammatory mediators that in turn insult the hepatocytes.

In a review of consecutive liver biopsies at Colorado State University histology grouped as non-specific reactive changes made up the largest category of abnormalities (approximately 25%) In this group we were able to identify an associated disease in many that could explain the likely cause for the hepatic enzyme increases and histological changes observed. Concurrent diseases identified included neoplasia, gastrointestinal, renal, autoimmune, dermatologic, dental, infectious and cardiac disease as a few examples. In some cases an underlying disease is not identified. The ALT values on the average are 1-2 X normal and the ALP values 1-3 X normal. It is interesting to note that in a series of 32 dogs having reactive hepatopathies, 8/8 cases in which serum bile acids were run, all were within the normal reference range again suggesting hepatic function tends to remain intact.

This category appears to be the most common histological change to occur in dogs and is by far the most common cause of elevated liver enzymes. Based on this fact, dogs presented with elevations in ALT and ALP should always have primary non-hepatic disease ruled out first. These changes are usually very reversible and no specific hepatic therapy is required short of treating the primary disease. The liver changes resolve once the primary etiology is successfully treated. Therapy providing good liver support such as antioxidants may be warranted.

Summary

Abnormal liver enzymes should not be ignored and should be investigated in a systematic manner as previously discussed. Asymptomatic animals with no evidence of significant or treatable disease or in situations where financial constraints limit further work up the patient should be fed a quality maintenance diet for the patient's stage of life and the possibility of instituting specific liver support therapy should be explored.

COMMON LIVER DISEASES IN THE DOG

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Abnormal liver enzymes are a common encounter in the dog and can be due to a number of etiologies. The following discussion includes some common conditions. Another common histological diagnosis is chronic hepatitis but this will be discussed elsewhere as there are important implications of specific diagnostic testing,therapy, and prognosis.

Reactive Hepatopathies. These occur secondary to non-hepatic disease with in increased serum biochemical hepatic tests (ALT, AST, GGT, ALP) and histomorphologic abnormalities. In most cases there are little if any changes in tests that evaluate hepatic function (bilirubin, albumin, glucose, BUN and bile acids). Histological findings associated with secondary reactive changes include descriptors such as vacuolar degeneration, hydropic degeneration, swollen hepatocytes, lipidosis, intracellular or intrahepatic cholestasis, mild multifocal hepatitis and periportal or variable hepatic necrosis. These changes are devoid of the typical progressive chronic inflammatory cell infiltrates characteristic of chronic hepatitis. The reason the liver often undergoes these changes revolves from the fact that the liver is involved in many metabolic and detoxification functions. Endogenous toxins, anoxia, metabolic changes, nutritional changes and endogenous stress related glucocorticoid release are examples of conditions responsible for the majority of these changes. Even non-specific mild liver changes routinely also occur following general anesthesia. In a review of liver biopsies at Colorado State University reactive hepatopathies made up the largest category of abnormalities (approximately 25%).

Vacuolar Hepatopathies. Hepatic vacuolar change is a common histological diagnosis in dogs but not cats. When we reviewed 150 consecutive liver biopsies performed at Colorado State University approximately 12% of the cases had predominately a vacuolar hepatopathy (VH) as the major histological finding. By definition according to the WSAVA Liver Standardization Group VH refers to a reversible parenchymal change that is characterized by swollen hepatocytes with clear cytoplasm due to glycogen without displacement of the nucleus from the center. The distributionand the extent of the lesion can vary being either diffuse, zonal, or involve individual cells. VH is a relatively easy histological diagnosis to make however Periodic acid Schiff (PAS) staining with or without diastase can be used to demonstrate glycogen accumulation. Vacuolated hepatocytes can also result from fat accumulation secondary to abnormal fat metabolism and is referred to as hepatic steatosis or lipidosis. Hepatic steatosis is a distinct histological vacuolar classification associated with abnormal fat metabolism and will not be discussed in this chapter.

VH in dogs is most often associated with hyperadrenocorticism (HAC). The dog is particularly sensitive the effects of glucocorticoids that both induce serum alkaline phosphatase (ALP) steroid isoenzyme activity and causes hepatic glycogen accumulation. (see chapter Evaluation of Elevated Alkaline Phosphatase in Evolve). Congenital glycogen storage disorders, breed specific disorders, hepatic nodular

hyperplasia and a variety of stress-associated secondary diseases are conditions that can cause this typical hepatic vacuolar changes. In a large study of 336 histological liver specimens having VH (defined as making up greater than 25% of the hepatocytes) were retrospectively reviewed for an underlying etiology (Hill et al., 2006). The authors report 55% of the cases were associated with either endogenous or exogenous glucocorticoids with the remaining 45% having no known glucocorticoid exposure. Most all of the dogs with no glucocorticoid exposure had other identifiable concurrent illness. Conditions such as renal, immune-mediated, cardiac, hepatic, gastrointestinal disease, or neoplasia accounted for many cases. The author's hypothesis was that stress-induced hypercortisolemia associated with acute or chronic illness likely contributed to the development of the VH. A second *in vivo* study showed that by experimentally inducing a chronic four to five-fold elevations in plasma cortisol concentrations to simulate a stress-like state in normal dogs inhibited non-hepatic glucose utilization and increased hepatic gluconeogenesis and glycogen formation through enhanced substrate delivery to the liver.

Idiopathic Vacuolar Hepatopathy. There is a subset of dogs having elevations in serum alkaline phosphatase and excessive hepatic glycogen accumulation that do not have evidence of either a stress induced illness, evidence of HAC based on cortisol testing, a history of recent glucocorticoid administration or have a specific hepatic disease. These dogs are referred to as having an idiopathic vacuolar hepatopathy (IVH). They generally have no clinical signs and are usually identified during investigation of unexplained elevations in serum alkaline phosphatase (ALP) found on a routine health screen. Several theories have been put forward as to the cause of IVH. Some believe adrenal progestagens; most likely increases in 17-hydroxyprogesterone and progesterone are responsible as these changes as they are frequently identified to be abnormal when a commercial adrenal steroid panel is performed. However, critical evaluation and validation of the adrenal steroid panel (17-hydroxyprogesterone, progesterone, estradiol, testosterone and androstenedione) is as yet still lacking and a direct association has not be made. Because the VH changes are typical of glucocorticoid excess it is entirely possible that a yet to be identified adrenal steroid could be responsible for the VH. Obviously future research is necessary to delineate this syndrome and the relationship to adrenal steroids.

Scottish terriers are also reported to have a breed-specific syndrome associated with a VH and elevated serum ALP. These affected dogs generally have no clinical signs. The authors found that the elevated ALP was predominately the corticosteroid isoform and following ACTH stimulation test in conjunction with an adrenal steroid panel found increases in one or more non-cortisol steroid hormones. The authors conclude that affected Scottish terriers have a type of hyperadrenocorticism on the basis of exaggerated adrenal hormone response. We have also observed similar non-cortisol steroid hormone increases in Scottish terriers but also in Scottish terriers without VH or increases in ALP adding more confusion to this syndrome. The reader should refer to Chapter 51, Occult hyperadrenocorticism: Is It Real? for further information concerning adrenal steroids.

Dogs with IVH generally have no clinical signs. They are usually identified serendipitously on a biochemical profile identifying elevations in serum ALP concentrations that subsequently initiates a diagnostic work-up. Most affected dogs are

middle-aged or older at the time of diagnosis. There does not appear to be a breed or sex predisposition other than the syndrome described above in the Scottish terrier. A small percent of dogs may have reported polyuria and polydipsia (PU/PD) but the other signs typical of HAC are generally absent. The work up of the asymptomatic dog having an IVH usually begins after the identification of an elevation in serum ALP. The ALP increases are often 5 to 10 times normal concentrations; the other liver enzymes are usually normal or there are occasional mild elevations in alanine aminotransferase (ALT) and gamma glutamyl transferase (GGT). Marked elevations in liver enzymes other than ALP is not typical of this syndrome and if present other types of liver disease should be investigated. The work-up should first rule out common causes for an elevated ALP such as drug administration (including topical or systemic steroids, phenobarbital, or herbal medications), cholestatic liver disease, or bone disorders. Next adrenal testing (ACTH stimulation or low dose dexamethasone suppression) would be prudent to perform to eliminate possibility of HAC. Determining the percent of ALP steroid isoenzyme is generally not helpful. Dogs with IVH will have predominately a steroid-induced ALP isoenzyme but this is neither specific for HAC or IVH and other non-adrenal illness may also have similar increases in the steroid-induced ALP isoenzyme. Basic tests of liver function tend to be normal however the author has seen a few cases having very mild elevations in serum bile acids. Abdominal ultrasound of the liver is helpful to rule out hepatic nodular hyperplasia, occult hepatic neoplasia or cholestatic disorders that all could be differentials for an elevated ALP. Affected IVH dogs generally have an enlarged uniformly hyperechoic liver with rounded borders. Adrenal glands are generally normal. Fine needle aspiration of the liver with cytology supports a diffuse vacuolar change. A PAS stain of the cytology sample can help confirm the presence of hepatic glycogen. A liver biopsy confirms diffuse vacuolar change but is rarely necessary. I generally make the diagnosis of IVH based on the above diagnostic findings and after exclusion of HAC, drugs, hepatic nodular hyperplasia, hepatic neoplasia or cholestatic liver disease.

At this time I believe adrenal sex steroid panel testing for most cases is not necessary for two reasons; first, our inability to adequately interpret the tests results and second, most all IVH dogs are generally asymptomatic and information obtained from the testing offers little important diagnostic or therapeutic information. Several labs offer adrenal hormone analysis and currently the most extensive adrenal steroid hormone profile is offered by the Clinical Endocrinology Laboratory at the University of Tennessee. The protocol for running the test is identical to that for a standard ACTH stimulation test.

Both proteinuria or hypertension are occasionally identified in cases of IVH and the affected dos should be periodically monitored for these complications and if identified, managed appropriately. Dogs with IVH are also thought to have an increased risk for developing biliary mucoceles and there is also some anecdotal evidence to suggest that some Scottish terriers with VH are at an increased risk of development of hepatic neoplasia (hepatocellular adenoma or carcinoma). Consequently it would be prudent to monitor IVH dogs from time with an ultrasound of the liver and biliary system.

The management of IVH is controversial at best and there are no studies critically evaluating therapy for this syndrome. I believe that specific therapy is unnecessary unless complicating factors such as hypertension, proteinuria or significant

PU/PD exist. Problem associated with therapy arise from the fact we do not know what the endpoint of therapy should be; is it normalization of adrenal hormones, return of ALP into the normal range or histological resolution of the VH? There are anecdotal reports of dogs with IVH being successfully treated using low doses of mitotane and monitoring clinical parameters and measuring adrenal steroid concentrations including cortisol to assure hypoadrenocorticism does not result. Trilostane often shows a similar clinical response however concentrations of 17-hydroxyprogesterone and progesterone are frequently higher following this therapy. Ancedotal reports of clinical improvement in dogs having IVH using either oftherapy does suggesting abnormal adrenal steroid production may be involved in the pathogenesis of this syndrome. However these treatments beg the question if therapy is warranted due to the expense of medication and monitoring and the potential complications associated with the therapy alone. Until more is known about this syndrome this author can't recommend specific adrenal therapy unless significant clinical findings would warrant a trial therapy.
Alternative therapies suggested include melatonin and flax seed products. Melatonin has been shown to decrease sex hormone concentrations in normal dogs. It is reported to be beneficial in some dogs with alopecia X syndrome, and has also been suggested for IVH. Doses of 3 mg/15 kg q 24h PO has been recommended however here is no published data showing effectiveness for dogs with IVH. Flaxseed hull products with lignans have also been suggested because they compete with estridiol production but again there is no reported evidence of benefit for IVH syndrome.

Liver support therapy using products such as s-adenosylmethionine (SAMe), the milk thistle products, or other antioxidants may have some beneficial effects. One study showed dogs given glucocorticoids and treated with SAMe failed to show a decrease in serum ALP or amount of VH but did have improvement in hepatocyte oxidative status through increased glutathione concentrations. The above products are generally safe for liver support but will unlikely have any effect in the resolution of IVH.

Hepatic Nodular Hyperplasia. This is a benign process causing an increase in hepatic values and histomorphologic changes that include macroscopic or microscopic hepatic nodules containing vacuolated hepatocytes. Liver function remains unchanged. Grossly, the appearance may be suggestive of chronic hepatitis or neoplasia. The etiology is unknown but appears to be an aging change in dogs; most of those affected are greater than 10 years of age. Laboratory findings include an ALP increase (mean ALP ~ 600 IU/L), but some may have mild increases in ALT and AST concentrations as well. Ultrasound may be normal or may demonstrate larger nodules (many can be only microscopic and not observed on ultrasound). Biopsy confirms the diagnosis, however a wedge section is preferred. A needle aspirate or needle biopsy may only demonstrate show a vacuolar hepatopathy There is no specific therapy and it does not progress to a neoplastic process.

Hepatic Neoplasia. In the dog liver tumors can be either metastatic or primary. Metastatic tumors are more common and would include the carcinomas and sarcomas. Hepatocellular ademoma is common in dogs and generally restricted to a single liver lobe. Previous terminology calls these tumors as hepatomas human terminology that is incorrect. These tumors are very slow growing and often are found as an incidental

finding on ultrasound as a work up for abnormal liver enzymes. There is no spread to this tumor. Often we will just watch them using ultrasound every several months and if they grow in size rapidly then surgery can be suggested. If they become large they may not lend to resection or may become necrotic and rupture causing abdominal bleeding. Hepatocellular carcinomas are malignant neoplasms that can be either solitary (more slowly growing) or diffuse having a poor prognosis. Sometimes telling the difference from adenoma and carcinoma is difficult FNA or a biopsy sample. It has also been reported that large liver masses may be associated with hypoglycemia due to production of a insulin like factor. The more diffuse cholangiocellular and hepatic carcinomas have poorer prognosis and do not respond well to chemotherapy.

CHRONIC HEPATITIS LATEST UPDATE IN THE DOG: DIAGNOSIS AND TREATMENT

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Chronic Hepatitis is an etiologic diverse and morphologically variable condition associated by mixed inflammatory cell infiltrates. It is characterized by hepatocellular apoptosis or necrosis, a variable mononuclear or mixed inflammatory infiltrates, regeneration and fibrosis. The proportion and distribution of these components vary widely. Plasma cells, lymphocytes and macrophages predominate with a lesser number of neutrophils. Because we see mild portal inflammation as a common non-specific reactive change it is important that pathologist conveys that there is moderate to severe inflammation and necrosis and that the disease is chronic. The presence of fibrosis in the hepatic biopsy usually denotes to me more serious consequences. As damage progresses cirrhosis can result with diffuse fibrosis, alteration in hepatic lobular architecture with the formation of regenerative nodules and abnormal vascular anastomoses. Cirrhosis is often associated with portal hypertension, ascites and multiple portosystemic collateral shunts. Some may show manifestations of liver failure, e.g., hyperbilirubinemia, coagulopathies, edema due to hypoalbuminemia, ascites and hepatic encephalopathy.

ETIOLOGY

The etiology of chronic hepatitis is generally never determined. To date, the definitive described etiology of chronic hepatitis is the copper associated hepatitis of the Bedlington terrier (see copper below). Copper associated chronic hepatitis has also been documented in a number of other breeds as well and the precise mechanism of copper accumulation in non-Bedlington terrier is poorly understood. But regardless of the etiology, as copper accumulates in hepatocyte it becomes toxic to hepatocytes.

Infectious chronic hepatitis in man is most often associated with viral etiologies. The search for a direct link to a viral etiology and hepatitis in the dog however has as yet been unrewarding. Chronic hepatitis has also been associated with leptospirosis with authors describing "atypical leptopsires" in a colony of dogs having a reactive type of hepatitis. Other infectious agents suggested by others as a possible etiology include *Helicobacter sp*, Bartonella, Leishmaniasis and others.

Chronic liver injury has also been reported in dogs with aflatoxicosis as well as various drug-induced hepatitis. Some dogs treated with anticonvulsant drug phenobarbital will develop chronic hepatitis. We have also observed some dogs being treated with NSAIDs to also have hepatitis that bears the questions of a link between NSAIDs and hepatitis. NSAIDs have been associated with acute hepatic necrosis. In man alpha-1-antitrypsin (AAT- also referred to as alpha one protease inhibitor) deficiency is known to cause chronic hepatitis and cirrhosis. Investigation by researchers in Sweden using immunostaining for AAT in hepatocytes found some dogs with chronic hepatitis to be positive for ATT in the hepatocytes but the dogs differ from man in that serum AAT remained in the normal range while humans have low concentrations. It is not known if the AAT accumulation is the cause or the result hepatocyte damage. The breed most often associated with AAT accumulation is thought to be the cocker spaniel.

Finally, immune associated hepatitis may also occur in the dog. Autoimmune liver disease in humans is an important cause of chronic hepatitis and is associated with

diagnostic circulating autoantibodies. Specific autoantibodies (ANA, antimitochrondial antibodies [AMA], smooth muscle antibodies [SMA], liver membrane autoantibodies [LMA]) are markers of autoimmune hepatitis in humans. A number of studies have been performed in dogs looking for liver associated antibodies and cell-mediated responses to support autoimmune disease as an etiology. Findings so far suggest autoimmune liver disease likely occurs but studies fail to conclusively prove its existence. The pathogenesis proposed is that an insulting agent damages the hepatocytes thus releasing liver antigens that initiate a secondary immune response perpetuating chronic hepatitis. Nonetheless, immune-mediated mechanisms are thought to occur in some cases of chronic hepatitis and this is further supported by the fact that some dogs respond favorably to immunosuppressive therapy.

There are also a number of breeds that have an increased incidence of chronic hepatitis and thought to be inherited. Some of these breeds have copper associated chronic hepatitis and are discussed below. Other breeds not yet associated with copper include the standard poodle, Cocker spaniel, English Springer spaniel and Scottish terrier. The pathogenesis of the hepatitis in these dogs is yet unknown. Cocker spaniels both English and American tend to be more commonly males. Standard poodles are more commonly females and tend to have prolonged survival with immunosuppressive therapy suggesting possible autoimmune mechanisms.

COPPER ASSOCIATED HEPATITIS

When we reviewed liver biopsies of 130 dogs having histological evidence of inflammatory liver disease we found 49% of those dogs also had abnormal hepatic copper (>400 ppm) with a mean copper content of 984 ppm. The mechanism of copper accumulation for most dogs is yet unknown. Abnormal hepatic copper accumulation may result from increased dietary copper intake, from defects in copper metabolism (copper located in zone 3 location) or secondary to cholestasis (zone 1 location). The Bedlington terrier has an inherited disorder of copper homeostasis as the result of a deletion of the COMMD1 gene involved in abnormal hepatic copper excretion. Some other breeds associated with abnormal copper accumulation include the Doberman pinscher, Dalmatian, West Highland white terrier and the Labrador retriever. The mechanism of copper accumulation in these and other breeds is yet to be elucidated.

We now speculate that a number of other dogs may have the inability to handle dietary copper resulting in hepatic copper accumulation. This theory comes about because the normal hepatic copper concentration for dogs has been increasing over the years and the fact that canine commercial diets are over supplementation with copper (if you compare that to copper requirements for humans). Further, in a study investigating feral dogs that were unlikely to have ever eaten commercial dog food were found to have significantly lower hepatic copper concentrations compared with normal control dogs eating a commercial diet. Consequently, we believe some dogs taking in excessive copper may have the inability to handle the high copper will develop copper associated hepatitis.

The definitive diagnosis of abnormal hepatic copper requires a quantitative analysis of liver tissue Cu. A semi-quantitative estimation involves histochemical staining for hepatic Cu. Reliable tissue bound copper stains include used rhodanine and rubeanic acid. A grading system estimating the quantity of Cu granules correlates roughly with quantitative determination of hepatic Cu.

CLINICAL FINDINGS

The incidence of chronic hepatitis makes up approximately one fourth of the cases having liver biopsies at Colorado State University (based on a review of 150 consecutive liver biopsies). Chronic hepatitis is more common in female dogs. The average of presentation ranges from 4 to 10 years. It is interesting to note that in both our series and in studies by others it is uncommon to observe chronic hepatitis/cirrhosis in dogs older than 10-11 years of age. As a general rule old dogs (> 11 years of age) don't generally present with chronic hepatitis/cirrhosis or if they do they are at or near end stage disease.

The clinical signs parallel the extent of hepatic damage. Early in the disease there are usually no or minimal clinical signs. Only after the disease progresses do the clinical signs specific for liver disease becomes evident. Frequent early signs are gastrointestinal associated with vomiting, diarrhea and poor appetite or anorexia. Ascites, jaundice and hepatic encephalopathy may then occur as the disease progresses. With development of these late signs the long-term prognosis is generally poor.

The laboratory findings include consistently elevated ALT and ALP. The magnitude of rise need not be marked however. One report found 75% of the cases with abnormal bilirubin elevation (mean elevation of 2.6 mg/dl). Serum proteins are variable. As the lesions become more severe albumin levels decline. Serum bile acids are abnormal in most cases having significant chronic hepatitis and measurement of bile acids appear to be a good screening test for the patient with unexplained elevations in ALT and ALP. In our study all dogs evaluated with chronic hepatitis had abnormal bile acid concentrations. In a second study only 8/26 dogs with chronic hepatitis had normal fasting bile acids. However, postprandial samples were not determined in these cases. Determining postprandial bile acids has been shown to increase the sensitivity of this test.

A presumptive diagnosis is made based on the clinical features and persistent increases in ALT values. A definitive diagnosis requires a hepatic biopsy showing characteristic morphological patterns. Needle aspirates are not helpful in making the diagnosis of chronic hepatitis because it is important to see the architecture of the liver and location and extent of the inflammation. One must work with the pathologist when making the diagnosis of chronic hepatitis and to be certain that characteristic abnormalities found in chronic hepatitis are present.

PROGNOSIS

There is little information of the prognosis with and without therapy. The prognosis in dogs with advanced chronic hepatitis and cirrhosis is guarded. In a study by Strombeck found mean survivals ranging from 6 to 16 months with therapy. This study also identified that dogs with hypoalbuminemia, hypoglycemia and coagulopathies have very guarded prognostic factors and many died within 1 week of diagnosis. A second study of 79 dogs found that dogs with cirrhosis had a survival of less than one month and dogs with chronic hepatitis had a mean survival in the range of about 20 to 30 months. Most of these dogs were not advanced in their disease and had concurrent corticosteroid treatment.

TREATMENT

There should be four general goals of therapy: 1) remove the etiology, 2) provide an adequate diet, 3) give specific therapy and 4) providing general liver support. First step in the therapy for chronic hepatitis and other liver diseases involves removing the primary etiology if it can be identified. Short of treating the primary etiology all other therapies suggested are unproven in the management of liver disease in dogs. Much of the therapy

is directed at providing adequate liver support. This often involves the use of multiple therapies.

Diet. Adjusting diet therapy should be considered and formulated for the individual case. However a few general guidelines should be kept in mind. First, palatability is important to assure adequate energy requirements are met. Next, there is a misconception about protein and liver disease as many believe all patients should be placed on a protein-restricted diet. Protein restriction should only be instituted in the patient that has clinical evidence of protein intolerance (i.e. hepatic encephalopathy). The goal of dietary therapy is to adjust the quantities and types of nutrients to provide nutrient requirements but to avoid the production of excess nitrogen by-products associated with liver disease. As a general recommendation the dietary protein should represent 17 to 22% of digestible Kcal. High carbohydrate and moderate fat content is important to supply caloric needs. Mineral supplementation containing high concentrations of both copper and iron should be avoided.

Diets low in copper are recommended for the dogs that have copper associated liver disease based on liver biopsy. However the restriction of dietary copper may do little to lower hepatic copper concentrations in diseased dogs having already large amounts of hepatic copper but diet will lessen further absorption of the metal. It is difficult to limit dietary copper because most commercial dog foods contain supplemental copper that likely exceeds the dog's actual dietary requirements. Most formulated "liver diets" have lower copper concentrations and are recommended. Homemade diets can also be prepared so that they do not to contain excess copper. These diets should exclude liver, shellfish, organ meats and cereals that are all high in copper content. Vitamins or mineral supplements should not contain copper or iron. The company Balance It™ makes a copper free dietary vitamin mineral supplement that can be used with homemade diets.

Antiinflammatory Therapy. Decreasing inflammation with anti-inflammatory therapy is indicated for chronic hepatitis in the dog. The treatment of chronic hepatitis however is controversial and there are as yet no good controlled studies in dogs that support corticosteroids or immunosuppressive drugs. Antiinflammatory therapy is indicated in suspected immune mediated chronic hepatitis in humans and likely indicated in immune mediated hepatitis in dogs.

One study by Strombeck found some dogs with chronic hepatitis had a prolonged survival when treated with corticosteroids when compared to dogs not given corticosteroids. This retrospective study is flawed because of the wide diversity of different breeds and multiple other concurrent therapies used. But none-the-less, it appears that corticosteroids offer benefit with prolonged survival in at least some cases (around 25% in Strombeck study). A suggested initial dose of 1 to 2 mg/kg/day of prednisolone is given. When clinical improvement is evident or after several weeks of therapy the dose is then gradually tapered eventually to a dose of 0.5 mg/kg/day or given every other day. The only accurate way to evaluate a response to corticosteroid therapy is to re-biopsy the patient after approximately 6 months to 1 year of therapy. During therapy it is impossible to interpret liver enzymes or predict improvement because the patient has a concurrent steroid hepatopathy. Short of biopsy one could also stop corticosteroids and then after a period of time (approximately 1 to 2 months later) determine if there is improvement in liver enzymes.

Because of the side effects of corticosteroids and the failure to successfully monitor liver enzymes while receiving steroid therapy other immune suppressive therapy may be a more rational approach. Azathioprine is an effective immunosuppressant drug that has

shown to increase survival in man when treated for chronic hepatitis in conjunction with corticosteroids. This therapy may also be beneficial in dogs (don't use in cats) by increasing the immunosuppressive response and enabling a reduction of both steroid dose and their side effects. A dose of 2.2 mg/kg/day is the suggested starting dose and after several weeks given every two days. The level of glucocorticoids can frequently be reduced when using azathioprine. It is important to note that azathioprine has occasionally been associated with a drug induced hepatic necrosis or acute pancreatitis. We have more recently been using cyclosporine in many cases with a very good clinical response. Our experience using 5 mg/kg bid or q 24 hrs (without steroids) has been very encouraging in dogs that are thought to have immune mediated chronic hepatitis. The veterinary formulation Atopica™ is a microemulsified preparation with the identical properties to the human product Neoral™ and is also sold as modified generic cyclosporine that ensures more consistent bioavailability and better than the other human product Sandimmune™. I will get a blood level at the trough (right before the next pill) if I feel the patient is not responding adequately to the therapy. The ideal range of blood levels are within 400-600 ng/ml. Many dogs will develop gingival hyperplasia at the higher concentrations of cyclosporine. Azithromycin 10 mg/kg/day for 4-6 weeks will decrease the gingival hyperplasia. With evidence of clinical response at 5 mg/kg bid (normalization of ALT) I will often decrease to once a day or even every other day therapy. The advantage of using cyclosporine alone is one can follow the liver enzymes making the need for a liver biopsy less frequently required.

Copper Reduction. If the liver biopsy of a dog with chronic hepatitis indicates significant abnormal hepatic copper accumulation, a low copper diet and copper chelation or zinc therapy should be started. I believe hepatic copper levels of greater than 750 µcg/g dry weight (dw) liver (normal <400 µg/g dw) requires therapy to reduce copper concentrations. Animals having greater than 1,500 µcg/g dw should all have chelator therapy because that is a concentration considered to definitely be toxic to hepatocytes.

Zinc given orally as the acetate, sulfate, gluconate or other salt has been shown to be effective in preventing hepatic copper absorption from the GI tract in Wilson's disease patients that have been previously decoppered with penicillamine. Oral zinc therapy works by causing an induction of the intestinal copper-binding protein metallothionein. Dietary copper binds to the metallothionein with a high affinity that prevents transfer from the intestine into the blood. When the intestinal cell dies and is sloughed, the metallothionein bound copper becomes excreted through the stool. I will sometimes use zinc after a course of chelation therapy or as a primary therapy in a dog having modest hepatic copper accumulation or when the client can not afford penicillamine therapy. An initial induction dose of 5-10 mg/kg body weight divided BID of elemental zinc. Following one to 3 months of induction period the dose can be reduced in approximately half. The goal is to get serum zinc concentrations greater than 200µg/dl but less than 500 so I will often check serum zinc concentrations several times during a course of therapy. The zinc must be administered on an empty stomach and has the frequent side effect of vomiting. Zinc also has anti-fibrotic and hepatoprotective properties as well.

Chelator treatment using penicillamine is the primary therapy for copper associated liver disease. Penicillamine binds with copper and then promotes copper removal through the kidneys. Penicillamine is the most frequent copper chelator recommended for use in dogs. The dose is 10-15 mg/kg bid given on an empty stomach. Side effects include anorexia and vomiting but can be managed by starting at a lower dose and then increasing the dose over time or by giving a small amount of food with the drug. Therapy using

penicillamine is a slow and prolonged process taking months to cause a substantial reduction in hepatic copper concentrations. Penicillamine also has been shown to have a protective effect in the liver beyond chelation therapy. It is believed penicillamine induces a hepatic copper binding protein, metallothionein, thus binding and sequestering copper in a nontoxic form in the liver. A second copper chelator is trientine (Syprine™) that has been produced to use in patients intolerant to penicillamine. This drug is also given at a dose of 15 mg/kg bid and has less gastrointestinal adverse side effects but is expensive and sometimes difficult to obtain. The length of chelation therapy is variable but based on past experience some general recommendations can be made. Ideally repeat liver biopsies should be obtained to determine success of the chelation and to direct duration of therapy. The following is only a general recommendation; if copper is less than 1000 I will generally treat for 3-4 months, if 1000-2000 I treat for 4-6 months and if greater than 2000 6-8 months. I monitor ALT levels and if they become normal I often discontinue therapy, maintain on a low copper diet and will in some cases consider zinc supplementation as well. Ideally repeat liver biopsies with copper quantitation is the gold standard to direct therapy.

Antifibrotic Drugs. Corticosteroids, zinc and penicillamine all have anti-fibrotic effects. Colchicine is a drug that has been used in treating persons with chronic hepatitis and other types of liver fibrosis. This drug interferes with the deposition of hepatic collagen and also stimulates collagenase activity to breakdown deposited fibrous tissue in the liver. It also is shown to have anti-inflammatory properties. There is still the lack of convincing data in humans and dogs with liver disease that colchicine is beneficial. A critical appraisal of colchicine in human liver disease having chronic hepatitis now questions its effectiveness and failed to show benefit in a placebo controlled meta analysis of over 1000 patients. There are only 3 case reports of colchicine in dogs having questionable results. A dose of 0.03 mg/kg/day has been suggested. Recently it was found that angiotensin II enzyme inhibitors such as Losartan (Zestril™, 0.25-0.5 mg/kg/day) has effects in reducing or preventing fibrosis in humans by inhibiting hepatic stellate (fibrosis producing) cells. We have used losartan in dogs having a primary fibrotic component of their liver disease but no controlled studies are available to determine effectiveness.

Choleretic Drugs. Decreasing cholestasis has been shown to be of benefit in humans and animals having cholestatic hepatobiliary disease. As serum bile acid concentrations increase (these are predominately cytotoxic bile acids) they can cause cell membrane permeability changes and fibrogenesis. Ursodeoxycholic acid (Ursodiol) is a choleretic agent developed to dissolve gallstones but later fond to have positive effects in patients with chronic hepatitis. This drug is a synthetic hydrophilic bile acid that essentially changes the bile acid pool from the more toxic hydrophobic bile acids to less toxic hydrophylic bile acids. Ursodeoxycholic acid has been shown to increase bile acid dependent flow, reduce hepatocellular inflammatory changes, fibrosis and possibly some immunomodulating effects. The hepatoprotective characteristics of ursodeoxycholic are that of a super antioxidant. The dose for ursodeoxycholic acid is 10-15 mg/kg daily. No toxicity has been observed in dogs and cats at this dose. There has been a concern raised by some that it should not be used if there is any possibility of a bile duct obstruction for fear of biliary rupture. Ursodeoxycholic acid is not a prokinetic and will not cause a gallbladder rupture. In fact, in experimental bile duct obstructions there was less secondary "toxic" changes in the liver in rats given ursodiol than placebo.

Antibiotics. Antibiotics are indicated for primary hepatic infections. However secondary bacterial colonization may also take place in a diseased liver due to Kupffer cell

dysfunction. Kupffer cells function as the primary filter of portal blood entering the liver. It is known that portal blood is not sterile and with hepatic disease bacteria may enter the liver. It may be prudent for antibiotic therapy trial for several weeks in patients having significant hepatic disease (i.e. chronic hepatitis). Amoxicillin, cephalosporin, or metronidazole is suggested. If metronidazole is given we suggest 7.5-10 mg/kg bid which is a much lower dose used for other bacterial infections because of hepatic metabolism of the drug.

Antioxidants. There has been recent interest in the management of certain types of liver disease using various antioxidants as liver support. Antioxidants in general may help promote optimal hepatic function. Considerable evidence shows that free radicals are generated in chronic hepatitis and participate in the pathogenesis of oxidative liver injury in dogs and cats. Normally there is an extensive system of cytosolic and membrane bound enzymatic and non-enzymatic antioxidants which function to prevent oxidative damage by "scavenging" or "quenching" free radicals that are formed. It is reported that close to half the dogs and cats with liver disease have reduced glutathione concentrations in the blood and liver supporting that oxidative damage is present.

Vitamin E, d-alpha tocopherol, functions a major membrane bound intracellular antioxidant, protecting membrane phopspholipids from peroxidative damage when free radicals are formed. Vitamin E is shown to protect against the effects of copper, bile acids and other hepatotoxins. A suggested vitamin E dose is 50 to 400 IU a day.

S-Adensosylmethionine (SAMe) is a naturally occurring molecule found in all living organisms and is involved in a number of metabolic pathways that appear to be beneficial to the liver as well as other tissues. SAMe is involved in three major biochemical pathways. It is involved in cell replication and protein synthesis, has a modulating influence on inflammation and plays a role as a precursor of the antioxidant glutathione in the hepatocyte.

Milk thistle has been used for centuries as a natural remedy for diseases of the liver and biliary tract. Silymarin the active extract consists of bioflavonoligans that have been reported to work as antioxidants, scavenging free radicals and inhibiting lipid peroxidation. Several recent human clinical trials have assessed the efficacy of silymarin in the treatment of liver disease. The data is somewhat difficult to interpret because of the limited number of patients, poor study design, variable etiologies, lack of standardization of silymarin preparations with different dosing protocols. There is however compelling evidence to suggest silymarin has a therapeutic effect in acute viral hepatitis, alcoholic liver disease, patients with cirrhosis, and in toxin or drug-induced hepatitis. Unfortunately, the purity of commercial products, and therapeutic dosage is unknown. Milk thistle is reported to have an extremely low toxicity in humans and animals and has been used extensively in clinical patients with little concern for side effects. Silibin appears to be a principle active isomer of the silymarin extract. Bioavailibility is increased by complexing with phosphatidylcholine. A new compound Denamarin™ is available containing SAMe and silybin and is available in a chewable formulation.

General Support Therapy. The remainder of the therapy for chronic hepatitis involves treatment of secondary complications. These occur as the disease becomes advanced. Hepatic encephalopathy, GI ulceration and ascites are common clinical occurrences in advanced hepatitis or cirrhosis.

EMERGING NEWER LIVER DISEASES

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Several hepatobiliary disorders have in the last few years come under increased recognition and interest in dogs. Understanding theses specific conditions is essential in the diagnosis and management of canine liver disease.

GALLBLADDER MUCOCELE

To date greater than 130 cases of gallbladder mucocele have been documented in the literature. A gallbladder mucocele is a condition that is described as an enlarged gallbladder with immobile stellate or finely striated patterns of mucoid material within the gallbladder lumen detected with ultrasound. The changes described can result in biliary obstruction or gallbladder perforation and peritonitis. Smaller breeds and older dogs are overrepresented. Shetland sheepdogs and Cocker Spaniels are most commonly affected. Most dogs are presented for nonspecific clinical signs such as vomiting, anorexia and lethargy. Abdominal pain, icterus and hyperthermia are common findings on physical examination in advanced cases. Most have serum elevations in bilirubin, ALP, GGT and variable ALT although some dogs are asymptomatic and a mucocele is diagnosed as an incidental finding on abdominal ultrasound. The Shetland sheepdogs tend to have hyperlipidemia and were first thought to have a genetic defect in the $ABCB_4$ hepatobiliary transporter gene involved phosphocholine transport into the bile. That theory is now questioned in a reported second larger study. Risk factors identified in mucocele cases include endocrine disease (hypothyroidism, Cushing's disease) and idiopathic vacuolar hepatopathy, hyperlipidemia and dogs on high fat diets.

Gallbladder mucoceles appear ultrasonographically as an immobile accumulation of anechoic-to-hypoechoic material characterized by the appearance of stellate or finely striated bile patterns (wagon wheel or kiwi fruit appearance). This should be differentiated from biliary sludge (bile sludge can be found in normal animals), by the absence of gravity dependent bile movement while the mucocele is non-movable. The gallbladder wall thickness and wall appearance are variable and nonspecific. The cystic, hepatic or common bile duct may be normal size or dilated suggesting biliary obstruction. Gallbladder wall discontinuity on ultrasound indicates rupture whereas neither of the bile patterns predicted the likelihood of gallbladder rupture.

Cholecystectomy is the treatment of choice for biliary mucoceles. Following cholecystectomy and recovery of postoperative period the prognosis is excellent especially when the liver enzymes are normal. Mortality rates have been reported to be in the 20% range and some may persist in having liver disease with elevated liver enzymes. There are reports of resolution of some mucoceles using ursodeoxycholic acid (ursodiol) and a low fat diet but this should only be attempted in the healthy patient and with careful monitoring. Ursodeoxycholic acid is thought to up-regulate biliary excretion of phospholipids and increase bile salt dependent flow.

On histopathology the gallbladder demonstrates cystic mucinous hyperplasia. The pathophysiology of this condition is unknown. It is possible biliary stasis and abnormal bile composition or lack of solubility results in gallbladder mucosal irritation and subsequent mucinous hyperplasia. Infection does not appear to be a factor in this condition. A mucocele is reported the most common cause of a gallbladder perforation.

PORTAL VEIN HYPOPLASIA

Portal vein hypoplasia (PVH), also referred to as microvascular dysplasia (MVD), is a common syndrome in the dog associated with abnormal microscopic hepatic portal circulation. It is thought that PVH is 15 to 30 times more common that a congenital portosystemic shunt (PSS). Hepatic PVH has been suggested as the terminology by the WSAVA Liver Standardization Group that may better reflect the etiology of this condition although MVD is ingrained in the veterinary liturature. It is believed that the primary defect in affected dogs is the result of hypoplastic small intrahepatic portal veins. This condition is thought to be a defect in embryologic development of the portal veins. With paucity in size or number of portal veins there is a resultant increased arterial blood flow in attempt to maintain hepatic sinusoidal blood flow. The hepatic arteries become torturous and abundant in the triad. Sinusoidal hypertension occurs under this high pressure system. Lymphatic dilation results and it is thought that this opens up of embryologic sinusoidal vessels to reduce pressure and thus acquired shunts develop to transport some (but not all) of the blood to the central vein thus by-passing the sinusoidal hepatocytes. This results in abnormal hepatic parenchymal perfusion and lack of normal trophic factors bathing the sinusoids causing hepatic atrophy. With portal shunting of blood increased iron uptake also occurs that results in hepatic iron granuloma formation. Ascites or portal hypertension generally do not occur in this condition.

Because similar histological changes occur in dogs having PVH and PSS (i.e., hepatic hypoperfusion) the diagnosis can be confusing. If an intrahepatic or extrahepatic macroscopic shunt is not observed then PVH becomes the probable diagnosis. Angiography or transcolonic portal scintigraphy fails to demonstrate macroscopic shunting in this condition. Often a needle biopsy is not sufficient to provide enough portal areas to make the diagnosis, and consequently a wedge or laparoscopic biopsy may be necessary.

The condition that was first described in Cairn terriers and now is felt to occur in other breeds of dogs. Yorkshire Terriers and Maltese may be over represented. Animals show no outward clinical signs and are usually identified because of elevated liver enzymes (ALT). All patients have abnormal serum bile acid concentrations (usually moderate elevations) but generally they are less than 100 µmole/L. It is reported PVH dogs have normal protein c concentrations while PSS dogs have concentrations less than 70% normal. There is no specific therapy. Some suggest antioxidants (i.e., SAMe, milk thistle etc.). The long-term prognosis is uncertain because of lack of experience with this relative new disease. There may be a small number of dogs developing portal hypertension over time.

PORTAL VEIN HYPOPLASIA AND SECONDARY PORTAL HYPERTENSION

Portal vein hypoplasia with portal hypertension and ascites occurs as a fibrosis variant of portal vein hypoplasia. It has also been called congenital hepatic fibrosis and idiopathic noncirrhotic portal hypertension but may in fact could be a congenital ductal plate abnormality. The ductal plate is the embryological precursor to development of bile ducts in the portal region. Some ductal plate abnormalities result in proliferation of small bile ducts and fibrosis with secondary portal hypertension. This subgroup of dogs with portal vein hypoplasia that have moderate to marked fibrosis of the portal tracts, a varying proliferation of arterioles and bile ductules, particularly at the periphery of the portal area. Ascites, portal hypertension and secondary acquired portosystemic shunts occur.

The hepatic histology demonstrates portal tracts associated with multiple arterioles, small or absent portal veins with variable portal fibrosis, lymphatic distention and variable bile duct proliferation. The pathology is void of inflammatory infiltrates. There are also increased amounts of hepatic iron deposited in the liver.

This latter condition is observed in dogs are under 2.5 years of age and there is no breed prevalence however Doberman Pinschers, Cocker Spaniels and Rottweilers may be over represented. The clinical presentation is similar to dogs having either congenital intra or extrahepatic shunts except most dogs have ascites. The liver enzymes are generally increased with a hypoalbuminemia and very high bile acid concentrations. Work up of these patients fails to identify a single shunting vessel, but rather these cases have marked portal hypertension associated with multiple acquired portosystemic shunts. These dogs will generally present with ascites and signs of hepatic encephalopathy. Ultrasound is often helpful showing microhepatia, hepatofugal portal blood flow and multiple abnormal extrahepatic collateral shunts. Portal contrast studies demonstrate acquired portal shunts and pressure measurements document portal hypertension. The prognosis for this condition is generally guarded but some dogs are reported to have a prolonged survival using anti-fibrotic agents and hepatic encephalopathy therapy.

ACUTE HEPATITIS

Acute liver damage is an uncommon condition that can result in rapid deterioration of liver function depending on the extent of damage occurring in a previously healthy animal. It is generally characterized by severe hepatocyte death due to aptoposis or cytolytic necrosis. The extent and location of the hepatocyte death depends on the etiology.

Drugs are the most common known cause acute liver damage in dogs and cats. Drugs can affect the liver in one of two ways. First, they may have a direct toxicity to hepatocytes or becomes metabolized to a toxic compound that then causes damage. This first classification is referred to as a direct hepatotoxin and is dose related and reproducible. An example would be acetaminophen poisoning. More common however are drugs associated with an idiosyncratic drug reaction. Idiosyncratic drug reactions are unpredictable and not dose related but most often associated with abnormal or aberrant metabolism of the drug to a toxic compound. Listed below are some of the more common drug associated hepatotoxicities. It should be noted however any drug metabolized by the liver has the potential to be a hepatotoxin. The common incriminators causing an idiosyncratic reaction include the NSAIDs, trimethoprim-sulfa, lysodren, ketoconazole (and other antifungals), and

diazepam (in cats) to name but a few. We have also more recently identified toxicity associated with azathioprine. See table of common drug associated with liver disease. Some herding breed dogs lack p-glycoprotein that plays an important role in metabolism of many drugs. Thus it is not surprising that lack of P-glycoprotein, which occurs in many herding-breed dogs leads to increased susceptibility to drug toxicosis.

Other causes of acute liver damage include infectious agents such as Leptospirosis. Environmental toxins such as industrial solvents, plants, insects, chemicals, envenomation, sago palm seeds, heavy metals, Amanita phalloides (mushroom) and aflatoxin have been incriminated to cause liver disease. Several years ago there was a large outbreak of liver failure in many dogs in the Eastern part of the United States due to contaminated dog food with aflatoxin. In most cases aflotoxin is an isolated event. Xylitol an artificial sweetener found in chewing gum can result in a sudden drop in glucose due to increase insulin release and in some cases also causes acute liver disease as well.

Damage to the liver may range from mild to moderate hepatic necrosis resulting in minimal clinical signs. Signs may be associated with vomiting, lethargy and anorexia. Massive hepatic necrosis will result in ALF and produce significant clinical signs of liver failure and possibly death. The signs of ALF are variable but usually will always include anorexia, depression, lethargy and vomiting. Neurological signs from hepatic encephalopathy may progress to coma or seizures. Jaundice is invariably present. ALF can also result in evidence of hemorrhage either from lack of coagulation factors or from DIC. GI ulceration is common. Septicemia may occur from uptake of enteric bacteria. Hepatic pain may be observed on abdominal palpation.

The clinicopathologic changes reflect the extent of necrosis and loss of hepatocyte numbers. The hepatic transaminases (ALT and AST) are released when the cell membrane is damaged and the cytosol enzymes leak out. A marked increase in AST to ALT ratio suggests more severe hepatocellular damage. Generally ALP and GGT increases are associated with hepatic necrosis and are only mild to moderately elevated. Hyperbilirubinemia is common when significant hepatic necrosis is present and frequently very high when massive necrosis occurs. Changes in the liver function test will reflect the magnitude of hepatic damage. When the necrosis is massive and liver function is compromised these function changes will occur.

When there is acute ingestion of a hepatotoxin toxin vomiting should be induced followed by administration of activated charcoal to prevent absorption of the toxin or drug absorption. In most cases the animal is clinical and too advanced for gastric lavage and charcoal to have any benefit.

The next step is to prevent further hepatocyte damage by providing an environment for optimal hepatic function. There is considerable evidence showing that free radicals are generated in acute liver damage and participate in the pathogenesis of liver injury. Free radicals are molecules with an unpaired electron that form by the injurious effects of certain drugs or various other toxic agents or events. Free radicals, if not inactivated, damage cellular macromolecules via lipid peroxidation and thus participate in cellular injury when produced in excess. Depletion of antioxidants primarily glutathione parallels hepatic damage. N-acetylcysteine (NAC, Mucomyst™) is thiol (SH) donor and promotes the production

of glutathione. Glutathione is the most important detoxifier of toxic cellular xenobiotics. There is also evidence that NAC protects against hepatic ischemia-reperfusion damage possibly by inhibiting Kupffer cell function. Further NAC has beneficial effects on liver blood flow, oxygen extraction, and the formation of non-glutathione products that protect against cell injury. Experimentally NAC has protective effects against aflatoxin damage as well. The suggested dose for NAC is 140 mg/kg IV followed by 70 mg/kg IV bid or tid for one to three days. The injectable NAC should be diluted 1:4 in 5% dextrose and water and given slowly over 30 minutes to 1 hour. When vomiting has resolved NAC therapy can be switched to oral medications. Oral S-Adensosylmethionine (SAMe) also protects against liver damage in dogs and cats by increasing hepatocyte glutathione concentrations being a SH donor. It also acts as a methyl donor and enzyme activator for key reactions that maintain membrane structure and function. Reports show protection against acetaminophen toxicity in the dog and cat. SAMe is given orally at the dose of 20 mg/kg bid or daily. SAMe in combination with milk thistle products is commercially available and would be of benefit as well.

The use of other antioxidants is warranted in management of the liver disease including vitamin E and milk thistle or its by-products. Vitamin E, d-alpha tocopherol, functions a major membrane bound intracellular antioxidant, protecting membrane phopspholipids from peroxidative damage when free radicals are formed. Vitamin E is shown to protect against the effects of copper, bile acids and other hepatotoxins. A suggested vitamin E dose is 50 to 400 IU a day. Other antioxidants that have been investigated but lack clinical experience in dogs and cats include allopurinol and desferoxamine.

Milk thistle has been used for centuries as a natural remedy for diseases of the liver and biliary tract. Silymarin the active extract consists of bioflavonoligans that have been reported to work as antioxidants, scavenging free radicals and inhibiting lipid peroxidation. In a number of human clinical studies on patients having either acute or chronic liver disease has provided mounting evidence of the benefit of milk thistle. These studies must be interpreted with care because of the variable experimental design and limited number of cases. One canine study showed that dogs poisoned with amanita mushrooms that were treated with milk thistle had less clinical signs and complete survival while one-third of dogs in the untreated group died. Due to the lack of standardization of milk thistle preparations it is difficult to provide an appropriate dosage. Suggestions have included 50-250 mg/kg bid. Milk thistle is reported to have an extremely low toxicity in humans and animals and has been used extensively in clinical patients with little concern for side effects. It appears to have a synergistic effect with vitamin E.

Other therapy includes fluid therapy, antibiotics, management of gastrointestinal ulceration and treatment of hepatic encephalopathy.

HEPATOCUTANEOUS SYNDROME

Hepatocutaneous syndrome, also known as superficial necrolytic dermatitis or metabolic dermatosis, is an uncommon disease observed in middle aged to older dogs. The skin lesions have characteristic histological changes (superficial necrolytic dermatitis or necrolytic migratory erythemia) and when combined with the hepatic changes typify this syndrome. The liver has mistakenly been described by some as cirrhotic because of the nodular appearance of the liver. The hepatic

changes are best described as an idiopathic hepatocellular collapse with nodular regeneration. Changes are generally devoid of major inflammation. The hepatic nodular regeneration consists of vacuolated hepatocytes. To date the pathogenesis of the hepatic disease is still controversial. In humans other types of liver disease have been noted to produce the similar cutaneous lesions however the hepatocellular collapse described in the canine hepatocutaneous syndrome has not been reported. It is not known if the liver dysfunction is the major mediator of the necrolytic skin lesions or whether another metabolic disease produced both the skin and hepatic lesions. Affected dogs almost all have pronounced reductions in amino acid and albumin concentrations. Some authors believe this condition to be the result of exaggerated amino acid catabolism. Uncommonly some dogs and humans have hyperglucagonemia secondary to a glucagon-secreting tumor. Diabetes mellitus occurs in some dogs. Recently hepatocutaneous syndrome has also been associated with chronic long-term phenobarbital therapy.

Most dogs are presented because of the skin disease. Abnormal liver enzymes are identified and in most, ALP and bile acids are increased. The albumin is typically below normal and almost every affected dog has hypoaminoacidemia if measured. The liver has a characteristic ultrasound appearance looking like "Swiss cheese" due to the hypoechoic nodules. It is thought that the necrolytic skin lesions are directly related to the hypoaminoacidemia. The hypoaminoacidemia may be responsible for the hepatic changes as well. This is supported in part by observations that dogs fed a protein deficient diet for prolonged periods develop hypoalbumenia and hepatic changes that resemble hepatic changes described in the hepatocutaneous syndrome, however skin lesions were not observed. The importance of hypoaminoacidemia in this disease is further supported in that administration of intravenous amino acid solutions transiently improved the lesions in many but not all dogs. The cause of the amino acid deficiency is unknown. The affected dogs appear to have been feed adequate protein content diets. The reported prognosis for this disease is grave and invariably most succumb either due to liver dysfunction or to the severity of the skin lesions, or both.

Our current therapy includes administration of intravenous amino acid solution. We give approximately 500 ml of Aminosyn™ (10% solution, Abbott) over 8-12 hours. If given too fast, hepatic encephalopathy can occur. Repeated infusions are given weekly or more frequently. If after four weekly amino acid infusions and if there is no improvement it is unlikely the patient will respond to therapy. Some dermatologists suggest that daily infusion of amino acids for the first week results in a quicker response. With a positive response repeated the amino acid infusions are given as needed. In addition, we generally treat the patient with a dietary protein supplement of egg yolks (as an amino acid source) and other protein supplements. Additional support includes antibiotics if a secondary skin infection exists, omega 3 fatty acids, ursodeoxycholic acid, vitamin E and/or zinc.

FELINE LIVER DISEASE: WHAT'S NEW?

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Liver disease is common in the cat and the finding of icterus is a frequently a clinical clue that the cat has primary liver disease. The types of liver disease as well as differences in laboratory tests for the cat are very different from disorders observed in the dog. This is due in part to specific anatomical and metabolic differences of the cat. The following includes an overview of theses differences with updates of newer information on feline hepatic disease and their treatments.

LABORATORY TESTING

A sick cat may become icteric (jaundice) without having primary liver disease. This is because of the complexities of bilirubin metabolism combined with cat's weak ability to conjugate compounds. Normal hepatic bilirubin metabolism must go through several steps in the hepatocyte before excretion into the bile. This metabolism can be affected by inflammatory cytokines or endotoxins and from nutritional alterations due to mobilization of free fatty acids delivered to the liver or from protein deficiencies resulting from catabolic conditions. Cats also have inherent low concentrations of glucuronyl transferase, an enzyme required to convert bilirubin to water-soluble form prior to hepatic excretion. It is this complex pathway that can result in icterus without evidence of significant structural liver disease. We recently reviewed 180 cats having elevated bilirubin concentrations and cases were grouped them into those clinically icteric (bilirubin>3.0 mg/dl, 51 µmol/L) or those with biochemical icterus (having only icteric serum with bilirubin ranging from 0.5 to 2.9 mg/dl). Clinically icteric cats (bilirubin > 3.0 mg/dl) likely have primary hepatobiliary disease when hemolytic disease is ruled out. Cats having biochemical icterus (bilirubin < 3.0 mg/dl) do not always have primary hepatobiliary disease and many have other non-hepatic disorders with the liver being secondarily affected with what is often referred to as a reactive hepatopathy. For example, it is not unusual to find elevations in bilirubin concentrations in cats with inflammatory disease such as pyothorax, abscesses or tissue necrosis. We also found the higher the bilibubin the poorer the survival rate. Those having only mild increases in bilirubin tended to have a better prognosis however the prognosis was influenced by the underlying primary liver disease.

A study evaluating the utility of liver biochemistries in the diagnosis of feline liver disease found the best predictive tests for primary liver disease includes ALP, GGT, total bilirubin and bile acids. ALP increases with hepatic cholestatsis. ALP is unique in cats in that the half-life of the enzyme is short (6 hours compared to 72 hours in the dog) and the feline liver is reported to contain only one-third the concentrations found in dogs. Consequently, increases in serum ALP with cholestasis are not expected to increase with the same magnitude as observed in dogs with similar diseases. ALP is also not induced by corticosteroids nor do they cause a steroid hepatopathy. Gamma-glutamyl transpeptidase (GGT) is a similar enzyme to ALP that increases with cholestasis and is more sensitive for feline inflammatory liver disease than ALP. Presumably this is because GGT is found in higher concentrations in the bile ducts than the hepatocyte where ALP predominates. Uniquely cats with idiopathic hepatic lipidosis usually have marked increases in ALP while GGT concentrations show only mild increases. Cats with cholangitis often

have high elevations in both GGT and ALP. Bile acids in the cat are most useful in screening for portosystemic shunts.

The ALT and AST are quite variable and reflect hepatocellular leakage from either degeneration or necrosis. These liver enzymes are less predictive of primary inflammatory liver disease than ALP and GGT (tests that reflect cholestasis). No published values exist for ALT half-life but it is presumed that ALT is much shorter (around 6 hours) than that of dogs (2.5 days). AST half-life is 77 minutes in the cat. The short half-lives may explain the variability of ALT and AST values in liver disease of cats and if marked elevations are found tend to reflect a relative acute episode. Increases in ALT alone without other enzyme elevations is often observed in cats having secondary liver involvement from some other primary non-hepatic condition for example hyperthyroidism.

LIVER DISEASE IN CATS

The incidence of liver disease in the cat is unknown but considered to be common. In an unpublished review of 175 consecutive liver biopsies performed on cats at Colorado State University several large categories were observed. Making up 87% of the liver biopsies were 4 groups: Lipidosis (26%, both idiopathic and secondary), Cholangitis (25%), Neoplasia (20%) and Reactive hepatopathies (16%). Hepatic cysts are also an occasional finding in some cats but rarely cause problems. Lipidosis and cholangitis were the most common conditions and will be discussed below. Reactive hepatopathies refer to changes in the liver that occur secondary to a primary non-hepatic disorder such as inflammatory bowel disease, hyperthyroidism and cardiac disease as a few examples. Usually there is also a degree of secondary lipidosis associated with reactive hepatopathies. Hepatic neoplasia was also common. Cats are differ from dogs in the fact that benign tumors are more common than malignant hepatic neoplasia. Bile duct adenomas (cyst adenomas) were the most common benign tumor and bile duct carcinoma the most common malignant neoplasia when hematopoietic tumors (ie, lymphoma) are excluded from the hepatic neoplasia group.

HEPATIC LIPIDOSIS

Lipidosis is common in the cat but relative uncommon in the dog. Hepatic lipidosis can occur as either a primary idiopathic syndrome or secondary to a number of other primary disease conditions. Lipid accumulation in the liver is simply the result of nutritional, metabolic or toxic insults to the hepatocyte and the degree of lipid accumulation can be quite variable but the process is reversible. For example, a common secondary disease associated with significant hepatic triglyceride accumulation is diabetes mellitus. Hepatic lipid accumulation can also result secondary to a number of other disease syndromes associated with anorexia and weight loss such as pancreatitis, inflammatory bowel disease or other major organ dysfunction. These secondary conditions generally have less severe lipidosis than the clinical syndrome associated with idiopathic hepatic lipidosis in which there is no identifiable etiologic factor. Basically any conditions leading to anorexia can also cascade into secondary hepatic lipidosis. I believe anorexic cats develop hepatic lipidosis easily. Interestingly in recent years we have seen fewer cases of the idiopathic form of hepatic lipidosis.

The etiology of idiopathic hepatic lipidosis is unknown and several theories have been put forward without substantial documentation. One proposal is that there is a defect in hepatic lipid mobilization and decreased ability for hepatic fat oxidation, decreased synthesis of apoproteins and decreased lipoprotein removal from the liver. In the idiopathic form affected cats generally are older and obese and usually have undergone a stressful episode in the recent history followed then by a period of complete anorexia with a dramatic aversion to food. There is rapid weight loss (up to 40-60% body weight over 1-2 weeks), depression and icterus. The weight loss involves muscle mass while abdominal and inguinal fat stores often being spared. The diagnosis of idiopathic hepatic lipidosis is supported by the clinical history and laboratory findings. Icterus and marked elevations in ALP are consistent findings. ALT levels are variable and GGT concentrations are normal or only moderately increased. Icterus with a very high ALP and normal GGT should be a clue to likely idiopathic lipidosis when appropriate clinical features are present. Hypercholesterolemia, hyperammoniemia and abnormal bile acid levels are characteristic. About 1/3 of the cats have a nonregenerative anemia, hypokalemia and clotting abnormalities and about 1/2 the cats demonstrate poikilocytes in the RBC's. Finding severe hypokalemia, anemia or other concurrent disease (ie pancreatitis) with lipidosis has a poor survival rate. A definitive diagnosis requires a liver biopsy or presumptive diagnosis supported by a fine needle aspirate of the liver with cytological evidence of many vacuolated hepatocytes.

The therapy for idiopathic hepatic lipidosis requires aggressive management. I believe up to an 86% or higher survival rate should be expected. Initial therapy requires fluid and electrolyte replacement. Adequate nutrition next becomes the most important part of the therapy for hepatic lipidosis. Placement of 20 French red rubber esophageal feeding tube is necessary for nutritional support. The nutritional recommendations for idiopathic hepatic lipidosis are completely empirical and poorly documented. Recovery formulations providing adequate calories and protein are used. There is also no good data on the benefit of various dietary supplements. The prognosis is good with aggressive nutritional therapy and most cats recover.

INFLAMMATORY LIVER DISEASE

Cholangitis is an inflammatory disorder of the hepatobiliary system. It is a disease complex that may be concurrently associated with duodenitis, pancreatitis, cholecystitis and/or cholelithiasis. The terminology has been somewhat confusing but using the histological classification of the WSAVA Liver Standardization Group this complex has is separated into three important histological groups; neutrophilic cholangitis, lymphocytic cholangitis and cholangitis associated with liver flukes.

Neutrophilic Cholangitis. This classification has previously been referred to as suppurative or exudative cholangitis /cholangiohepatitis and is the most common type of biliary tract disease observed in cats in North America. Neutrophilic cholangitis is thought to be the result of biliary tract infection from bacterial translocation from the gastrointestinal tract. In the acute neutrophilic form (ANF), the lesions are exclusively neutrophilic or suppurative but over time it is thought that some cases may progress to a chronic neutrophilic form (CNF) with a mixed inflammatory pattern containing variable numbers of neutrophils, lymphocytes and plasma cells.

In the ANF coliforms (predominately E. coli) are frequently cultured from the liver or bile. Inflammation can also extend into the hepatic parenchyma causing a cholangiohepatitis. Cats with this syndrome tend to be younger (~3-7 years) and present with illness usually a week or less in duration. They may have evidence of a fever, anorexia, vomiting or lethargy. A leukocytosis may be identified on the CBC. The ALT/AST and ALP/GGT are usually increased but quite variable and cats are frequently icteric. Ultrasound should be performed to rule out pancreatitis, biliary obstruction or other intra-abdominal disorders. In some cases we will perform an ultrasound-guided cholecystocentesis for cytology and culture. It is generally considered to be a safe procedure and may provide important diagnostic information. A liver biopsy is required for histology and will confirm the diagnosis. The liver biopsy should always also be cultured because of the relationship of bacteria and cholangitis. If obstruction is identified surgery becomes indicated to decompress and flush the biliary system. However, I always try to avoid surgical diversion surgery of the biliary system unless it becomes the last resort and temporary stent placement should be considered. Concurrent pancreatitis may be diagnosed with an elevated feline PLI and pancreatic ultrasound changes. Inflammatory bowel disease (IBD) is diagnosed by presence of GI signs, intestinal ultrasound changes and or an intestinal biopsy showing chronic inflammation.

Therapy first includes fluid and electrolyte replacement if needed. Antibiotics are also a critical part of the therapy in ANF. Culture and sensitivity of the liver or bile will drive antibiotic selection. Without a positive culture I would consider the likelihood of E. coli or other enteric aerobe (i.e., enterococcus). Ampicillin, ampicillin-clavulanic acid, cephalosporins and aminoglycosides have been suggested as likely effective antibiotics. Ampicillin or ampicillin-clavulanic acid is often my choice because of the likelihood of E. coli and the fact that both antibiotics are concentrated in the bile. It is recommended that affected cats be treated for at least 1 month or even longer with antibiotics as a short duration of therapy may result in reoccurrence of clinical signs. Ursodeoxycholic acid (Ursodiol 10-15 mg/kg/day) is also recommended. Abdominal discomfort and vomiting may be associated with hepatobiliary pain and buprenorphine should be administered.

The CNF (neutrophilic, mixed or lymphocytic-plasmacytic) cholangitis may be the result of progression of the acute neutrophilic cholangitis. In the chronic stage the liver lesions are associated with the presence of a mixed inflammatory infiltrates in the portal areas consisting of neutrophils, lymphocytes and plasma cells. Possibly fibrosis, ductular proliferation or extension of inflammation into the hepatic parenchyma can occur as well.

In a recent study using FISH analysis we identified the presence of bacteria in 2/3 of the cases having the CNF. The most common bacteria identified was E. coli followed by enterococcus. Historically the CNF was treated with corticosteroid therapy but in light of our findings we recommend if cultures are negative that antibiotic therapy be instituted prior to corticosteroid therapy. Remainder of the management is similar to the acute form. It has been argued that many cases do not improve until corticosteroids are given. Steroid improvement may be due to the fact many cats also have concurrent inflammatory bowel disease and/or chronic pancreatitis. One study found 83% of affected cats had inflammatory bowel disease (IBD) and 50% had concurrent chronic pancreatitis. The association of the three

together has been referred to as "feline triaditis syndrome". IBD is generally treated with corticosteroids and diet and clinical improvement may actually be due to the IBD therapy.

The pathogensis of the triaditis syndrome is not well delineated. Possibly the common channel theory where the pancreatic ducts and bile ducts join before entering the duodenum could explain ascending bacteria. Also unique to the cat is the high bacterial concentration in the proximal small bowel. With concurrent IBD there is the likelihood of increased enteric bacterial translocation to the liver and pancreas. In a yet unpublished FISH study we also found approximately 1/3 of cats with moderate to severe acute or chronic pancreatitis to have bacteria in the pancreas. Cats with concurrent pancreatitis may also have increases feline pancreatic lipase immunoreactivity (fPLI) and or ultrasound changes.

So in summary, when ever possible cats suspected of having cholangitis should have hepatic biopsies but also hepatic and biliary cultures, pancreatic biopsies and small intestinal biopsies.

Lymphocytic Cholangitis

This condition (severe lymphocytic portal hepatitis, progressive lymphocytic cholangitis or nonsuppurative cholangitis) is described as a very chronic inflammatory biliary tract disorder that is progressive over months and years. Some describe it as also being acute in nature. This disorder appears to be more common in European cats than in cats in North America. The pathology of the liver is characterized by a consistent moderate to marked infiltration of small lymphocytes predominately restricted to the portal areas, often associated with variable portal fibrosis and biliary proliferation. The later stages result in considerable distortion of liver architecture. The bile ducts can also become irregular with dilation and fibrosis. In some cases lymphocytic infiltrates in the portal areas may be confused with well-differentiated lymphocytic lymphoma. It is postulated that lymphocytic cholangitis could be the result of immune mediated mechanisms based on preliminary immunologic studies. We have found bacteria to be less commonly associated with this condition using special fluorescent stains (FISH) for enteric bacteria.

The syndrome is usually chronic progressing over months to years. The clinical features are often similar to the neutrophilic form but advanced disease can result in ascites, jaundice, and hypergammaglobulinemia (in almost all cases). In advanced cases, ultrasonographic examination may demonstrate dramatic changes intra and extra-hepatic bile ducts with marked segmental dilations and areas of stenosis that may lead the operator to believe there is an obstruction. Ascites and hepatic encephalopathy occur late in the disease as a result of acquired portal hypertension and hepatic dysfunction.

The treatment for the chronic lymphocytic cholangitis involves using anti-inflammatory (prednisolone) and/or immunosuppressive therapy (I frequently use chlorambucil in severe cases) in addition to supportive therapy as described with neutrophilic cholangitis. Ursodeoxycholic acid has been shown to have a positive treatment effect in humans having chronic primary biliary cirrhosis having a very similar histologic pattern to these chronic cases and may be a helpful adjunct therapy.

FELINE TRIADITIS SYNDROME

The term "triaditis" is used to describe concurrent inflammation of the pancreas, liver and small intestines and is based on histological conformation. However, the specific conditions that constitute the diagnosis of triaditis include any inflammatory process within these organs but is most often is associated with a combination of pancreatitis, cholangitis and inflammatory bowel disease (IBD). Triaditis has been reported in 50-56% of cats diagnosed with pancreatitis and 32-50% of those with cholangitis or inflammatory liver disease.

Although there appears to be a direct association between the three organ involvement, the etiology and pathophysiology of this syndrome is yet unknown. Likely causes of inflammation include bacterial infection, immune mediated or idiopathic mechanisms. When all three organs (liver, pancreas and intestine) become inflamed it becomes triaditis. Because the etiology of this syndrome is unknown it is difficult to know how to best treat it. Since it is likely several etiologies are responsible and the specific therapies are also variable and will different from case to case.

Bacterial Theory. One theory for triaditis is that both acute and chronic pancreatitis could be the result of an extension of ductular inflammation from the biliary system. This is because the common bile duct and pancreatic duct both merge into a common channel before entering into the intestine. It is possible bile and enteric bacteria from the common channel enter both the pancreatic duct and common bile duct and are responsible for both inflammatory liver and pancreatic changes. With the theory of ascending bacteria from the intestine bacteria may be responsible for both cholangitis and pancreatitis. It is known that cats also have on the order of 100 times higher concentrations of bacteria in the proximal duodenum than do dogs or humans (dogs 10^3cfu/g vs cats 10^5 to 10^8cfu/g). High enteric bacterial concentrations coupled with inflammatory changes in the intestine would be a likely source of bacterial seeding either via the common channel or through intestinal translocation with hematogenous seeding. In either case IBD would likely potentiate bacterial movement.

FISH analysis (fluorescence in situ hybridization [FISH] using a 16S rDNA probe that recognizes a specific class of enteric bacteria) is a non-culture method staining technique for bacteria. In a published study we found through FISH analysis that enteric bacteria was present in liver tissues of 69% of the cats having a chronic or acute inflammatory liver disease. The most common bacteria identified in the livers with cholangitis are *E coli* and *Enterococcus*. In yet another, but yet unpublished study, we used FISH to examine the pancreas of cats with either acute or chronic pancreatitis and found a relatively high frequency of bacteria in that organ (35% or 11/31 cases). Infection was most prevalent in cats with moderate to severe acute or chronic pancreatitis. The localization and type of intra-pancreatic bacteria suggests translocation of enteric bacteria. The most common organisms identified were *E. coli*, *Streptococcus* spp and *Enterococcus* spp. Further, an experimental pancreatitis study in cats clearly demonstrated that *E. coli* translocated from the intestines into experimentally induced acutely inflamed pancreas as well as into the liver and gallbladder supporting the intestinal translocation theory. These findings have substantial implications for the diagnosis and management of cats with pancreatitis.

Immune-mediated Theory. Cats having chronic lymphocytic pancreatitis or lymphocytic cholangitis invasive bacteria are less commonly visualized. With the combination of lymphocytic (chronic) pancreatitis, lymphocytic or mixed lymphocytic and neutrophilic cholangitis and lymphocytic plasmacytic enteritis may all be a consequence of an immune-mediated process rather than active bacterial infection. In people and experimental animals autoimmune pancreatitis and cholangitis are recognized as extra-intestinal complications of IBD, with immune attack frequently directed against bile and pancreatic ducts. Immune mediated damage may either be a consequence of immune responses against bacteria (that may or may not have established an active infection) that cross-react with host tissues with

resultant innocent by-stander immune responses in the intestines, liver and pancreas, or immune attack directed against host antigens unmasked by tissue damage. In further support for an immune etiology are human studies demonstrating that a variety of autoantigens have been implicated again suggesting that immune responses to translocated bacteria, perhaps facilitated by a leaky gut, and may promote an immune inflammation in a susceptible individuals. We also know feline IBD when not dietary or antibiotic responsive often improves with immunosuppressive therapy supporting again a possible the immune theory. At this point there are no reliable clinical tests to detect an immune response.

Diagnosis. The definitive diagnosis involves histopathology from each organ. It is important when ever doing an exploratory surgery for a biopsy of intestine, pancreas or liver that all three organs should be carefully inspected and biopsied even if they appear normal because triaditis is so common. Evidence of liver disease is based on identification of elevations in liver enzymes and or total bilirubin. Liver ultrasound findings in cats are quite variable and many affected livers can appear normal. Abnormal ultrasound changes in cholangitis include prominent portal areas, duct distention and thickened gallbladder wall. In some cases bile duct obstruction can occur from duct inflammation, cholelithiasis or thick bile sludge. Surgical flushing or even temporary stent placement may be required in these cases. I will also always culture the liver biopsy and bile that has been obtained from a gallbladder aspirate. A presumptive diagnosis of pancreatitis includes an elevated serum pancreatic lipase immunoreactivity test (fPLI) and abdominal ultrasound showing abnormal pancreatic changes. In one study the fPLI sensitivity is reported to be 67% and the specificity of the fPLI to be 91%. Ultrasound will detect anywhere from 35 to 67% of cats with pancreatitis. Pancreatic biopsies are safe and easy to perform either at surgery or via laparoscopy. I also now culture most of my pancreatic biopsies as well. Intestinal disease is often diagnosed based on signs of GI disease (vomiting or diarrhea) and ultrasound changes in the bowel with mucosal thickening or loss of layering. Some cats may also have decreased folate of cobalamin (B_{12}) serum concentrations with triaditis. Intestinal biopsies confirm inflammatory intestinal disease and are obtained via endoscopy or surgery. It is ideal to biopsy each segment of the small intestine because the IBD can be regional. Further, the most common area for GI T-cell lymphoma is the ileum that must be reached endoscopically via colonoscopy.

Treatment Considerations. Since the etiology of feline triaditis is unknown it is almost impossible to make absolute treatment recommendations. The first step in the therapy should be directed to the organ that is thought to be primarily responsible for the clinical signs. Because we believe that both bacterial and immune-mediated theories are possible one should use all the clinical information available to help direct the course of therapy.

Inflammatory Bowel Disease (IBD). The etiology of IBD is unknown. Possibly dietary constituents, bacterial causes or an abnormal immune response are all thought to be likely etiologies. Lymphocytic plasmacytic enteritis frequently responds to dietary modification with an antigen restricted (novel protein) or a hydrolyzed diet. Refractory patients typically escalate to diet plus antimicrobial therapy using enteric antibiotics such as tylosin (15 mg/kg bid), metronidazole (7-10 mg/kg bid) or amoxicillin. If the patient fails to respond to more conservative therapy then I will then institute anti-inflammatory therapy using prednisolone (1-2 mg/kg q 24h with gradual dose reduction based on response). Often B_{12} supplementation is required (250 µg SQ weekly). Concurrent low-grade small T-cell intestinal lymphoma can respond well to therapy with chlorambucil (2 mg PO given 3 times a week), prednisolone and supplementation of B_{12}.

Pancreatitis. *Acute pancreatitis* is less common than chronic pancreatitis but acute can often progress to chronic pancreatitis or even exocrine pancreatic insufficiency. Acute (suppurative) pancreatitis carries a particularly poor prognosis. Complicating factors that can modify the situation are bacterial translocation and biliary obstruction. Fluid therapy,

analgesics, antiemetics and assisted alimentation are the basis of therapy. Antimicrobial therapy is warranted in moderate to severe cases and is supported by the finding of positive FISH staining in over 1/3 of the cases investigated. *E. coli*, *Streptococcus* spp and *Enterococcus* spp are the most common organisms identified. Amoxicilin-clavulanic acid, cephalosporins, fluorquinolones or metronidazole are reasonable considerations. In cats with suspected disease exploratory laparotomy with biopsy of the pancreas, liver and intestine with appropriate cultures of pancreas and liver is frequently required to optimize therapy. Persistent biliary obstruction from pancreatitis is another indication for surgery and may be amenable to stenting or cholecystojejunostomy. It should be noted that corticosteroids are not typically employed in the treatment of feline acute pancreatitis.

Chronic pancreatitis is more common than acute pancreatitis in the cat. Lymphocytic or lymphocytic plasmacytic pancreatitis with fibrosis is the characteristic finding. In some cases the pancreatic damage can be so severe resulting in exocrine pancreatic insufficiency requiring pancreatic enzyme supplementation. Bacteria can also be a component of chronic pancreatitis so I generally begin with antibiotic (same listed above) and antioxidant therapy (i.e. SAMe, milk thistle, vitamin E). If there is a failure to respond to antibiotics or with evidence of IBD and or lymphocytic cholangitis then corticosteroid therapy would be indicated. Many cats will also require vitamin B_{12} supplementation.

Cholangitis. The management of cholangitis is based in part on culture results and histopathology. The *acute neutrophilic (suppurative) cholangitis or chronic neutrophilic (lymphocytic plasmacytic neutrophilic) cholangitis* are often associated with bacteria. The specific antibiotic therapy to use is best determined based on culture and sensitivity of the liver biopsy or bile aspirate. Short of a positive culture antibiotic therapy should be directed at enteric coliforms as suggested in the pancreatitis section. Other adjunct therapy may include ursodiol (ursodeoxycholic acid 10-15 mg/kg q 24h or divided bid), SAMe, milk thistle products or other antioxidants. The acute form usually responds quickly while the chronic form is less predictable. Generally a 4-week course of antibiotic therapy is indicated. If the patient fails to improve after several weeks of antibiotics I will begin prednisolone therapy. The *lymphocytic cholangitis* is thought to be likely immune mediated and rarely has a bacterial component. But because pancreatitis is common with cholangitis and bacteria could play a role in both I will usually also institute a course of antibiotic therapy. Cats having lymphocytic cholangitis will however generally require prednisolone therapy and sometimes even immunosuppressive therapy such as chlorambucil or others. A recent study found ursodiol was inferior to steroids based on follow up biopsies after a course of therapy. I use ursodiol as an additional adjunct therapy in these cases. General supportive therapy, antioxidants and vitamin B_{12} are generally used in these cases.

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ACUTE PANCREATITIS IN THE DOG

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It is generally believed that pancreatitis develops when there is activation of digestive enzymes within the gland and subsequent autodigestion. The location of the initiation of enzyme activation is thought to begin at the intercellular level, but the exact mechanism is unclear at this time. Experimental studies have shown that excessive acinar stimulation may be involved. Other observations suggest that the depletion of acinar glutathione in the pancreas may stimulate oxidative stress and that contributes to tissue injury. Certain drugs are also associated with development of pancreatitis.

Pancreatitis and subsequent autodigestion may be mild associated with an edematous pancreatitis or may become more severe associated with pancreatic acinar necrosis. It is the more severe pancreatic necrosis that tends to have the severe clinical signs and a poorer prognosis associated with systemic disease, such as systemic inflammatory response syndrome (SIRS) or multiple organ dysfunction (MODS).

CLINICAL CONDITIONS

In most cases the etiology of pancreatitis is never determined. In many over nutrition is a common factor likely causing excessive acinar enzyme secretion. The ingestion of high-fat diets especially in the obese patient is a well-accepted risk factor. Animals getting into the trash also have a higher risk of developing pancreatitis. Hyperlipoproteinemia is common with pancreatitis and whether this is a result of fat necrosis secondary to the pancreatitis or possibly the hyperlipidemia resulting in pancreatic ischemia is unknown. It is postulated that high concentrations of triglycerides may become activated by pancreatic lipase and produce pancreatitis. Pancreatitis is common in Schnauzers and other dogs that have a primary hyperlipidemia. A number of drugs are also shown to cause pancreatitis including thiazides, furosemide, tetracycline, L-asparaginase, and azathioprine. I personally believe azathioprine is by far the most common drug causing pancreatitis. The role of corticosteroids as a cause of pancreatitis has been suggested but as yet is unproved and is still controversial. In a study of 70 dogs with confirmed pancreatitis certain risk factors were identified (note that the animals included in this study were all necropsy cases and thus likely had severe disease). It was concluded that the breed, overweight body condition, small breed size, prior gastrointestinal diseases, diabetes mellitus, hyperadrenocorticism, and hypothyroidism were risk factors for developing acute pancreatitis. It is thought that around one fourth of the dogs presented with acute diabetes mellitus also have concurrent pancreatitis. No concurrent medications, glucocorticoid therapy, anesthesia, or trauma were associated with increased risk. Dogs having surgery (within 2 weeks before onset of signs) is also a risk factor. The breeds most commonly involved include Yorkshire terriers, toy poodles, and miniature Schnauzers.

Acute or chronic vomiting is a major clinical sign associated with pancreatitis. The clinical spectrum can vary dramatically from case to case. In the above study of 70 dogs with severe pancreatitis, vomiting (90%), weakness (79%), abdominal pain (58%), dehydration (46%), and diarrhea (33%) were reported. In experimental pancreatitis, colitis signs (often a bloody mucoid stool) were common presumably due to the extension of inflammation from the inflamed pancreas to the transverse colon that lies in close proximity to the pancreas. Severe cases also have systemic clinical signs such as fever or even cardiovascular shock.

Diagnosis

Laboratory findings are quite variable and to some extent parallel the severity of the clinical disease. Leukocytosis is usually present and biochemistry profile will show variable changes. Azotemia, elevated liver enzymes, increases in total bilirubin, hyperglycemia and hypokalemia may also be present. When disseminated intravascular coagulopathy (DIC) and coagulopathies occur, it generally reflects a poor prognosis.

Amylase and lipase have been used for years to diagnose pancreatitis in the dog but unfortunately they are not consistently reliable. The specificity of amylase and lipase is approximates 50%. Factors such as azotemia increases serum amylase and lipase due to decreased renal removal and dexamethasone will increase serum lipase levels. More recently cPLI or Spec cPL was found to be more diagnostic. In a prospective study of cases with clinical evidence of pancreatitis found the test had a 93% sensitivity and a 78% specificity using the IDEXX

cutoff value of <200 µg/L as normal. The conclusion was if the Spec cPL was < 200 µg/L (normal) that it was likely that the patient did not have pancreatitis. If the value was above the normal reference range pancreatitis should be included in the differential diagnosis and other tests are required to support the diagnosis.

Traditional lipase is measured using a catalytic assay. More recently newer lipase assays including a DGGR lipase and a Fuji dry chemistry assay appear to have better correlation with PLI activity. Antech now offers a Precision Pancreatic Specific Lipase (Precision PSL) on their profiles. Further studies are required to support these initial observations.

Abdominal radiographs may reveal increased density, diminished contrast and granularity in the right cranial abdomen with displacement of the stomach to the left, and widening of the angle between the stomach and the duodenum. A non-homogenous mass and loss of echodensity in the area of the pancreas is often noted on ultrasonographic examination. Occasionally dogs having pancreatitis may also have thoracic effusion as well, probably due to extension of inflammation through the diaphragm. One study found the sensitivity of ultrasound to be 68% but this varies based on operator skill. We will frequently perform a fine needle aspiration of suspected areas of pancreatitis; cytology showing suppurative inflammation also supports the diagnosis. We consider cytology to be safe as a diagnostic tool. Abdominocentesis and cytology is also very helpful if effusion is present. Suppurative nonseptic inflammation is the typical finding and is rarely septic.

Treatment

For humans suffering from acute pancreatitis there is an important short therapeutic window for successful management. It is considered to be the first 36-48 hours after hospital admission. Survival rate decrease and complication rates increase if treatment is delayed. The importance of rapid fluid therapy to maintaining adequate microcirculation within the pancreas and to prevent inflammatory cytokine release improves survival. These principles can also be extrapolated to the management of canine acute pancreatitis, rapid recognition and appropriate therapy.

Fluid and electrolyte therapy is given in virtually every case of pancreatitis for improving pancreatic perfusion and correcting the effects of fluid loss into the peritoneal cavity, and vomiting losses coupled with the vasoactive factors released from the pancreas producing a hypovolemic or possibly endotoxic shock. Fluid losses through vomiting may also result in a hypochloremic metabolic alkalosis. Most cases, however, usually have a metabolic acidosis with depletion of total potassium stores. A balanced crystalloid electrolyte solution often supplemented with additional potassium is indicated in almost all cases. Careful monitoring of electrolyte concentrations and patient hydration and renal output is essential in the severe pancreatitis case. Colloids such as Hetastarch have been recommended in the past but recent information suggests it is associated with acute kidney injury and consequently we do not use this product. Experimental studies of pancreatitis found aggressive fluid replacement prevented progression of edematous to the more severe necrotizing pancreatitis.

When protein levels decline plasma therapy has been suggested for improving oncotic pressure, pancreatic perfusion, and replacing protease inhibitors. More recently there have been questions on the benefit of fresh frozen plasma for protease replacement and one study failed to demonstrate the benefit in patients given plasma compared with those only given crystalloids. Probably the most important use of plasma is for factor replacement associated with coagulopathies or DIC.

Analgesics should be considered in all patients with pancreatitis, even if there is no outward evidence of abdominal pain. For mild pain buprenorphine (0.1- 0.2 mg/kg intravenously [IV], intramuscularly [IM] q 4-6 has needed) is suggested. Moderate to more severe pain morphine (0.1–0.5 mg/kg IV, subcutaneously [SC], or IM as needed) fentanyl is given as a continuous rate infusion (CRI, 2–5 µg/kg/hour) or 4–10 µg/kg SC, IM not to exceed 500 µg/dog. With severe pain we increase the dose of fentanyl (5–10 µg/kg/hour) and may add either ketamine (0.2–0.4 mg/kg/hour CRI) or lidocaine (5–30 µg/kg/min CRI). The animals should be monitored for side effects, particularly respiratory depression. Narcotics do decrease gastrointestinal motility that is in theory are a potential downside for their use. In some cases there is severe wind-up pain and alternative measures may be required to block the pain before traditional analgesics are effective. Spinal blocks and local analgesia should be considered in this case. We have treated some patients having severe abdominal pain with some success using intrathoracic or intra-abdominal placement of local anesthesia. Either lidocaine (1.5 mg/kg) or bupivacane (Marcaine, 1.5 mg/kg) can be used. Bupivacane has a longer duration of action and is my preference. We generally use a

butterfly catheter or over-the needle-catheter placed in the 8th mid-intercostal space or peritoneal cavity near the pancreas. Following injections the dog is rolled around and placed on its back so the anesthesia will drain into the area of the vagal nerves.

Antiemetics usually are given routinely if the patient has nausea and vomiting to help prevent fluid loss and make the patient more comfortable and possibly enhance return to early nutrition. The ideal antiemetic for pancreatitis should work both centrally and peripherally. Metoclopramide is suggested by some for their antiemetic effects and to improve gastrointestinal tone (0.2–0.4 mg/kg four times daily (QID) PO or SC, or 0.01–0.02 mg/kg/hr CRI). Metoclopramide, a dopamine antagonist, has poor prokinetic effects and is limited as an antiemetic in that it only works centrally. The dopamine antagonists may also decrease pancreatic perfusion. Anticholinergic agents are contraindicated because of profound effects on decreasing GI motility and little if any effects in decreasing pancreatic secretion. The serotonin antagonists such as ondansetron is a broad spectrum antiemetic but may have some effects in decreasing GI motility as well. My antiemetic of choice is maropitant (Cerenia, 1 mg/kg every 24 hours given SC or IV slowly or 2 mg/kg every 24 hours given PO). It is a broad-spectrum antiemetic that works both centrally and peripherally. Recent evidence by us has shown that maropitant also blocks visceral pain – at least in a visceral pain model given at the dose 1 mg/kg. There is also evidence that maropitant also helps with nausea as well although this is a subjective concept. Maropitant is a neurokinin-1 antagonist that blocks receptors found in the emetic center, CRTZ, and in peripheral afferent nerves. At higher doses it is effective blocking vestibular input from motion sickness.

Antibiotics should be considered for prophylactic therapy in the severe case or whenever there is evidence of sepsis or pancreatic infection. Infectious etiology of pancreatitis is rare in dogs but an experimental pancreatitis study in dogs suggests antibiotic therapy improves survival. Broad-spectrum antibiotics effective against aerobes and anaerobes should be given. I generally place my severe pancreatitis cases on a second-generation cephalosporin or a combination of amoxicillin and enterofloxacin for this purpose.

Nutritional supplementation in severe pancreatitis cases very important. Enteral nutrition is favored over parenteral nutrition. Pancreatic rest in the form of fasting has been the traditional recommendation for any patient with pancreatitis by giving nothing per OS (NPO) for several days. The belief is that feeding results in the release of pancreatic secretory stimuli that will stimulate pancreatic secretions and exacerbate the pancreatitis. Studies have now shown, however, that adequate nutrition improves survival in experimental and human pancreatitis pancreatitis. We now believe that severe vomiting and/or pain associated with eating would be the only reasons to fast patients. If the patient is not expected to be eating on its own within 3 days nutritional support is indicated. Nutrition not only improves patient survival but improved gut integrity. Parenteral nutrition is expensive and fraught with complications. It appears that enteral feeding does not significantly increase pancreatic secretions and actually improves gut integrity, with clinical improvement in the patients being fed. Free choice feeding or tube feeding (nasoesophageal, esophageal, gastrostomy or jejunostomy tube feeding) should be considered in moderate to severe cases. We generally begin feeding CliniCare™ Canine/Feline Liquid Diet (Abbott Animal Health) through a small-diameter feeding tube. During recovery I generally feed a low-fat diet given in small frequent meal.

Surgery for pancreatitis is controversial and indications would include septic peritonitis, to lavage the abdomen, treatment of pancreatic abscesses, feeding tube placement, or possibly for treatment of a biliary obstruction. Surgery for pancreatitis or obstructive biliary tract disease generally has a guarded prognosis. However we have a small series of cases that underwent laparoscopic exploration, lavage and jejunostomy tube placement that did well. Most obstructive biliary complications will resolve as the pancreatic inflammation obstructing the common bile duct resolves. In some cases we will place a temporary biliary stent if there is significant cholestasis.

Other therapy should be considered only after careful evaluation of the individual case. Because oxidative damage is thought to be the result of cellular membrane death antioxidants may be of benefit in the acute management of cases. Studies show that perfusion of the pancreas with free radical scavengers ameliorates the severity of pancreatitis in experimental canine models. Vitamin E is a potent membrane antioxidant and S-adenosyl L-methionine (SAMe) replaces glutathione stores that may have some benefit in pancreatitis. Pancreatic enzyme supplementation has been reported to decrease the pain that accompanies chronic pancreatitis in humans by the feedback inhibition by endogenous pancreatic enzyme secretion. It is not known if enzymes are helpful in

acute cases. NSAID therapy is contraindicated and there is yet no evidence that corticosteroids are indicated or beneficial for acute pancreatitis. Hypertriglyceridemia is common in the Schnauzer and contributes to secondary pancreatitis. Triglycerides >500 mg/dL present after a 12- to 18-hour fasted sample should be treated first with a low fat diet (RC Low Fat or Hills I/D Low fat). If they persist omega-3 dose (70–100 mg/kg body weight) should be added and increased as needed up to the National Research Council safe upper limit (200 mg/kg body weight). Lastly I would consider gemfibrozil (dogs, 7.5 mg/kg body weight PO q12h; cats, 10 mg/kg body weight PO q12h). Gemfibrozil does have side effects and should only be considered only when diet cannot maintain serum triglyceride <500 mg/dL.

Complications of pancreatitis include diabetes mellitus, septic peritonitis and pancreatic abscess formation. Diabetes is treated with insulin therapy. Septic peritonitis or pancreatic abscess formation requires surgery. In both conditions the prognosis is guarded to poor.

DRUGS COMMONLY USED IN PANCREATITIS THERAPY

Action	Drug	Dose	Route	Frequency
Analgesic	Fentanyl	2-10 µg/kg/h	IV	CRI
Analgesic	Morphine	0.1-1 mg/kg	IV, IM	Prn
Analgesic	Butorphanol	0.1-1 mg/kg	SQ	q6h
Analgesic	Hydromorphone	0.1-0.2 mg/kg	IV, IM, SQ	q6-8h
Analgesic	Methadone	0.1-0.5 mg/kg	IV, IM, SQ	q6-8h
Analgesic	Ketamine*	10-20 µg/kg/min	IV	CRI
Analgesic	Lidocaine*	30-50 µg/kg/min	IV	CRI
Antiemetic	Chlorpromazine	0.2-0.5 mg/kg	IV, IM, SQ	q8h
Antiemetic	Metoclopramide	1-2 mg/kg 0.1-0.4 mg/kg	IV IM, SQ	CRI q24h q8h
Antiemetic	Ondansetron	0.1 mg/kg	IV	q8-12h
Antiemetic	Maropitant	1 mg/kg	SQ, IV	q24h

PRINCIPLES OF GI SURGERY

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If you would like a copy of the illustrated version of these notes on CD and a video of this surgical procedure on DVD go to www.videovet.org.

Key Points

- Pay attention to basic surgical principles
- Submucosa is the layer of strength
- Use synthetic absorbable suture materials
- Appositional techniques are best
- Identify breakdown via abdominal tap

General principles of small intestinal surgery

The small intestine is a very forgiving organ system when considering surgical intervention. It has an excellent blood supply with many collateral mesenteric vessels. If the blood supply can be preserved during surgical manipulations, small intestinal incisions can be expected to heal rapidly, gaining almost 70% of their original unwounded tensile strength in 14 - 21 days. It should be remembered that the small intestine is a low pressure conduit system that contains primarily liquid contents and has a relatively low bacterial content proximal to the ileocecocolic valve (compared to the colon). These properties make sugical manipulations of the small intestine predictably successful if basic principles of tissue handling, preservation of blood supply, and hemostasis are followed.

Principles of intestinal surgery include:
1) Incorporation of the collagen laden submucosal layer in the surgical closure.
2) Minimize trauma and contamination.
3) Maintain good blood supply to the surgical site.
4) Avoid tension across the suture line as this may increase the possibility of leak and/or breakdown.
5) Pay attention to your established criteria when suturing intestinal defects.

Preoperative preparation

Preoperative assessment should include a thorough historical and physical examination. This can often be helpful in localizing the problem to an upper versus lower GI obstruction, complete or partial obstruction, or strangulating versus nonstrangulating obstruction. Minimum data base should include complete blood count, electrolytes (i.e., sodium, potassium, chloride), glucose, and BUN. If available, blood gas analysis should be done on patients with severe vomiting, dehydration, or possible sepsis.

Criteria for Use of Prophylactic or Therapeutic Antibiotics

Prophylactic antibiotics should be considered in the following situations:
1. Old age (e.g., >7 years old), debilitated patient
2. Likely to open devitalized bowel
3. Estimated surgical time greater than 90 minutes
4. "Break" in aseptic surgical technique

Therapeutic antibiotics should be considered in the following situations:
1. Non GI associated infection that cannot be treated prior to surgery (e.g., severe dental disease, pyoderma)
2. Gross peritoneal contamination at surgery
3. Operation involving strangulation obstruction
4. Operation in patient with existing peritonitis (e.g., gun shot wound to abdomen with bowel perforation)
5. Reoperation of intestinal surgical breakdown with peritonitis

Operative Considerations
1) Proper **"packing off"** of the surgical field using moistened laparotomy pads should be performed around the **exteriorized** bowell to prevent accidental abdominal contamination from intestinal contents.
2) Keep abdominal contents warm and **moist** throughout surgery with a warm, balanced electrolyte solution.
3) Handling abdominal viscera should be kept to a minimum. **Gentle manipulation** of intestine with moistened gloves or stay sutures is helpful in preventing unnecessary tissue trauma. **DeBakey** forceps are the most atraumatic forceps for handling abdominal visceral organs.
4) The collagen laden, tough **submucosa** is the layer of strength in the small intestine; this layer must be incorporated into any small intestinal closure (i.e., enterotomy, anastomosis).
5) It may be difficult to visualize the submucosal layer due to **mucosal eversion**. Visualization of submucosa may be enhanced if everted mucosa is trimmed away.
6) Intestinal contents should be "milked" away from the anastomosis or enterotomy site. **Intestinal clamps** (e.g., Doyen intestinal clamps, Alice tissue forceps with a rubber feeding tube interposed, hair clips, or Penrose drains) may be used to prevent intestinal contents from contaminating the surgical site whilst manipulating intestine during anastomosis or enterotomy.
7) The enterotomy or anastomosis should be **irrigated** prior to its return to the abdominal cavity and instruments and gloves changed prior to abdominal closure.
8) **Abdominal lavage** with 2-3 liters of body temperature, sterile, physiologic saline solution should be accomplished prior to closure. The objectives of repeated abdominal lavage include dilution of bacteria and endotoxin and mechanical removal of fibrin and necrotic debris. The fluid of choice is body temperature, sterile, physiologic saline solution with no additives (i.e. betadine solution, chlorhexidine, antibiotics, etc). Lavage solution is poured into the abdominal cavity using a sterile stainless steel bowl, the abdominal viscera gently aggitated, and fluid and debris suctioned out with a suction device and a sump suction tip.

Suture Material
Absorbable suture
Catgut. Catgut is NOT recommended in contaminated, infected, hypoproteinemic, or debilitated cachexic patients. Its unpredictable absorption and rapid loss of tensile strength in such situations may result in an unacceptably high number of anastomotic leaks and /or breakdowns. Use of catgut suture in gastrointestinal surgery is not recommended.

Dexon, Polysorb, and Vicryl. Synthetic absorbable braided suture (i.e., polyglactin, poly-glycolic acid) have become very popular. The braided nature however does result in increased tissue drag and difficult knotting ability.

Biosyn and Monocryl. These sutures have similar properties to Dexon, Polysorb and Vicryl however they are monofilament. They were developed to overcome the problem of tissue drag and knot slipping found in the braided synthetic absorbables. Their predictable hydrolytic absorption is unaffected by their immediate environment (i.e., infection, contamination, hypoproteinemia). They retain high tensile strength for a long period of time (2-3 weeks) and have very good handling characteristics. These suture materials are ideal for use in gastrointestinal surgery. These sutures are the authors choice for gastrointestinal surgery.

PDS and Maxon. PDS and Maxon, are synthetic absorbable monofilament suture materials with similar properties to that of Dexon and Vicryl. They have been shown to retain approximately 70% of their tensile strength at 3-4 weeks, and are absorbed by hydrolysis (unaffected by infection, contamination, hypoproteinemia). These suture materials are ideal for use in gastrointestinal surgery. Possible disadvantages include stiffness, a tendency to kink and prolonged absorbtion time.

Nonabsorbable suture
Nylon, Polypropylene, Polybutester. Monofilament, nonabsorbables are excellent suture materials for use in contaminated or infected surgical sites. They have a high tensile strength, are relatively inert in tissue, noncapillary, and do not act as a nidus for infection. These materials pass through tissue with essentially no tissue drag and have excellent knot tying security at sizes 3-0 to 5-0. For their properties, effectiveness, and cost, these are the author's nonabsorbable sutures of choice for intestinal anastomosis and enterotomy closure. Possible disadvantage of these materials is their memory.

Silk, Mersilene, Bronamid, Vetafil. In general, stay away from burying multifilament or braided nonabsorbable suture material. These sutures may harbor infection for years and may result in suture related abdominal abscesses or draining tracts. They should never be used in gastrointestinal surgery.

Suture size
For the majority of small intestinal surgical procedures in dogs, 3-0 or 4-0 size suture material is adequate; in cats, size 4-0 or 5-0 is recommended. The tensile strength of this size suture is greater than the tensile strength of the tissues that are being sutured (i.e., intestinal wall). Larger size suture may contribute to anastomotic failure by increased trauma to tissues and its effect on the blood supply of tissue margins.

Needles
Swaged-on "atraumatic" reversed cutting, narrow taper point, or fine taper-cut needles can all be used for gastrointestinal surgery. The author prefers a narrow taper point needle.

Suture Placement
When suturing intestine, sutures should be placed 3 - 4 mm from the cut edge of the intestine and no more than 2 - 3 mm apart. It is important to recognize everted mucosa and be sure the 3 - 4 mm bite in the intestinal wall is not just in mucosa but engages all layers of the intestinal wall. Measure your intestinal wall bite from the cut edge of the serosa.

Suture Patterns
There is considerable controversy regarding specific suture pattern for use in small intestinal surgery. Everting, inverting, and appositional suture patterns have been used experimentally

and clinically for suturing enterotomies and anastomoses. Appositional patterns are recommended as they cause little lumen compromise postoperatively.

Everting: Everting patterns (i.e., horizontal mattress) have been shown to encourage adhesions and result in lumen stenosis. This technique is NOT recommended. The everting technique is not to be confused with the mild eversion of mucosa that occurs in the appositional techniques described below.

Inverting: In small animals adequate lumen diameter is an important consideration with any technique. Inverting patterns result in substantial lumen compromise of the small intestine and are NOT recommended in dogs and cats.

Apposition: Anatomic apposition of individual layers of the bowel wall (i.e., mucosa, submucosa, muscularis, and serosa) result in primary intestinal healing. This technique is superior to inverting or everting techniques because apposition of intestinal margins eliminates lumen compromise. This is the authors preferred technique for suturing all hollow viscus organs in the abdominal cavity. Suture patterns of choice include:

1) Simple interrupted apposing. This technique involves suturing **all** layers of the intestinal wall and tying the knots on top of the serosa to approximate cut edges. The sutures should be tied tight enough to effect a watertight seal, yet not so tight as to blanch the tissue and cause ischemia of intestinal margins. This technique is simple, fast, reliable, and does not result in lumen compromise.

2) Simple continuous apposing. This technique is similar to the simple interrupted appositional technique however, a continuous suture pattern is used rather than an interrupted pattern. Advantages include faster anastomosis, equal suture tension over the entire anastomosis, airtight-watertight seal, and mucosal eversion is minimized.

Commonly performed small intestinal surgical procedures

Key Points

- intestinal sutures should engage at least 3 - 4 mm of submucosa and be no further apart than 2 - 3 mm
- always handle bowel wall with atraumatic technique
- examine the integrity of your anastomsis visually
- 50 - 60% of the small intestine of dogs and cats can be resected

ENTEROTOMY:

See the DVD for a detailed video description of this technique (www.videovet.org).
An enterotomy incision may be necessary for removal of intraluminal intestinal foreign bodies (e.g., balls, rocks, toys, linear foreign bodies), intestinal biopsy, exploration of the bile duct papilla or intestinal lumen, or rarely intestinal decompression. The segment of bowel to be incised should be removed from the abdominal cavity and packed off with moistened laparotomy pads. An incision parallel to the long axis of the bowel (i.e., longitudinal) or perpendicular to the long axis of the bowel (i.e., transverse) may be made on the antimesenteric border, preferably in healthy bowel (i.e., the aboral side of the foreign body). Closure is performed using the appositional techniques previously described (i.e., simple

continuous or simple interrupted). Omentum can be placed over the enterotomy, but need not be sutured.

Transverse closure: If a large full thickness piece of intestine must be excised (i.e., mural mass) longitudinal closure may result in stenosis. To prevent this, transverse closure of the linear incision is recommended. This ensures adequate lumen diameter without the need for intestinal anastomosis.

INTESTINAL ANASTOMOSIS: Intestinal anastomosis is indicated for resection of nonreducible intussusception, necrotic bowel wall secondary to complete intestinal obstruction, intestinal volvulus, stricture secondary to trauma, linear foreign body with multiple perforations, and intestinal neoplasia (e.g., leiomyoma, leiomyosarcoma, adenocarcinoma).

After a complete abdominal exploration, the affected length of bowel is delivered from the peritoneal cavity and isolated with the use of moistened laparotomy pads and crib towels. If possible, the intestinal anastomosis should be performed on a water resistant surface (e.g., plastic drape, crib towel) to prevent 'strike' through contamination.

Once the level of resection has been determined, the appropriate mesenteric vessels are identified and ligated, and the portion of intestine to be resected is isolated by clamping the bowel at a 60° angle away from the mesenteric border. This angle ensures adequate blood supply to the antimesenteric border.

Everted mucosa: Occasionally when the segment of intestine to be removed is amputated mucosa 'everts' from the cut edge of the intestinal wall making it difficult to visualize the cut edge of the serosa. If this occurs it is 'highly' recommended to excise the everted mucosa to enable the surgeon to easily visualize the cut edge of the intestinal serosa. It is vital that the surgeon engage at least 3 – 4 mm of intestinal wall with each suture to guarantee adequate bites in the collagen laden submucosa.

Bowel lumen diameters: In cases where the oral end of the bowel is dilated and the aboral end is normal size, several options exist to create intestinal lumens of equal diameter:

1) Increase the angle of resection on the smaller diameter segment of bowel (i.e., aboral segment). This will increase the orifice size by 5-10 mm depending upon bowel diameter (e.g., dog vs cat).
2) In larger lumen size discrepancies the antimesenteric border of the smaller diameter stoma can be incised longitudinally to enlarge the lumen diameter.
3) An end-to-side anastomosis can be performed by closing the larger diameter stoma of the intestinal resection with a single layer continuous apposing suture pattern then anastomosing the smaller diameter segment of bowel to an appropriate size enterotomy made in the antimesenteric border of the larger diameter segment of bowel.
4) The larger diameter segment of bowel can be made smaller in diameter by suturing its cut edge until its lumen is equal in size to the smaller diameter intestine (this technique is often used for subtotal colectomy in cats).

Intestinal Anastomosis Technique:
See the DVD for a detailed video description of this technique (www.videovet.org).

When suturing an anastomosis, atraumatic handling of bowel wall and perfect anatomic apposition of incised margins is important. It is recommended to begin suturing at the mesenteric border as this allows adequate visualization of mesenteric vessels and helps prevent encircling these vessels when placing the first few sutures. Any of the appositional suture patterns previously described (i.e., simple continuous or interrupted) will result in a high success rate, both in the short-term (i.e., leakage, breakdown) and long-term (i.e., stricture, stenosis).

The following tips may prove helpful when performing an intestinal anastomosis (see the anastomosis video clip at www.videovet.org for detailed description of the surgery tips below:
1) First, place a stay suture to hold the mesenteric border of each segment of bowel in apposition. Tie this suture, leave the ends long, and place a hemostat on the suture end without the needle.
2) Place a second stay suture in the antimesenteric borders of each segment to be sutured to bring the ends of the intestinal segments into apposition. Place a hemostat on the ends of this suture.
3) Place gentle traction on the mesenteric and antimesenteric stay sutures to bring the two intestinal segments into apposition.
4) Using the needled segment of suture from the mesenteric stay suture, begin a simple continuous appositional anastomosis being careful to get a 3 - 4 mm bite in the submucosa and placing each suture no more than 2 - 3 mm apart (2 mm apart in cats). When the anastomosis is complete, tie the suture to the mesenteric stay suture.
5) If a simple interrupted apposing suture pattern is used, be careful to get a 3 - 4 mm bite in the submucosa and place each suture no more than 2 - 3 mm apart.
6) Evaluate the integrity of the anastomosis. The author's preference for evaluating the integrity of anastomotic closure is to **visually** examine each suture to be certain that suture placement is no more than 2 - 3 mm apart and that each suture has a 3 mm bite in the submucosa.

Postoperative care
Intravenous fluids to maintain hydration and ensure renal function are continued postoperatively, until the patient begins to eat and drink. Intravenous fluids should then be tapered over a 24 to 48 hour period.
Systemic antibiotics are continued postoperatively for 5-7 days; 10 - 14 days in cases with peritonitis and/or sepsis.

Feeding: Early return to enteral feeding is best for the overall health of the intestine. Feeding the postoperative gastrointestinal surgical patient is generrally based on the following criteria:
a) preoperative condition of the patient
b) the condition of the bowel at the time of surgery
c) surgical procedure performed (i.e., enterotomy, anastomosis, pylorectomy)
d) presence or absence of peritonitis
e) postoperative condition of the patient.
The earlier patients can be returned to oral alimenation the better.

Complications
The most common postoperative complication of small intestinal surgery is leakage; leak is either associated with breakdown of the anastomosis or improper surgical technique (i.e.,

improper suture placement, inappropriate suture material, knot failure, sutures to far apart, inappropriate bite in the collagen laden submucosal layer, suturing nonviable bowel).
A presumptive diagnosis may be accomplished by the following:
1) Body temperature (may be up if acute or down if moribund).
2) Abdominal palpation: periodic, gentle abdominal palpation for pain (gas or fluid?).
3) General attitude (depression-anorexia).
4) Incision: examination of the patients incision for drainage (look at cytology if drainage is present)
5) CBC: leukocytosis followed by leukopenia (sepsis), or a degenerative left shift may imply breakdown.
6) Glucose: low glucose generally implies sepsis (this occurs early in sepsis and may be used as a screening
test).
7) Abdominal radiographs: generally not helpful, they are difficult to critically assess due to the presence of postoperative air and lavage fluid. It can take 1 - 3 weeks for peritoneal air to diffuse from the abdominal cavity after routine abdominal surgery. Time variation is dependant upon the amount of air remaining in the abdominal cavity postoperatively (i.e., large deep chested animal vs a small obese animal).
8) **Abdominal tap** (paracentesis): a four quadrant abdominal tap is accomplished by aspirating fluid using a 5cc syringe and 20 gauge needle or placing a plastic IV catheter into the peritoneal cavity and allowing fluid to drip onto a slide. This may be the most sensitive diagnostic test for determining the presence or absence of intestinal leak.
9) Peritoneal lavage (if paracentesis is not productive): infuse 10-20cc/kg of sterile physiologic saline solution into the abdominal cavity, then gently palpate the abdomen and repeat the four quadrant paracentesis. This technique increases the sensitivity of paracentesis to 90%.
Once fluid has been obtained, a smear should be stained and evaluated microscopically. Depending upon the cell types seen, a determination of the presence of leakage can be made.

Below are examples of expected cytology in patients with and without leak.
1) Healthy PMNs with few degenerate PMNs and a moderate number of red blood cells: This cytology may be expected in any postoperative abdominal procedure (e.g., OHE, abdominal exploratory, cystotomy). Your index of suspicion for anastomotic breakdown should be low. However, if clinical signs continue to deteriorate, repeat paracentesis (2 - 3 times daily, if necessary) to determine the "trend" of the abdominal fluid cytology is recommended.
2) Healthy polymorphonuclear leukocytes with bacteria located intra or extracellularly, degenerate PMNs with intracellular bacteria, free bacteria, or food particles--imply breakdown. Exploratory laparotomy is indicated.

In a recent morbidity/mortality study of patients undergoing intestinal surgery it was found that animals requiring a second abdominal surgery to treat intestinal disorders were less likely to survive than patients requiring only one laparotomy. Also, the longer it took to determine whether or not intestinal leakage had occured the less likely the patient would survive reoperation. The take home message is: pay attention to detail during the first surgery and if a leak occurs, diagnose it as soon as possible.

Prognosis The overall prognosis for uncomplicated GI surgery is excellent. The surgeon must pay attention to detail when suturing any hollow viscus organ with liquid contents.

VISCERAL ORGAN BIOPSY

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If you would like a copy of a video of this surgical technique on DVD, go to **www.videovet.org**.

Key Points

- Open the abdomen from xyphoid to pubis
- Use the same method of exploration in each case
- When in doubt, biopsy, biopsy, biopsy
- Close the linea alba using a continuous suture pattern

General Considerations and Indications

The systematic, thorough observation and palpation of all abdominal structures is mandatory with any abdominal exploratory procedure. It is easy to miss a second intestinal foreign body, an area of metastasis or a 'second' tumor if one does not get in the habit of performing a complete exploratory.

An exploratory can be done in any order but it is best to establish a routine and follow it for every case. With experience the procedure can be completed in less than five minutes. The best way to recognize an abnormal finding is to know the normal. Take advantage of any laparotomy to observe normal structure, color, consistency and position of all abdominal organs.

Abdominal exploratory may be indicated in following situations:

Abdominal mass
Undiagnosed GI disorders
Urogenital abnormaities unresponsive to medical management
Abdominal disorders of unknown origin
Penetrating trauma
Acute abdomin
Generalized peritonitis
Diagnosis and treatment of portosystemic shunts
Spleenic abnormalities
Uncontrolled abdominal hemorrhage

Preoperative Considerations

A midline abdominal incision from xiphoid to pubis is the easiest and most versatile approach. Positioning the patient's head toward the top of the table and tilting the table at a 30° to 40° angle will facilitate gravitation of abdominal viscera out of the thorax. Rarely is it necessary to extend the incision into the thorax via a median sternotomy however if your index of suspicion is high that this may be necessary (e.g., diaphragmatic hernia, chylothorax, porosystemic shunt) the animal should be properly and adequately prepared.

ABDOMINAL EXPLORATORY TECHNIQUE

Position, Preparation and Draping

The abdomen is always clipped and prepared wider and longer than you may anticipate for a "routine" procedure. This generally means from cranial to the xyphoid to a point 4-5 cm caudal to the brim of the pubis and laterally to include the ventral aspect of the abdomen. The animal is placed in dorsal recumbency in a V-trough with front and hind limbs secured with ropes to the table. If the penis or prepuce does not need to be accessible during surgery, the prepuce is clipped but not flushed. If the penis needs to be exposed and handled by the surgeon (lower urinary system exploratory), a prepucal lavage with a1:50 dilution of betadine solution in sterile saline is performed

prior to skin preparation. An example is when the surgeon feels it is necessary to pass a urinary catheter during surgery (i.e., urethral and cystic calculi). In this case, the prepuce is clipped then flushed using dilute Betadine or chlorhexidine prior to the prep. Standard skin preparation is performed.

A ventral midline incision is made from xyphoid to pubis. After identifying the linea alba, a scalpel blade is used to open the abdominal cavity via a stab incision. Mayo scissors are used to complete the abdominal incision. Make sure you can see or feel the internal side of the linea so that you do not damage abdominal viscera during abdominal wall incision. The falciform ligament is excised with scissors from its attachment to the abdominal wall midline and xyphoid. This will allow better inspection of viscera, particularly in the cranial quadrant, and facilitate easier closure of the abdomen. Moistened laparotomy sponges may be placed on the incision if viscera are to be brought out of the abdomen. All viscera should be kept moistened with saline solution.

Examination of abdominal viscera can be done in any order but it is best to establish a routine and follow it every time the abdomen is explored. Generally, start with proximal GI tract and move distally, then liver and pancreas, then urinary tract. Be thorough, and always be gentle when handling tissue. it is easy to miss a second intestinal foreign body or an area of metastasis if one does not get in the habit of performing a complete exploratory. With experience, complete exploration can be performed in less than five minutes. The best way to recognize an abnormal finding is to know the normal. Take advantage of any laparotomy to observe normal structure, color, consistency and position all of abdominal organs. You should be able to identify the following structures:

1. Skin, subcutaneous tissue and linea alba
2. Falciform ligament and fat should be removed with scissors from both sides of the incision, no ligation is usually necessary
3. Abdominal aorta and its major branches
4. Caudal vena cava
5. Portal vein
6. Kidneys - artery - frequently multiple; vein - frequently multiple; ureter - note its location at bladder neck (dorsolateral) and its path along psoas muscles
7. Liver lobes
8. Gallbladder
9. Pancreas (always be gentle handling this organ because you can induce pancreatitis) -left and right limbs
10. Diaphragm -left and right crus; aortic hiatus; esophageal hiatus; caval foramen; costal arch
11. Abdominal esophagus
12. Stomach - cardia; fundus; body; pylorus (note close relationship of common bile duct and pancreatic ducts); arterial supply; gastrohepatic ligament
13. Small bowel - note blood supply to each area
14. Cecum - note size and consistency, feel ileocecocolic junction
15. Colon - ascending, transverse and descending portion
16. Lymph nodes - mesenteric and sublumbar
17. Omentum and mesentary; greater omentum; lesser omentum; mesoduodenum - used to displace and pack off cranial portions of abdomen from the right to the left; mesocolon - used to displace and pack off caudal aspect of abdominal contents from the left to the right
18. Urinary bladder; ureter entrance on dorsal trigone area; apex and trigone; lateral ligaments
19. Female; ovary, ovarian bursa, proper ovarian ligament; uterine horn; uterine body; cervix; round lig; broad lig; suspensory lig (broken down to mobilize ovary during spay)
20. Male; prostate; ductus deferens (and relation to ureters)
21. Adrenal glands; phrenicoabdominal arteries and their position in relation to ureters)
22. Spleen - usually will be very large and turgid as a result of barbiturate anesthesia

Closure
The linea alba is closed with monofilament absorbable or nonabsorbable suture using a simple continuous pattern. If the abdominal incision was made directly on the midline (i.e., linea alba) closure requires full thickness bites of the linea alba. If the abdominal incision was slightly off the midline, suture the rectus sheath only (do not include rectus abdominus muscle or peritoneum). The most important tissue in the abdominal closure is the collagen dense external rectus sheath. Incorporation of the internal sheath (i.e., peritoneum) is unnecessary as the peritoneum has very little holding power. Sutures should engage approximately 5-7 mm of rectus sheath on each side of the incision line.

Subcutaneous tissues are closed separately with a simple continuous pattern using monofilament or multifilament synthetic absorbable suture. Tissues should be approximated and not strangulated. In cats, the subcutaneous closure is not recommended.

Skin is closed with simple interrupted monofilament nonabsorbable skin sutures or a continuous intradermal suture (i.e., subcuticular).

Postoperative Care
Postsurgical care may include systemic antibiotics, appropriate pain medication, careful monitoring of the patient's breathing, temperature, and color. Hypothermic patients should be kept in a warming cage or on a warm water circulating blanket for at least 24 hours. Analgesics may be used to relieve patient discomfort, however care should be taken to monitor the effects of various analgesic drugs on respiratory effort.

BIOPSY TECHNIQUES FOR ABDOMINAL ORGANS

A variety of visceral organ biopsy techniques are illustrated on a video DVD available through VideoVet at www.videovet.org.

Liver Biopsy
Liver biopsy is indicated whenever an abdominal exploratory is being performed in patients thought to have liver disease or in cases that liver disease was not the primary reason for exploratory but the liver appears grossly normal.

Liver biopsy is one of the most important diagnostic aids available for evaluation of liver disease. Samples for cytologic examination may be obtained via percutaneous needle biopsy, laparoscopy, or exploratory laparotomy. Percutaneous needle biopsy techniques are the most efficient in terms of time and expense.

Several techniques are available for obtaining liver specimens during exploratory laparotomy. The simplest method is performed by cutting a strip of liver parenchyma 5 to 6 mm thick along the border of the liver lobe. Excessive bleeding is rarely a problem with this technique; hemorrhage is controlled via cautery or direct pressure. Diffuse liver disease must be present if this method is to be diagnostic.

A second technique involves placing an encircling ligature around a pedicle of liver tissue. As the ligature is tightened, it cuts through the hepatic parenchyma, ligating hepatic vessels and bile ducts. This technique is widely known as the Guillotine technique. This method requires the presence of diffuse liver disease to obtain a diagnostic biopsy munless the lesion is present in the distal aspect of the liver lobe.

A technique that can be used in 'bulbous' liver lobes with no convenient edges to biopsy is performed by penetrating the central portion of the proposed biopsy site with 2-0 or 3-0 suture on a swaged-on curved taper needle. The suture ends are left long and a mosquito hemostat attached. A second pass of the suture is made through the same location as the first needle pass. A second stay suture is made. Each stay suture is tied individually to "cut" through the liver. A "V" wedge is cut through the liver when both strands of suture have been tied. A number 15 BP scalpel blade or fine Metzenbaum scissors is used to cut the V-shaped liver biopsy wedge from the sutures.

Another technique for use in patients with diffuse fibrotic liver disorders is performed by penetrating the affected liver lobe with a straight mosquito hemostat. The hemostat tip is placed on the surface of the liver lobe to be biopsied and gently plunged through the liver lobe until the tip of the hemostat is seen penetrating through the opposite side of the liver. The jaws of the hemostat are opened just wide enough to accept a piece of 2-0 or 3-0 Maxon or Biosyn suture. The suture is doubled on itself, the loop is passed into the jaws of the hemostats, and the loop pulled through the liver lobe. The exiting loop is cut leaving two strands of suture coursing through the liver lobe. Each strand is tied individually to "cut" through the liver. A "V" wedge is cut through the liver when both strands of suture have been tied. A number 15 BP scalpel blade is used to cut the V-shaped liver biopsy wedge from the sutures.

Occasionally it may be required to biopsy a small lesion located distant from the liver lobe margin. This can be accomplished using a 4mm or 6mm 'sharp' skin punch biopsy instrument. The skin punch is placed directly over the lesion on the surface of the liver. With mild downward pressure and a gentle back and forth twisting motion the punch biopsy instrument cuts a circular hole in the liver thus engaging a piece of the liver. The punch is then angled to attempt to cut the base of the biopsy specimen. The punch is removed and either the biopsy specimen comes out with the punch or a DeBakey forcep may be needed to remove the specimen from its remaining attachment to the liver. This technique results in a very small biopsy specimen and thus an additional marginal liver biopsy is performed.

Pancreatic biopsy

The old wives tale stating "don't touch the pancreas" needs to be put to rest. Gentle manipulation and biopsy of the pancreas is a predictably successful procedure with almost no incidence of postoperative pancreatitis.

Biopsy of the pancreas is performed in a similar manner as biopsy of the liver. In patients that have diffuse pancreatic disease, a segment of the right or left limb of the pancreas is identified. An encircling ligature of 3-0 Biosyn is placed around the pedicle. As the ligature is tightened, it cuts through the pancreatic parenchyma, ligating vessels and pancreatic ducts. The distal pedicle of pancreas is carefully removed with a number 15 BP scalpel blade or metzenbaum scissors. Care is taken to avoid cutting the suture. If a relatively large portion of pancreas is to be removed (e.g., removal of insulinoma), a similar technique is used. In this situation, 2-0 or 3-0 monofilament nonabsorbable suture should be used.

Stomach and Small Intestine

Patients with chronic vomiting or chronic diarrhea of unknown origin often require gastric and intestinal biopsies for definitive diagnosis. In many cases, the surgeon will examine the gastrointestinal tract carefully and conclude that there are no apparent abnormalities. In this situation, ALWAYS perform gastric and multiple intestinal biopsies (i.e., duodenum, jejunum, ileum). Remember these words of wisdom when concluding that you have a negative exploratory laparotomy "your eyes are NOT microscopes".

Gastric biopsy
The stomach should be visually examined for any obvious abnormalities on the serosal surface. In addition, the stomach should be carefully palpated to determine if there are mural or mucosal abnormalities present. In the case of an observed or palpated abnormality, the surgeon should plan the gastric biopsy to include a portion of the abnormal stomach, the margin of normal and abnormal stomach, and normal stomach. Full thickness biopsies should always be taken. In the case of diffuse disease or if an abnormality cannot be located, a 3-4 cm incision should be made in the ventral aspect of the stomach equidistant from the greater and lesser curvature. Stay sutures are placed at the midpoint of the incisied edges and the interior of the stomach visually and digitally examined. If a mucosal abnormality is detected, the area should be biopsied either from inside the stomach of from the serosal surface directly over the lesion.

Gastric wall incisions (e.g., biopsy, gastrotomy, partial gastrectomy) should be closed with a single layer, simple continuous or simple interrupted suture pattern being careful to get full thickness bites. Sutures should be placed no further apart than 3 mm and at least a 4 mm bite of gastric wall is recommended. Monofilament absorbable suture with a sharp taper or taper-cut (penetrating point) needle is the authors' preference.

Small intestinal biopsy
Several techniques can be used to successfully biopsy the intestine. Always remember; FULL THICKNESS biopsy is mandatory for the pathologist to give you the the most accurate diagnosis.

When taking an intestinal biopsy, the easiest way to guarantee you will get an adequate size, full thickness piece of intestine is to use a brand new 4mm skin punch biopsy instrument. The skin punch is placed on the antimesenteric border of the proposed segment of intestine and 'drilled' through all layers of intestine until the biopsy punch can be felt to enter the lumen of the intestine. The skin punch is removed and the biopsy retreived from the shaft of the skin punch biopsy. This technique is particularly useful for ileal biopsy as it is easy to biopsy between the mesenteric and antimesenteric vessels. Transverse closure of the biopsy site is recommended to eliminate the possibility of lumen compromise. Suture technique is as described above for enterotomy closure. This is the authors' preferred technique for intestinal biopsy.

An alternate technique for intestinal biopsy is to make a 2-3 mm long incision on the antimesenteric border of the intestinal segment. A #11 or #15 BP scalpel blade is used to penetrate the intestinal wall. The blade is withdrawn to create a 2-3 mm long incision. A second parallel incision is made 1 – 2 mm from the original incision. A DeBakey forcep is used to grasp one end of the parallel incisions, a Metzenbaum scissor is used to cut out the piece of intestine. The surgeon should be careful not to crush the specimen with forceps. Only handle one end of the specimen whilst excising the biopsy specimen. If excessive trauma is created during biopsy, the pathologist may not be able to determine if the pathology is real or surgically created. The excised piece of intestine is examined closely to ensure that all layers have been included in the specimen. The biopsy site is closed using a simple interrupted or simple continuous suture pattern. 3-0 or 4-0 monofilament absorbable suture with a swaged-on sharp taper or taper-cut (penetrating point) needle is recommended. Care is taken to ensure that at least 3 mm bites are taken into the intestine and the sutures are no more that 2-3 mm apart.

Biopsy of the duodenum, jejunum, and ileum is recommended whenever a chronic vomiting/diarrhea patient is explored.

Complications associated with multiple intestinal biopsies are rare. Even patients that present with protein loosing enteropathy. One study looking at the complication rate of intestinal surgical procedures in patients with normal protein levels and patients that were hypoproteinemic found no

difference. Complications in patients undergoing intestinal surgica procedures are generally related to the surgeons technical ability not the patients preoperative status.

SURGICAL MANAGEMENT OF GDV

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If you would like a copy of this surgical procedure on DVD go to **www.videovet.org.**

Key Points

- Survival is generally determined by early and appropriate presurgical management
- Patients referred for surgery should be decompressed prior to referral with continued decompression provided during transport
- Incisional gastropexy results in a fast, easy, permanent adhesion
- Ventricular tachycardia is a common postoperative complication
- Gastric necrosis signals an unfavourable prognosis

Introduction: Patients with GDV are considered critical care cases; every minute of presurgical treatment is vital to a successful outcome. Survival is generally determined by early and appropriate presurgical management; not surgery. Efficient presurgical treatment usually involves a minimum of two people. Gastric decompression and shock therapy should be done simultaneously. If this is not possible; decompression should be performed first. It is stated that gastric decompression is the single most important factor in reversing cardiovascular deficits in patients with GDV.

Decompression: Generally, orogastric intubation can successfully be performed in 80 - 90% of GDV patients. Decompression via flank needle puncture should be attempted in cases difficult to intubate or severely depressed metabolically deranged patients.

Technique: The stomach tube is measured to the last rib and marked with a piece of tape. A stiff foal or mare stomach tube with a smooth beveled tip works best (having several diameter and stiffness tubes is ideal). Apply adequate lubrication to the tube. Place a functional mouth speculum; generally a roll of 2" tape secured in the mouth with tape encircling the muzzle. As the stomach tube is passed, you will generally meet resistance at the esophageal-stomach junction. Pass the tube firmly in a twisting manner to pass the lower esophageal sphincter.

If unsuccessful, place the patient in various positions and attempt to pass the tube (i.e., elevate animal at 45 degree angle with rear feet on floor and forefeet on table, right lateral recumbancy, and left lateral recumbancy). This movement may encourage the stomach to rotate enough to allow tube passage. Be careful not to position the patient in dorsal recumbancy as this will increase abdominal visceral pressure on the caudal vena cava and may exacerbate signs of shock.

If still unsuccessful, try different diameter tubes; try a smaller diameter, more flexible tube and proceed as described above.

If still unsuccessful, attempt to remove some of the air in the stomach by placing an l8 gauge needle at the point of distention in the right flank region. Ping the area to make sure the spleen is not under the proposed trocarization

site. After trocar decompression, attempt to pass the stomach tube as described above.

If still unsuccessful, sedate the dog with a narcotic (e.g., Oxymorphone) and try to pass the tube again. Mild sedation is recommended if the patient strongly resists physical restraint.

Success in passing a stomach tube depends on the skill of the operator and available assistants.

If you are successful at passing a stomach tube, but plan to refer the patient to a referral surgical center for gastropexy, transport the patient with the tube remaining in the stomach (i.e., taped to the mouth) or bring the tube out through a pharyngostomy incision or place a nasogastric tube.

If a stomach tube was successfully passed, stomach contents should be evaluated for color and presence or absence of necrotic looking gastric mucosa. This may give an impression of gastric viability.

Fluids: Shock dosage of polyionic isotonic fluid is carefully administered to expand the vascular compartment. Patients are frequently monitored during fluid administration to help determine ultimate fluid rate and amount. One or two indwelling cephalic catheters are placed.

Referral: If you are successful at passing a stomach tube, but plan to refer the patient to a referral surgical center for gastropexy, transport the patient with the tube remaining in the stomach (i.e., taped to the mouth) or bring the tube out through a pharyngostomy as described below.

Pharyangostomy placement:
a. Orally palpate the fossa lateral to the hyoid apparatus until a lateral bulge is seen
b. Make a small skin incision over the bulge and press a curved forceps (substitute for finger) through the soft tissues and skin incision.
c. Pull the stomach tube through the incision with curved forceps; then pass the tube over the arytenoid cartilages, down the esophagus, and into the stomach (measure to the 13th rib).

Disadvantages include: heavy sedation or general anesthesia is necessary for placement of tube.

Rarely a temporary gastrostomy may need to be performed. The patient is placed in left lateral recumbancy with the right flank area clipped and surgically prepared. Heavy sedation and local infiltration of lidocaine or light general anesthesia is performed. A 4 - 5 cm incision is made in the skin over the point of greatest gastric distention (generally 1 - 2 cm caudal to the 13th rib and 2 - 3 cm distal to the transverse processes of the lumbar vertebrae). A grid technique is used to gain entrance into the peritoneal cavity. Due to severe gastric distention the stomach wall is pressed against the abdominal wall and easily identified through the flank incision. The stomach wall is sutured to the skin using a simple continuous pattern with 3-0 Maxon. This is done prior to incising into the stomach lumen. A #11 BP scalpel blade is used to puncture into the lumen of the stomach. Gas and stomach contents are expelled under pressure so stand back! The gastric mucosa is evaluated for viability. Disadvantages of

gastrostomy include: the stomach is sutured in its rotated position and more time is required when definitive surgical treatment is performed due to the necessity of closing the gastrostomy.

Successful stomach tube placement: Once the stomach tube has been passed into the stomach or gastrostomy performed, the stomach is lavaged with warm water. If a stomach tube was successfully passed, the stomach contents should be evaluated for color and presence or absence of necrotic gastric mucosa. This may give an impression of gastric viability.

Surgical Treatment: Surgical procedures utilized in the treatment of gastric dilatation-volvulus can be divided into two categories; 1) immediate decompression and 2) therapeutic gastropexy. Immediate decompression is performed with a successfully passed stomach tube secured to the patient or temporary gastrostomy as described above. Therapeutic or prophylactic gastropexy techniques are described below.

Gastric repositioning: Anatomic repositioning of the stomach is necessary to perform prior to permanent gastropexy. Repositioning occasionally occurs spontaneously at the time of gastric decompression. Knowledge of normal anatomy is necessary to understand how repositioning is performed.

A specific 'Surgical Plan' should be in mind before entering the operating room theatre. This will improve the efficiency of surgery and thus decrease overall surgery time. The 'authors' surgical plan is as follows:

Stand on the right side of the patient.
Provide generous abdominal exposure via xyphoid to pubis midline laparotomy.
Remove of all of the falciform ligament to the level of the xyphoid.
Place a 10" Balfour self retaining abdominal retractor with full retraction.
Confirm that the omentum is draped over the exposed surface of the stomach (pathagnomonic for GDV)
Exteriorize the spleen from the abdominal cavity. Evaluate color, texture, blood flow (splenomegaly is always present and is NOT an indication for splenectomy)
Splenectomy is rarely performed but may be necessary if splenic vessels are infarcted.
If the stomach is full of air or fluid it should be emptied, if possible, prior to attempting derotation. If the stomach is full of food and several attempts to derotate (see author's technique below) are unsuccessful, perform a gastrotomy and manually remove the food from the stomach lumen. Suture the gastrotomy and attempt derotation again.

Attempt derotation by:
Standing on the patients' right side, first reach your right hand across the abdomen and place it between the left body wall and dilated stomach.
Slide your right hand along the sublumbar body wall and grasp the deep (dorsal) aspect of the stomach.
Next, place the open palm of your left hand on the exposed surface of the right side of the dilated stomach.

Using both hands simultaneously, pull the deep part of the stomach with your right hand to begin derotation whilst you push the right surface of the stomach down toward the patients sublumbar body wall with your left hand. This maneuver will be successful in the majority of cases.

See this maneuver performed on the Emergency Surgery I, Gastrointestinal Surgery I, and Soft Tissue Surgery II DVD's available at www.videovet.org. Once the stomach is derotated, evaluate the stomach for evidence of viability abnormalities (particularly the greater curvature and fundus) and for evidence of gastric motility.

Commence your gastropexy procedure.

Incisional gastropexy: This technique is based on the construction of a seromuscular antral flap attached to a incised segment of transversus abdominus muscle. Prior to selecting the location on the transversus abdominus m for gastropexy, visualize the diaphragmatic muscle fibers as they radiate into the abdominal cavity and attach near the costal arch. It is important that the gastropexy site be distant from the diaphragm muscle insertion. In addition, it is important to locate the ideal position for the gastric antral incision. The incision is located equidistant between the pylorus and gastric incisure and equidistant between the greater curvature and lesser curvature. A 3-4 cm incision is made in the antral portion of the stomach. Once the antral incision has been made, the bleeding surface of the antrum is brought to the right body wall. With the stomach in a normal position, the bleeding antral surface is touched to the peritoneal wall approximately 2-3 cm deep to the abdominal wall incision and caudal to the insertion of the diaphragm. A blood mark is created on the peritoneum at this proposed location. This will be the site for the permanent gastropexy. The peritoneum and transverses abdominus muscle are then incised creating a mirror image defect of the stomach incision. The incisional defect in the stomach is then sutured to the incisional defect in the abdominal wall. The defects are sutured in two layers using a simple continuous pattern with 2-0 or 3-0 monofilament or multifilament synthetic absorbable suture.

Belt Loop Gastropexy: This technique is based on the construction of a sero-muscular antral flap attached around a segment of transversus abdominus muscle. A horseshoe shaped incision is made in the serosal layer of the antral portion of the stomach with its base at the greater curvature. The sero-muscular portion of the stomach is identified by grasping full thickness antral wall between the thumb and index finger and "slipping" the mucosal and submucosal layers away so only the sero-muscular portion of the wall remains between thumb and finger. The sero-muscular layer is incised with scissors and the horseshoe shaped sero-muscular antral flap is dissected and elevated of the submucosal layer. The stomach is replaced in the abdominal cavity in normal position and the sero-muscular flap lined up with the transversus abdominus muscle. Once this optimal location is discovered, two longitudinal incisions (along the fibers of the transversus m.) are made in the transversus abdominus m. The segment of muscle between the incisions is undermined. The sero-muscular flap from the stomach (i.e., belt) is passed through the

transversus abdominus m. (i.e., loop) and sutured to itself to complete the "Belt-Loop" gastropexy. 2-0 or 3-0 monofilament absorbable synthetic suture in a simple interrupted or continuous pattern is used to secure the flap in place. Advantages of belt loop gastropexy include: it is relatively easy to perform alone and in the middle of the night, it can be performed quickly, and it is an effective means of permanent gastropexy.

Postoperative management

In most cases 3 to 4 days of intensive monitoring is necessary for the successful management of GDV patients. Postoperative considerations are listed below:

a. Shock is a postoperative possibility and the patient should be monitored and treated accordingly.

b. Patients are generally held off food and water for 24 hours following surgery. During this time maintenance fluids should be supplied using polyionic isotonic crystalloid fluid. Vomiting may occur following surgery; the NPO period should be extended accordingly. Gastritis and gastric motility disorder may be seen in post op GDV patients.

c. After 24 hours of no vomiting, oral alimentation should begin gradually with a sequence of ice cubes, water, and finally canned dog food. This should occur over a 2-3 day period.

d. Antibiotics should be continued for 7 - 10 days.

e. Routine surgical complications such as infection, dehiscence, seroma, etc. should be watched for and treated accordingly.

f. EKG monitoring: the most common severe postoperative complication is cardiac arrhythmia. Approximately 75% of GDV patients will develop arrhythmia's in the immediate postoperative period. Arrhythmia's can be present at the initial time of presentation but most often occur within 24 - 72 hours after surgery. Ventricular premature contractions, progressing to ventricular tachycardia is most common. Etiology is unknown but shock, hypoxia, acid base alterations, endotoxins, myocardial depressant factor (MDF), reperfusion injury, release of free radicals, and hypokalemia have been identified. Occurrence of a total body potassium deficit has been proposed. Etiology of the hypokalemia includes anorexia, vomiting, tremendous outpouring of potassium rich fluids into a dilated stomach, and use of potassium poor fluids in treatment of shock. For this reason, adding 20-30 mEq of potassium chloride per liter of maintenance fluids during and after surgery are recommended.

g. Gastric motility: occasionally GDV patients will develop postoperatove gastric motility abnormalities. Patients with gastric hypomotility or gastric stasis should be treated with a motility modifier (i.e., metaclopramide, erythromycin, etc).

INTESTINAL ANASTOMOSIS

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If you would like a copy of this surgical procedure on DVD go to www.videovet.org.

Key Points

- Pay attention to basic surgical principles
- Submucosa is the layer of strength
- Use synthetic absorbable suture materials
- Appositional techniques are best
- Intestinal sutures should engage at least 3 - 4 mm of submucosa
- Intestinal sutures should be no further apart than 2 - 3 mm
- Always handle bowel wall using atraumatic technique
- Examine the integrity of your anastomsis visually
- 50 - 60% of the 'small intestine' of dogs and cats can be resected

General principles of small intestinal surgery

1) Incorporation of the collagen laden submucosal layer in the surgical closure.
2) Minimize trauma and contamination.
3) Maintain good blood supply to the surgical site.
4) Avoid tension across the suture line as this may increase the possibility of leak and/or breakdown.
5) Pay attention to your established criteria when suturing intestinal defects.

Operative Considerations

1) Proper **"packing off"** of the surgical field using moistened laparotomy pads should be performed around the **exteriorized** bowell to prevent accidental abdominal contamination from intestinal contents.
2) Keep abdominal contents warm and **moist** throughout surgery with a warm, balanced electrolyte solution.
3) Handling abdominal viscera should be kept to a minimum. **Gentle manipulation** of intestine with moistened gloves or stay sutures is helpful in preventing unnecessary tissue trauma. **DeBakey** forceps are the most atraumatic forceps for handling abdominal visceral organs.
4) The collagen laden, tough **submucosa** is the layer of strength in the small intestine; this layer must be incorporated into any small intestinal closure.
5) It may be difficult to visualize the submucosal layer due to **mucosal eversion**. Visualization of submucosa may be enhanced if everted mucosa is trimmed away.
6) Intestinal contents should be "milked" away from the anastomosis site. **Intestinal clamps** (e.g., Doyen intestinal clampS, Alice tissue forceps with a rubber feeding tube interposed, hair clips, or Penrose drains) may be used to prevent intestinal contents from contaminating the surgical site whilst manipulating intestine during anastomosis.
7) The anastomosis should be **irrigated** prior to its return to the abdominal cavity and instruments and gloves changed prior to abdominal closure.
8) **Abdominal lavage** with 2-3 liters of body temperature, sterile, physiologic saline solution should be accomplished prior to closure. The objectives of repeated abdominal lavage include dilution of bacteria and endotoxin and mechanical removal of fibrin and necrotic

debris. The fluid of choice is body temperature, sterile, physiologic saline solution with no additives (i.e. betadine solution, chlorhexidine, antibiotics, etc). Lavage solution is poured into the abdominal cavity using a sterile stainless steel bowl, the abdominal viscera gently aggitated, and fluid and debris suctioned out with a suction device and a Poole suction tip. Injecting antimicrobials or other products into the abdominal cavity is not recommended.

Suture Material

Absorbable suture

Catgut. Catgut is NOT recommended for any visceral organ surgery. Its unpredictable absorption and rapid loss of tensile strength in such situations may result in an unacceptably high number of anastomotic leaks and /or breakdowns. Use of catgut suture in gastrointestinal surgery is not recommended.

Dexon, Polysorb, and Vicryl. Synthetic absorbable braided suture (i.e., polyglactin, poly-glycolic acid) have become very popular. The braided nature however does result in increased tissue drag and difficult knotting ability.

Biosyn and Monocryl. These sutures have similar properties to Dexon, Polysorb and Vicryl however they are monofilament. They were developed to overcome the problem of tissue drag and knot slipping found in the braided synthetic absorbables. Their predictable hydrolytic absorption is unaffected by their immediate environment (i.e., infection, contam-ination, hypoproteinemia). They retain high tensile strength for a long period of time (2-3 weeks) and have very good handling characteristics. These suture materials are ideal for use in gastrointestinal surgery. These sutures are the authors choice for gastrointestinal surgery.

PDS and Maxon. PDS and Maxon, are synthetic absorbable monofilament suture materials with similar properties to that of Dexon and Vicryl. They have been shown to retain approximately 70% of their tensile strength at 3-4 weeks, and are absorbed by hydrolysis (unaffected by infection, contamination, hypoproteinemia). These suture materials are ideal for use in gastrointestinal surgery. Possible disadvantages include stiffness, a tendency to kink and prolonged absorbtion time.

Nonabsorbable suture

Nylon, Polypropylene. Monofilament, nonabsorbables are excellent suture materials for use in contaminated or infected surgical sites. They have a high tensile strength, are relatively inert in tissue, noncapillary, and do not act as a nidus for infection. These materials pass through tissue with essentially no tissue drag and have excellent knot tying security at sizes 3-0 to 5-0. For their properties, effectiveness, and cost, these are the author's nonabsorbable sutures of choice for intestinal anastomosis and enterotomy closure. Possible disadvantage of these materials is their memory.

Silk, Mersilene, Bronamid, Vetafil. In general, stay away from burying multifilament or braided nonabsorbable suture material. These sutures may harbor infection for years and may result in suture related abdominal abscesses or draining tracts. They should never be used in gastrointestinal surgery.

Suture size

For the majority of small intestinal surgical procedures in dogs, 3-0 or 4-0 size suture material is adequate; in cats, 4-0 is recommended. The tensile strength of this size suture is

greater than the tensile strength of the tissues that are being sutured (i.e., intestinal wall). Larger size suture may contribute to anastomotic failure by increased trauma to tissues and its effect on the blood supply of tissue margins.

Needles
Swaged-on "atraumatic" reversed cutting, narrow taper point, or fine taper-cut needles can all be used for gastrointestinal surgery. The author prefers a narrow taper point needle. Needle diameter should approach the diameter of the suture.

Suture Placement
When suturing intestine, sutures should be placed 3 - 4 mm from the cut edge of the intestinal serosa and no more than 2 - 3 mm apart. It is important to recognize everted mucosa and be sure the 3 - 4 mm bite in the intestinal wall is not just in mucosa but engages all layers of the intestinal wall. Measure your intestinal wall bite from the cut edge of the serosa.

Suture Patterns
There is considerable controversy regarding specific suture pattern for use in small intestinal surgery. Everting, inverting, and appositional suture patterns have been used experimentally and clinically for suturing enterotomies and anastomoses. Appositional patterns are recommended as they cause little lumen compromise postoperatively.

Everting: Everting patterns (i.e., horizontal mattress) have been shown to encourage adhesions and result in lumen stenosis. This technique is NOT recommended. The everting technique is not to be confused with the mild eversion of mucosa that occurs in the appositional techniques described below.

Inverting: In small animals adequate lumen diameter is an important consideration with any technique. Inverting patterns result in substantial lumen compromise of the small intestine and are NOT recommended in dogs and cats.

Apposition: Anatomic apposition of individual layers of the bowel wall (i.e., mucosa, submucosa, muscularis, and serosa) result in primary intestinal healing. This technique is superior to inverting or everting techniques because apposition of intestinal margins eliminates lumen compromise. This is the authors preferred technique for suturing all hollow viscus organs in the abdominal cavity. Suture patterns of choice include:

1) Simple interrupted apposing. This technique involves suturing **all** layers of the intestinal wall and tying the knots on top of the serosa to approximate cut edges. The sutures should be tied tight enough to effect a watertight seal, yet not so tight as to blanch the tissue and cause ischemia of intestinal margins. This technique is simple, fast, reliable, and does not result in lumen compromise.

2) Simple continuous apposing. This technique is similar to the simple interrupted appositional technique however, a continuous suture pattern is used rather than an interrupted pattern. Advantages include faster anastomosis, equal suture tension over the entire anastomosis, airtight-watertight seal, and mucosal eversion is minimized. This is the authors preferred suture pattern for suturing all hollow viscus organs in the abdominal cavity.

INTESTINAL ANASTOMOSIS: Intestinal anastomosis is indicated for resection of nonreducible intussusception, necrotic bowel wall secondary to complete intestinal obstruction, intestinal volvulus, stricture secondary to trauma, linear foreign body with multiple perforations, and intestinal neoplasia (e.g., leiomyoma, leiomyosarcoma, adenocarcinoma).

After a complete abdominal exploration, the affected length of bowel is delivered from the peritoneal cavity and isolated with the use of moistened laparotomy pads and crib towels. If possible, the intestinal anastomosis should be performed on a water resistant surface (e.g., plastic drape, crib towel) to prevent 'strike' through contamination.

Once the level of resection has been determined, the appropriate mesenteric vessels are identified and ligated, and the portion of intestine to be resected is isolated by clamping the bowel at a 60° angle away from the mesenteric border. This angle ensures adequate blood supply to the antimesenteric border.

Everted mucosa: Occasionally when the segment of intestine to be removed is amputated mucosa 'everts' from the cut edge of the intestinal wall making it difficult to visualize the cut edge of the serosa. If this occurs it is 'highly' recommended to excise the everted mucosa to enable the surgeon to easily visualize the cut edge of the intestinal serosa. It is vital that the surgeon engage at least 3 – 4 mm of intestinal wall with each suture to guarantee adequate bites in the collagen laden submucosa.

Bowel lumen diameters: In cases where the oral end of the bowel is dilated and the aboral end is normal size, several options exist to create intestinal lumens of equal diameter:

1) Increase the angle of resection on the smaller diameter segment of bowel (i.e., aboral segment). This will increase the orifice size by 5-10 mm depending upon bowel diameter (e.g., dog vs cat).
2) In larger lumen size discrepancies the antimesenteric border of the smaller diameter stoma can be incised longitudinally to enlarge the lumen diameter.
3) An end-to-side anastomosis can be performed by closing the larger diameter stoma of the intestinal resection with a single layer continuous apposing suture pattern then anastomosing the smaller diameter segment of bowel to an appropriate size enterotomy made in the antimesenteric border of the larger diameter segment of bowel.
4) The larger diameter segment of bowel can be made smaller in diameter by suturing its cut edge until its lumen is equal in size to the smaller diameter intestine (this technique is often used for subtotal colectomy in cats).

Intestinal Anastomosis Technique:
See the DVD for a detailed video description of this technique (www.videovet.org).

When suturing an anastomosis, atraumatic handling of bowel wall and perfect anatomic apposition of incised margins is important. It is recommended to begin suturing at the mesenteric border as this allows adequate visualization of mesenteric vessels and helps prevent encircling these vessels when placing the first few sutures. Any of the appositional suture patterns previously described (i.e., simple continuous or interrupted) will result in a high success rate, both in the short-term (i.e., leakage, breakdown) and long-term (i.e., stricture, stenosis).

The following tips may prove helpful when performing an intestinal anastomosis (see the anastomosis video clip at www.videovet.org for detailed description of the surgery tips below:
1) First, place a stay suture to hold the mesenteric border of each segment of bowel in apposition. Tie this suture, leave the ends long, and place a hemostat on the suture end without the needle.
2) Place a second stay suture in the antimesenteric borders of each segment to be sutured to bring the ends of the intestinal segments into apposition. Place a hemostat on the ends of this suture.
3) Place gentle traction on the mesenteric and antimesenteric stay sutures to bring the two intestinal segments into apposition.
4) Using the needled segment of suture from the mesenteric stay suture, begin a simple continuous appositional anastomosis being careful to get a 3 - 4 mm bite in the submucosa and placing each suture no more than 2 - 3 mm apart (2 mm apart in cats). When the anastomosis is complete, tie the suture to the mesenteric stay suture.
5) If a simple interrupted apposing suture pattern is used, be careful to get a 3 - 4 mm bite in the submucosa and place each suture no more than 2 - 3 mm apart.
6) Evaluate the integrity of the anastomosis. The author's preference for evaluating the integrity of anastomotic closure is to **visually** examine each suture to be certain that suture placement is no more than 2 - 3 mm apart and that each suture has a 3 mm bite in the submucosa.

Postoperative care
Intravenous fluids to maintain hydration and ensure renal function are continued postoperatively, until the patient begins to eat and drink. Intravenous fluids should then be tapered over a 24 to 48 hour period.
Systemic antibiotics are continued postoperatively for 5-7 days; 10 - 14 days in cases with peritonitis and/or sepsis.

Feeding: Early return to enteral feeding is best for the overall health of the intestine. Feeding the postoperative gastrointestinal surgical patient is generrally based on the following criteria:
a) preoperative condition of the patient
b) the condition of the bowel at the time of surgery
c) surgical procedure performed (i.e., enterotomy, anastomosis, pylorectomy)
d) presence or absence of peritonitis
e) postoperative condition of the patient.
The earlier patients can be returned to oral alimenation the better.

Complications
The most common postoperative complication of small intestinal surgery is leakage; leak is either associated with breakdown of the anastomosis or improper surgical technique (i.e., improper suture placement, inappropriate suture material, knot failure, sutures to far apart, inappropriate bite in the collagen laden submucosal layer, suturing nonviable bowel).
A presumptive diagnosis may be accomplished by the following:
1) Body temperature (may be up if acute or down if moribund).
2) Abdominal palpation: periodic, gentle abdominal palpation for pain (gas or fluid?).
3) General attitude (depression-anorexia).
4) Incision: examination of the patients incision for drainage (look at cytology if drainage is present)

5) CBC: leukocytosis followed by leukopenia (sepsis), or a degenerative left shift may imply breakdown.
6) Glucose: low glucose generally implies sepsis (this occurs early in sepsis and may be used as a screening
test).
7) Abdominal radiographs: generally not helpful, they are difficult to critically assess due to the presence of postoperative air and lavage fluid. It can take 1 - 3 weeks for peritoneal air to diffuse from the abdominal cavity after routine abdominal surgery. Time variation is dependant upon the amount of air remaining in the abdominal cavity postoperatively (i.e., large deep chested animal vs a small obese animal).
8) **Abdominal tap** (paracentesis): a four quadrant abdominal tap is accomplished by aspirating fluid using a 5cc syringe and 20 gauge needle or placing a plastic IV catheter into the peritoneal cavity and allowing fluid to drip onto a slide. This may be the most sensitive diagnostic test for determining the presence or absence of intestinal leak.
9) Peritoneal lavage (if paracentesis is not productive): infuse 10-20cc/kg of sterile physiologic saline solution into the abdominal cavity, then gently palpate the abdomen and repeat the four quadrant paracentesis. This technique increases the sensitivity of paracentesis to 90%.
Once fluid has been obtained, a smear should be stained and evaluated microscopically. Depending upon the cell types seen, a determination of the presence of leakage can be made.

Below are examples of expected cytology in patients with and without leak.
1) Healthy PMNs with few degenerate PMNs and a moderate number of red blood cells: This cytology may be expected in any postoperative abdominal procedure (e.g., OHE, abdominal exploratory, cystotomy). Your index of suspicion for anastomotic breakdown should be low. However, if clinical signs continue to deteriorate, repeat paracentesis (2 - 3 times daily, if necessary) to determine the "trend" of the abdominal fluid cytology is recommended.
2) Healthy polymorphonuclear leukocytes with bacteria located intra or extracellularly, degenerate PMNs with intracellular bacteria, free bacteria, or food particles--imply breakdown. Exploratory laparotomy is indicated.

In a recent morbidity/mortality study of patients undergoing intestinal surgery it was found that animals requiring a second abdominal surgery to treat intestinal disorders were less likely to survive than patients requiring only one laparotomy. Also, the longer it took to determine whether or not intestinal leakage had occured the less likely the patient would survive reoperation. **The take home message is:** pay attention to detail during the first surgery and if a leak occurs, diagnose it and treat it as soon as possible.

Prognosis The overall prognosis for uncomplicated GI surgery is excellent. The surgeon must pay attention to detail when suturing any hollow viscus organ with liquid contents.

GI SURGERY CASES

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If you would like a copy of the illustrated version of these notes on CD and a video of the surgical procedures described below (DVD), go to **www.videovet.org**.

LINEAR FOREIGN BODY

Clinical presentation: Linear foreign bodies (e.g., string, plastic bags, tinsel, tape deck tape, yarn, thread) occur in the dog and cat. The classic presentation is a patient four years of age or less with persistent vomiting, anorexia, and depression. These signs are common with many gastrointestinal disturbances and linear foreign body should be included in your differential diagnosis. Occasionally, patients are presented late in the course of the disease and may have a history of intermittent vomiting with anorexia, depression, and weight loss as the major presenting signs.

Diagnosis: A thorough physical examination should be performed with emphasis on oral examination and abdominal palpation. Oral examination often reveals the linear foreign body around the base of the tongue in cats. The foreign body itself may be seen or an area of inflammation may be present at the junction of the base of the tongue and frenulum. Abdominal palpation may reveal "bunched-up" small intestine due to the plication. When this finding is made, the clinician should be very gentle with further abdominal manipulations so as not to encourage bowel perforation.

Radiography: Definitive diagnosis is based on characteristic findings on survey and contrast radiography. Survey radiographs may reveal plicated bowel bunched up in one quadrant of the abdomen. Due to its plicated nature, air accumulation in the bowel lumen forms a characteristic "tapered enteric gas bubble". Three or more tapered gas bubbles are diagnostic for linear foreign body. Evidence of peritonitis (i.e., ground glass appearance), free gas in the abdominal cavity, ileus, or the presence of a needle are findings that may be present on survey radiographs.

Presurgical treatment: Surgery for the removal of linear foreign bodies should be accomplished as soon as possible. Pre-surgical preparation of patients diagnosed early and in good health include an intravenous catheter, maintenance fluids (22 ml/kg TID), replacement of fluid loss from vomiting and dehydration, and antibiotics prior to abdominal exploratory When fluid losses have been replaced and shock therapy instituted the patient is anesthetized for abdominal exploratory.

Surgical treatment: After a xyphoid to pubis ceiliotomy, the plicated bowel is gently exteriorized from the abdominal cavity. In order for a linear foreign body to result in intestinal obstruction and clinical signs, it must be lodged somewhere in the proximal gastrointestinal tract. The surgeons first task is to locate the area in which the foreign body is lodged and release it. If it is lodged under the tongue it should be cut at the time of exploratory laparotomy; if it is lodged in the stomach or pylorus, it is released via a gastrotomy; if it is lodged in the duodenum, it is removed via enterotomy.

Once the proximal end is released, the extent of the linear foreign body is evaluated, and 1-3 subsequent jejunal enterotomies may need to be performed to remove the remainder of the foreign body.

Care is taken to remove the linear foreign body in segments short enough that further cutting of the mesenteric border of the intestine does not occur during removal, yet long enough to perform a minimum number of enterotomies. All linear foreign bodies should be removed to the level of the ascending colon. Colotomies are **not** necessary, as once the linear foreign body is in the colon it can be passed with little danger of causing obstruction.

An alternate technique for removal of a linear foreign body is to identify and release the obstructed proximal aspect of the foreign body and attach the released end of the linear foreign body to the flanged end of a 12 - 18 French red rubber catheter/feeding tube. Pass the blunted end of the catheter into the gastrotomy or enterotomy and pass it aborally through the entire length of the intestinal tract and out through the anus. As the catheter is passed, it pulls the linear foreign body out of the GI tract and releases the bowel from its plication. This technique eliminates the need for multiple enterotomies to remove the foreign body. Difficulty can arise when attempting to pass the catheter through the small intestine. Care should be taken not to encourage further trauma to the mesenteric border while passing the catheter.

After the foreign body has been completely removed, a close examination of the mesenteric border is made for evidence of perforation. Any perforation should be debrided and sutured. If multiple perforations occur, a resection and anastomosis may be necessary.

Patients with multiple mesenteric perforations that cannot be sutured without severely compromising bowel viability should undergo massive bowel resection. Remember, you can successfully resect 60 - 70% of the small intestine and have a nutritionally acceptable animal. If the client is willing to treat their dog or cat with an acid blocking agent, this resection can be expanded to a 75 - 80% small intestinal resection.

The abdominal cavity is lavaged with copious quantities (e.g., 200-300 ml/kg) of sterile physiologic saline solution prior to closure. Placement of an enterostomy feeding tube should be considered in severely debilitated patients. Postoperative management (i.e., fluids, antibiotics, feeding) is as previously discussed.

Prognosis: Prognosis for patients with linear foreign body is directly related to the presence or absence of bowel perforation at the time of surgery. Patients without preoperative perforation have an 85% chance of survival while those with preoperative perforation have only a 50% chance of survival. This survival rate further reinforces the importance of early diagnosis and surgical treatment.

Massive bowel resection

A question often asked is; "How much small bowel can I resect and still have a nutritionally functional pet?"

Experimental surgical studies reveal that dogs with 75-80% of the small bowel removed usually die within 90 days of emaciation, cachexia, and massive diarrhea with undigested food in the stools when fed standard diets. However, dogs with 50-60% of the small bowel

removed will eventually undergo enough intestinal villous adaptation that a nutritionally sound pet can be expected.

Recently, it has been shown that dogs undergoing 75 - 80% small bowel resection (i.e, leaving 18 inches from the descending duodenum and 18 inches from the ileum in a 25 kg dog) will be nutritionally functional if given an H_2 receptor blocker or other acid blocking agent (i.e., cimetidine, ranitadine, famotadine, prilosec). This is probably due to the fact that massive small bowel resection results in gastric acid hypersecretion and lipid malabsorption. The cause of gastric acid secretion is unknown (possibly increased gastrin levels), but it results in a decreased pH of the small intestine. This acid intestinal environment inhibits lipase activity and the emulsification process. The use of H_2 receptor blockers improves patient response by decreasing acid production, increasing digestibility of lipids by 40%, and accelerating intestinal adaptation by increasing villous length, width, and numbers. It is recommended that patients with massive bowel resection (60% or greater) be placed on acid blocking agents.

INTUSSUSCEPTION

Intussusception is a sign not a disease. It most frequently occurs in young animals with a history of GI upset; generally secondary to parasitic infestation, parvovirus, etc. In older patients it may be associated with intestinal foreign body or GI neoplasia. Classic history is that of vomiting, diarrhea (with or without blood), and abdominal cramping or pain when lifted by the abdomen. Clinical signs are as with any gastrointestinal obstruction however, in puppies and kittens, the signs may "come and go". This is thought to be due to the effects of an intussusception that comes and goes (i.e., sliding intussusception). Physical examination generally reveals an easily movable, slightly painful, sausage-like abdominal mass.

Diagnosis is based on history, clinical signs, palpation of an abdominal mass, and pain on abdominal palpation. Radiographs may reveal an obstructive pattern. and _ A barium enema may outline the intussusception but is rarely necessary for the diagnosis. Be appreciative of the sliding intussusception that presents with periodic signs of an abdominal mass that seems to "come and go".

Treatment of intussusception in the dog and cat is generally surgical. Barium enemas rarely reduce the intussusception and maintain its reduction. Laparotomy generally reveals either an ileocecocolic, jejunal, or rarely a colonic intussusception. A thorough abdominal exploratory for multiple intussusceptions, foreign bodies, or other causes of GI obstruction should be done in all cases.

When attempting to surgically reduce an intussusception, very gently **push** distally and pull proximally (don't pull hard).

Frequently, intussusceptions can be reduced without serosal tears. Once reduced, examination of the bowel for intestinal foreign bodies, masses, etc. is performed (remember, intussusception is a **sign** not a disease). If the intussusception is reducible but there is questionable viability, inject fluorescein dye and make viability assessments as previously described.

If no obvious abnormality exists to explain the presence of the intussusception, an enteroplication should be performed.

Enteroplication: Technique. Enteroplicaiton is performed by exteriorizing the small intestine from the proximal jejunum to the ileum. The bowel is placed in an accordion-like manner and sutured together to form permanent adhesions. The seromuscular/submucosal layer (do **not** penetrate into the lumen) of one loop of bowel is sutured to the seromuscular/submucosal layer of the adjoining bowel using simple interrupted sutures of 4-0 Vicryl, Dexon, PDS, or Maxon.

The plicated bowel is replaced into the abdominal cavity and closure is routine. The planned adhesions prevent bowel from re-intussuscepting. Plicated bowel remains adhered for at least two months postoperatively and no abnormal gastrointestinal signs or nutritional disturbances result. Recurrence is essentially eliminated.

If reduction of the intussusception results in seromuscular tears or if bowel viability is assessed as poor, serosal patching or resection and anastomosis should be considered. Serosal patch and anastomotic techniques have previously been described. Any of the appositional techniques may be successfully used. If resection and anastomosis is performed, the resected bowel should be examined carefully to determine a possible cause. If there is no evidence of a foreign body, mass, etc., the remainder of the bowel should be plicated as described above. Postoperative treatment for patients with intussusception is as previously described for any intestinal foreign body.

Ileocecocolic and ileocolic valve resection

If bowel resection results in removal of the ileocecocolic valve (cat) or the ileocecal and cecocolic valves (dog) malabsorption syndrome and chronic diarrhea may result. These valves function to control bacterial numbers in the small and large bowel. The small bowel has a relatively low bacterial count, and the large bowel a high bacterial count. If the valve is removed in an intestinal resection (i.e., ileocecocolic intussusception), reflux of bacteria from the colon into the ileum may occur. Overgrowth of bacteria in the small intestine results in an increased deconjugation of bile acids and hydroxylation of dietary fatty acids as well as production of bacterial metabolites toxic to epithelial cells. The absorptive capacity of the epithelial cells is then decreased, resulting in malabsorption. The toxic effect on villi result in inflammation and edema causing fluid secretion into the lumen and further malabsorption resulting in chronic diarrhea. Treatment with intestinal antibiotics may help control the overgrown small bowel bacterial population. Given time, most dogs and cats recover to a normal GI function.

SURGICAL MANAGEMENT OF MEGACOLON IN CATS

Clinical presentation: Megacolon is a condition in which the ascending, transverse, and descending colon are chronically large in diameter and filled with inspisated stool. Patients generally present with a history of chronic constipation (i.e., weeks to years), tenesmus, and weight loss. Males are more commonly affected than females and the age ranges from one year to 12 years.

Etiology: The etiology of megacolon is either congenital, acquired, or idiopathic. The idiopathic form is the most common type seen in the cat.

Diagnosis: Diagnosis of idiopathic megacolon in cats is usually made on the basis of history, abdominal palpation, and radiography. Confirmation is based on exploratory laparotomy.

Treatment: The decision to operate is generally made on the basis of the constipation becoming progressively worse and responding only to multiple enemas and manual deobstipation. Exhaustive medical therapy is generally performed prior to surgical intervention.

Preoperative management: Preoperative bowel preparation, using antibiotics administered orally or multiple cleansing enemas is probably useless in cases of severe constipation or obstipation. A parenterally administered antimicrobial agent, with a spectrum of activity directed toward coliforms and anaerobes, is probably the most efficacious preoperative management.

Subtotal colectomy: Subtotal colectomy is the procedure of choice in cats with megacolon. This technique is performed regardless of how much of the colon appears diseased. The surgical objective is to remove all of the colon except what is necessary to reestablish bowel continuity. When the ileocecocolic valve is removed (i.e., which is done if the cecum appears grossly abnormal), a 1.5 - 2 cm segment of descending colon just proximal to the pubis (i.e., colorectal junction) is saved to accommodate the ileo-colonic anastomosis. When the ileocecocolic valve is retained, a 1 cm segment of ascending colon is preserved to accommodate the colonic anastomosis.

Several techniques have been described for performing the colonic anastomosis. The author's technique of choice is an end-to-end anastomosis. A detailed description of this technique is available at www.videovet.org. The procedure is performed using a single layer simple continuous or simple interrupted appositional pattern with 3-0 or 4-0 synthetic absorbable or monofilament nonabsorbable suture. Because of lumen diameter differences between the ileum and colon, it is necessary to place several sutures in the larger diameter bowel in order to produce an even, watertight anastomosis.

After the anastomosis is completed, the peritoneal cavity is thoroughly lavaged with 200 - 300 ml/kg of warm, sterile physiologic saline solution prior to closure. In situations where the anastomosis is under any question, particularly with respect to color and blood supply (i.e., tissue viability), it is advisable to place a serosal or omental patch over the anastomotic area to help prevent leak, provide a source of blood supply, and help support the anastomosis.

Postoperative care: Immediately postoperatively patients should be supported with a balanced electrolyte solution intravenously until they are able to maintain their hydration status. Antimicrobial agents are continued for five to seven days in all cases. Patients are returned to their normal diet within 24 hours and are allowed water ad libitum.

Results: Long term results have been somewhat variable from case to case, but generally:
1) all patients maintain fecal continence post-operatively
2) after a 10-15% weight loss 2 - 3 weeks postoperatively, BW is regained within 3 - 7 weeks
3) watery to mucoid stools occur during the first 3 - 7 weeks followed by mucoid to semi-solid to formed stools by 3-6 months
4) frequency of stools is approximately six per day initially followed in 1-2 months by four per day, then at six months to 2-3 stools per day (range 1-4 stools per day)
5) owner satisfaction has been excellent in the majority of cases.

OPEN PERITONEAL DRAINAGE

Prior to abdominal closure, especially in cases with peritonitis secondary to intestinal perforation, the peritoneal cavity should be lavaged with copious quantities (200-300 ml/kg body weight) of sterile physiologic saline solution. The use of rubber drains for postoperative drainage and/or lavage of the peritoneal cavity is a controversial subject among surgeons. Several types of drains can be used, the most common include Penrose drains, single lumen fenestrated tubes, and double or triple lumen sump drains. Although these drains may be efficient for the first 12-24 hours, omentum quickly and effectively seals them off, precluding further drainage.

Jackson Pratt drains offer a more efficient means of post operative peritoneal drainage. These drains should be placed in the crania abdomen between the liver and diaphragm. Large dogs (>40 lbs) should have a second drain placed in the caudal abdomen. Drains should always be exited from the abdomen at a point distant from the midline abdominal incision. Abdominal wall closure is generally performed using absorbable or nonabsorbable monofilament suture material in a simple continuous pattern.

An alternative technique for treating patients with generalized suppurative peritonitis is termed open peritoneal drainage and intermittent lavage.

SEROSAL PATCH

A technique has been described for successfully treating hollow viscous organ perforation and leakage and for reinforcing areas of potential leakage. The technique involves suturing the surface of a loop of healthy bowel (generally jejunum) over the leaking or devitalized area to form a serosal patch.

In the small intestine, serosal patching is most helpful when debridement and closure of an intestinal defect would result in significant lumen compromise. Serosal patching is also indicated for support of an enterotomy or intestinal anastomosis that is of questionable viability. It is effective in preventing leakage even if the anastomosis breaks down as the patch seems to retain its integrity in the face of peritonitis or protein-calorie malnutrition.

Technique: When using a serosal patch to cover a defect, the defect is first debrided to healthy bleeding margins and irrigated. A loop of jejunum is brought into apposition with the defect and sutured using a simple continuous apposing pattern of 4-0 or 5-0 polypropylene (Prolene) suture. Sutures are placed 2-3 mm apart and about 3 mm from the edge of the defect; be sure sutures are in viable bowel wall. Polypropylene suture is used for its nonreactive properties as well as its continued tensile strength in the face of peritonitis, hypoproteinemia, and prolonged illness. Sutures are placed 360° around the defect making sure to suture submucosa of both structures with each bite. Advantages of serosal patch over omentum include: its strong subserosal layer, it withstands higher intralumen pressures, and it holds sutures well. It may also help to "support" the anastomosis during healing. When defects in the duodenum and colon are patched with a loop of jejunum, the serosal surface becomes lined with mucosa similar to the organ repaired.

MESENTERIC VOLVULUS

Mesenteric volvulus is an uncommon but often fatal disorder in dogs; it is rarely diagnosed in cats. Clinical presentation is a young to middle age, male, medium sized to large breed dog (German Shepherd Dogs appear to be most commonly affected), presenting with an acutely

distended and painful abdomen, hematochezia, +/- vomiting, and rapid onset of shock. The abdomen is moderately distended and tympanic. Abdominal distention occurs rapidly; generally less than 6 hours. Presumptive diagnosis is based on history, clinical presentation, physical examination, and radiographs. Abdominal radiographs reveal distended loops of small intestine suggesting obstruction or adynamic ileus. The stomach is generally not distended with air. Differential diagnosis includes GDV, intestinal obstruction, parvovirus, garbage gut, and generalized adynamic illeus. Treatment is emergency surgery. A xyphoid to pubis midline abdominal exploratory is performed. Adequate exposure is necessary to visualize and evaluate the volvulus for appropriate derotation. As in any strangulation obstruction, endotoxin is released to the systemic circulation when the vascular occlusion is relieved. Pretreatment with shock dose of polyionic isotonic fluids, glucose, broad spectrum antibiotics, and corticosteroids or flunixin meglumine are recommended. As these patients are also experiencing reperfusion injury, specific drug therapy shown to improve patient outcome should be considered (at this time no drug has been shown clinically effective in treating dogs with reperfusion injury).

GASTROINTESTINAL NEOPLASIA

The overall incidence of gastrointestinal tract neoplasia in animals is low (16% of canine neoplasms and 28% of feline neoplasms originate in the alimentary tract). Clinical signs associated with the presence of small intestinal neoplasia vary with the location of the tumor in the bowel (i.e., high or low), the degree of obstruction (i.e., partial or complete), and the rate of growth of the tumor causing the obstruction. Intermittent vomiting and diarrhea, hyporexia to anorexia, depression, and cachexia are commonly seen with slow growing mural neoplasms that cause chronic partial obstruction. An abdominal mass may be palpable on physical examination. A presumptive diagnosis can generally be made by characteristic findings on an upper gastrointestinal contrast study (i.e., barium). Definitive diagnosis requires abdominal exploration and intestinal biopsy (generally excisional biopsy).

Leiomyosarcoma in dogs

Leiomhosarcoma is a slow-growing, malignant tumor of smooth muscle origin. It is the second most common intestinal tumor in dogs. Dogs with leiomyosarcoma of the small intestine have no breed or sex predilection and present at a median age of 10 years (range, 8 - 15 years). Clinical signs include vomiting, lethargy, anorexia, and diarrhea. Occasionally, patients present with weight loss and distended abdomen. Radiology reveals an abdominal mass in 60% of cases. Jejunum is the most common site in the small intestine and duodenum is second. If surgical resection and anastomosis is feasible, median survival can be expected to be 1.1 year (range, 7 months to 5.3 years). Prognosis in dogs treated surgically for leiomyosarcoma of the small intestine is favorable to excellent.

Intestinal adenocarcinoma in the cat.

This tumor most often affects older male Siamese cats (11 years old is the mean). Presentation is often nonspecific and includes weight loss, depression, intermittent vomiting and diarrhea, and hyporexia to anorexia. Clinical signs may last from a few days to several months. Tumors are most commonly found in the jejunum, ileum, and ileocecal colic region (i.e., rarely colonic). Diagnosis is often made by performing an upper GI barium series. _ and At laparotomy, they appear as pale annular strictures affecting 1-5 cm segments of the intestine. and They are firm on palpation and may be associated with a pre- and post-stenotic dilatation of the intestinal tract. Treatment includes wide excision of the tumor. Since most recurrences are at the previous anastomotic site, it is recommended that 7-10 cm of

grossly normal intestine be included on each end of the resection. Remember, 60 to 70% of the small intestine can safely be resected in the dog and cat. A routine intestinal anastomosis as previously described is performed. Resection or incisional biopsy of a regional mesenteric lymph node should be performed and submitted with the intestine for histopathologic evaluation and tumor staging. It is important that the pathologist read the "margins" of the intestinal resection as well as the tumor and regional lymph node. This may help determine the appropriate prognosis. Postsurgical survival time varies from 5-28 months. Survival times may increase if wider resections are accomplished at laparotomy.

Intestinal adenocarcinoma in the dog presents in a similar fashion as in the cat. Surgical therapy is similar, as is prognosis. This tumor is relatively rare in the dog as compared to the cat.

DIFFUSE GASTROINTESTINAL DISORDERS

Abdominal exploration with representative gastrointestinal biopsies is a valuable adjunct in diagnosing diffuse gastrointestinal disorders (i.e., lymphangectasia, idiopathic inflammatory bowel disease, lymphosarcoma, lymphocytic-plasmacitic gastroenteritis, eosinophilic enteritis). The preoperative condition of the patient should not preclude the use of gastric and intestinal biopsies as a diagnostic tool. Even severely hypoproteinemic patients will prioritize what protein they have to the healing of wounds. Delayed wound healing should be anticipated and appropriate measures taken to ensure wound tensile strength until healing is complete. A ventral midline celiotomy that allows complete abdominal exploration is performed. After examination of viscera the proper sequence of organ biopsies follows the general rule that clean procedures should be done first (i.e., lymph node, liver, duodenal aspirate) and potentially contaminating procedures done last (i.e., gastric, duodenal, jejunal, ileal). The recommended sequence of samples and biopsies are listed below:

1) Liver, spleen, etc. as needed, 2) Mesenteric lymph node, 3) Duodenal aspirate, 4) Stomach bx, 5) Duodenal bx, 6) Jejunal bx, 7) Ileal bx.

When taking gastric and intestinal biopsies for diffuse gastrointestinal disorders a **full thickness** biopsy is necessary for adequate histopathologic evaluation. Gastric biopsy is performed in the ventral body of the stomach. A 1 - 2 cm incision is made and a full thickness biopsy specimen is taken. Care is taken not to traumatize the specimen with excessive tissue handling during biopsy. Closure is routine.

When taking an intestinal biopsy, the easiest way to guarantee you will get an adequate size, full thickness piece of intestine is to use a 4mm brand new skin punch biopsy instrument. The skin punch is placed on the antimesenteric border of the proposed segment of intestine and 'drilled' through all layers of intestine until the biopsy punch can be felt to enter the lumen of the intestine. The skin punch is removed and the biopsy retreived from the shaft of the skin punch biopsy. This technique is particularly useful for ileal biopsy as it is easy to biopsy between the mesenteric and antimesenteric vessels. Transverse closure of the biopsy site is recommended to eliminate the possibility of lumen compromise. Suture technique is as described above for enterotomy closure.

An alternate technique required the use of a scalpel. A small longitudinal or transverse enterotomy is made (i.e., 5 - 10 mm long) with a #11 Bard-Parker scalpel blade (see video on intestinal biopsy www.videovet.org). One end of the enterotomy is grasped with atraumatic

forceps. Metzenbaum scissors are used to cut a 2 - 3 mm wide full thickness biopsy. The mucosa tends to evert when the enterotomy is made (especially with diseases that infiltrate mucosa), so be sure to include serosa, muscularis, submucosa, and mucosa in the biopsy.

Closure of all tissues (i.e., stomach, intestine, linea alba, subcutaneous tissues, skin) should be accomplished with suture material with predictabl absorbtion characteristics and that will retain a significant part of its original tensile strength 2-4 weeks postoperatively (e.g., nylon, polypropylene, Novafil, PDS, Maxon). As with all intestinal surgery patients the surgeon provides careful postoperative evaluation for possible signs of intestinal breakdown.

Esophagostomy Feeding Tube Placement in the Cat

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If you would like a copy of the illustrated version of these notes on CD and a video of this surgical procedure on DVD, go to **www.videovet.org** or contact videovet@me.com .

Key Points
- feeding tubes should not pass the LES
- "if the gut works, use it"
- learn how to do a Chinese finger trap friction suture
- keep a column of water in the tube between feedings

As a general rule, the closer one comes to the oral route of food intake and digestion, the more efficient is the assimilation and digestion of nutrients and the greater the flexibility in formula composition. Conversely, the further aboral one gets, the less efficient is the assimilation and digestion of nutrients and greater care must be taken when choosing formula composition. Route of administration also dictates feeding tube diameter; tube diameter in turn dictates usable feeding formulas due to varying formula viscosity and particulate matter size. The most common routes of administration for enteral hyperalimentation include oral, nasoesophageal, esophagostomy, gastrostomy, and jejunostomy. Techniques for placement of an esophagostomy feeding tube will be presented.

Esophagostomy

Indications: Esophagostomy tube feeding is indicated in anorexic patients with disorders of the oral cavity or pharynx, or anorexic patients with a functional gastrointestinal tract distal to the esophagus.

Contraindications: Esophagostomy tube placement is contraindicated in patients with a primary or secondary esophageal disorder (e.g., esophageal stricture, after esophageal foreign body removal or esophageal surgery, esophagitis, megaesophagus) and patients with a history of vomiting.

Advantages: Advantages of esophagostomy tube feeding include ease of tube placement, tubes are well tolerated by the patient, large bore feeding tubes can be used allowing use of blenderized diets, tube care and feeding is easily performed by the client, patients can eat and drink around the tube, and tube removal can be performed anytime after placement. Esophageal tube placement eliminates local pharyngeal irritation, coughing, laryngospasm, or aspiration occasionally associated with pharyngostomy tubes.

Disadvantage: The major disadvantage of esophagostomy tube is the need for general anesthesia during placement.

Placement Technique: Provide general anesthesia. Place the patient in right lateral recumbency with the left side uppermost. The tube can be placed on either the right or left side of the midcervical region, however the esophagus lies slightly left of midline making left sided placement more desirable. Aseptically prepare the lateral midcervical area from the angle of the mandible to the thoracic inlet. Slightly extend the neck and hold the mouth open with a mouth speculum.

Pre-measure and mark a 20 to 24 French feeding tube for dogs and a 16 – 18 French feeding tube for cats from the level of the mid-cervical region (i.e., exit point of feeding tube) to the level of the seventh or eighth intercostal space; ensuring mid- to caudal esophageal placement. Make certain the tube does not cross the lower esophageal sphincter (LES) as this may cause sphincteric incompetence, gastric reflux of acid, esophagitis and subsequent vomiting or regurgitation. Prior to tube placement, enlarge the two lateral openings of the feeding tube to encourage smoother flow of blended diets.

Eld Esophagostomy Tube Placement Technique

The following technique requires the use of an Eld feeding tube placement device and is illustrated in the esophagostomy video labeled E-tube. Place the oblique tip of the instrument shaft through the oral cavity and into the esophagus to the level of the mid cervical region (i.e., equal distance between the angle of the mandible and thoracic inlet) and palpate the tip as it bulges the cervical skin. Make a small skin incision over the device tip. Activate the spring loaded instrument blade until it penetrates esophageal wall, cervical musculature, subcutaneous tissue and is visible through the skin incision. Carefully enlarge the incision in the subcutaneous tissue, cervical musculature and esophageal wall with the tip of a #15 scalpel blade to allow penetration of the instrument shaft. Place a 2-0 Nylon suture through the side holes of the feeding tube and through the hole in the instrument blade. Tighten the suture until the tip of the instrument blade and feeding tube tip are in close apposition. Retract the instrument blade into the instrument shaft so the feeding tube tip just enters the instrument shaft (i.e., deactivating the instrument blade. Place sterile water-soluble lubricant on the tube and instrument shaft. Retract the instrument and pull the feeding tube into the oral cavity to its predetermined measurement. Remove the 2-0 Nylon suture to free the feeding tube from the instrument. Place a stylet through one of the side holes of the feeding tube and against its tip (do NOT use a stylet when placing an E-tube in cats). Lubricate the feeding tube and advance it into the esophagus until the entire oral portion of the tube disappears. Gently retract the stylet from the oral cavity being careful to ensure its release from the feeding tube. If you encounter resistence and cannot pass the feeding tube into the esophagus you may have engaged the endotracheal tube. If this happens remove the feeding tube and replace it under direct visualization. Secure the tube to the cervical skin with a Chinese finger-trap suture of #1 Novafil.

Curved Carmalt Hemostate Technque

Instead of the Eld device a curved Carmalt hemostat can be used to place an esophagostomy feeding tube. Patient and feeding tube preparation is identical to that stated above for the Eld technique.

The curved Carmalt forceps is placed into the cats oral cavity with the curve of the hemostate directed toward the cervical region. The Carmalt is directed to a point equidistant between the ramus of the mandible and point of the shoulder midway between the dorsal and ventral aspect of the neck. The hemostat is pushed laterally so as to make a 'buldge' in the cervical region at the desired exit point described above. A scalpel blade is used to incise over the tip of the Carmalt until the tip protrudes through the skin. The tip of the feeding tube is then grasped with the Carmalt hemostat and the tube is exited out through the oral cavity. The tube is pulled out until the flanged end of the tube just comes in contact with the cervical skin. The tip of the tube is then turned back on itself, grasped with the Carmalt forceps, and redirected into the oral cavity of the cat. The tube should remain in the jaws of the Carmalt hemostat until the tip of the tube is beyond the cervical exit point of the tube. The feeding tube is then released from the Carmalt and pushed into the esophagus until the tube is in the mid-esophagus (i.e., 7 or 8th intercostals space). The tube is secured using a Chinese finger-trap friction suture.

Regardless of technique used, the exit point of the tube can be left exposed or bandaged. A column of water is placed in the tube and the exposed end capped with a 3 cc syringe; this prevents intake of air, reflux of esophageal contents, and occlusion of the tube by diet. Most patients tolerate the tube without the need of an Elizabethan collar.

Esophagostomy tubes can be removed immediately after placement or left in place for several weeks to months. Care of the tube exit site may require periodic cleansing with an antiseptic solution. Tube removal is performed by cutting the finger-trap suture and gently pulling the tube. No further exit wound care is necessary; the hole seals in one or two days and heals by 7 - 10 days.

Complications: Complications associated with esophagostomy tube placement include early removal by the patient or vomiting the tube No significant long-term complications have been reported (e.g., esophagitis, esophageal stricture, esophageal diverticulum, or subcutaneous cervical cellulitis). Reflux esophagitis can occur from improper tube placement (i.e., through the lower esophageal sphincter) or esophageal irritation from the tube itself. Mid-esophageal placement of silicone rubber tubes greatly reduces the incidence of esophageal injury and eliminates reflux esophagitis.

ANAL SACCULECTOMY; A NOVEL APPROACH

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Key Points

- knowledge of anorectal anatomy and neuroanatomy is important to the surgeon
- remove all anal sac epithelium during anal sacculectomy
- use of a Foley catheter may facilitate anal sacculectomy

If you would like a video of this surgical procedure on DVD go to www.videovet.org or contact videovet@me.com. You may click on the 'Seminar Price' for any DVD you would like to purchase.

Introduction: Disorders involving the anus and rectum occur frequently in small animal practice. In order to appropriately diagnose and treat these disorders, knowledge of the regional anatomy, physiology, common clinical signs they produce, and proper physical examination techniques are necessary.

Anatomy: The location and function of the following anatomic structures should be reviewed prior to surgical management of diseases of the anus and rectum: internal and external anal sphincter muscle, anal sac and duct, circumanal glands, caudal rectal artery, vein and nerve, and columnar zone of the anus. These structures are commonly involved in many of the disease processes discussed below and their preservation or removal plays an important part in the patient's ultimate recovery.

The Anal Sphincter Muscle (From the introduction of a report on hemorrhoidectomy written by WC Bornemeier and published in Am J of Proc, Feb, 1960.): "The prime objective of a hemorrhoidectomy is to remove the offending varicosity with as little damage as possible to the patient. Of all the structures in the area, one stands out as the king. You can damage, deform, ruin, remove, abuse, amputate, maim, or mutilate every structure in and around the anus except one. That structure is the sphincter ani. There is not a muscle or structure in the body that has a more keenly developed sense of alertness and ability to accommodate itself to varying situations. It is like the goalie in hockey...always alert."

"They say man has succeeded where the animals fail because of the clever use of his hands yet, when compared to the hands, the sphincter ani is far superior. If you place into your cupped hands a mixture of fluid, solid, and gas and then, through an opening at the bottom, try to let only the gas escape, you will fail. Yet the sphincter ani can do it. The sphincter apparently can differentiate between solid, fluid, and gas. It apparently can tell whether its owner is alone or with someone, whether standing up or sitting down, whether its owner has his pants on or off. No other muscle in the body is such a protector of the dignity of man, yet so ready to come to his relief. A muscle like this is worth protecting."

Physiology: The rectum has little importance in digestion, and acts as a reservoir or collecting tube for undigested waste. The most important physiologic function of the rectum and anus is in the controlled act of defecation (i.e., continence).

Clinical Signs: Common clinical signs associated with diseases of the anus and rectum include: dyschezia, hematochezia, tenesmus, anal licking, ribbon-like stools, matting of anal hair, anal discharge, scooting, excessive flatulence and diarrhea. Patients that present with any of the above clinical signs should have a thorough physical examination with emphasis on the anorectal region, including a digital rectal examination.

Physical Examination: A complete physical examination should be performed in all patients with clinical signs specific for anorectal disease in order to rule-out systemic disorders that manifest themselves with anorectal abnormalities (i.e.,pemphigus).

Specific examination of the anorectal region should include close visual examination of the perineum, circumanal area, and base of the tail, as well as careful digital rectal palpation. In many instances this may be all that is necessary to obtain a definitive diagnosis. If a more detailed examination is needed, the use of an anal dilator or proctoscope may be indicated.

These techniques require heavy sedation or general anesthesia to adequately perform. Epidural anesthesia has proven to be an effective anesthetic regime for examination of the anus and rectum. Excellent muscle relaxation allows easy anal sphincter dilation and visualization of the anal canal and rectal mucosa. The patient is placed in a perineal position for examination.

Sphincter muscle atonia or areflexia: This form of incontinence occurs when the peripheral nervous supply to the external anal sphincter muscle or the muscle itself has been partially or totally severed. The external anal sphincter muscle is made up of striated muscle fibers, and is partially responsible for the voluntary control of defecation.

Isolated injury of the pudendal nerve to the external anal sphincter is uncommon, but may occur from iatrogenic causes. Injury can occur during the following surgical procedures:
1. Perianal fistula repair-cryosurgery or excision
2. Perianal gland adenoma removal-cryosurgery or excision
3. Perineal hernia repair
4. Anal sacculectomy
5. Anoplasty procedures
6. Removal of malignant neoplasm

When this type of injury occurs, the patient may still be considered an appropriate house pet. With loss of anal sphincter tone, fine control of defecation is lost, but the patient still has the ability to sense the urge to defecate and can position

properly. However, the fine control necessary to terminate a bowel movement without dropping a piece of stool is compromised. Also, when the patient is excited, startled, or barks loudly causing increased intra-abdominal pressure; a piece of stool may drop out of the rectum. The important thing to remember is that the patient retains the *urge* to defecate and can control, to some extent, bowel movements.

Anal Sacculitis: Anal sac impaction and abscessation is the most common anorectal disorder diagnosed by the small animal practitioner. Diagnosis is confirmed by clinical signs, visual and digital rectal examination. Relief of impaction by digitally expressing the anal sacs is easily performed during rectal examination. If abscessation is present, infusion of an antibiotic preparation may be sufficient to eliminate the infection. Systemic antimicrobial treatment may be required in resistant cases. If abscessation becomes a chronic recurrent problem, surgical excision of both anal sacs is the treatment of choice. Surgery should be delayed however until the immediate infection or abscess has been controlled medically as described above.

Surgical Techniques: There are a variety of techniques currently used to successfully remove anal sacs. One such technique includes using a pair of Metzenbaum scissors to cut into the anal sac through the duct. The sac is opened to expose the glistening greyish colored interior lining. Hemostats are used to grasp the full thickness of the anal sac wall, being careful to avoid the external anal sphincter muscle fibers. A number 15 BP scalpel blade is used to carefully scrape the gland from the underlying external anal sphincter muscle. The external anal sphincter m., subcutaneous tissue and skin are closed with a synthetic absorbable suture material in a simple interrupted pattern.

An alternate method is to incise over the anal sac, dissect through the subcutaneous tissue, locate the sac and excise it toward the duct.

Regardless of the procedure used, if the entire anal sac is removed and the caudal rectal nerve avoided the prognosis is excellent.

Foley Catheter Technique (the authors' preferred technique)
A novel approach for safely and completely removing anal sacs relies on the use of a 6 French Foley catheter with a 3cc bulb. The Foley catheter is placed into the anal sac through the anal sac orifice and its cuff inflated. Once introduced into the sac, the Foley catheter bulb is inflated with 2-3 cc of air or saline. The bulb distends the anal sac making identification and palpation of the gland simple. The protruding catheter allows the surgeon, or the surgeon's assistant, to place gentle traction on the gland during dissection. A 360-degree skin incision is made around anal sac duct and the protruding catheter. Care is taken to leave at least 2mm of skin from the anal sac duct and the incision. Metzenbaum scissors (curved) are then used to dissect to the plane of tissue between the anal sac wall and external anal sphincter. Identification of the wall is made by identifying its grayish color in comparison to the deep red color of external anal sphincter muscle fibers that will be carefully dissected off of the anal sac wall. As the dissection progresses constant traction is placed on the Foley catheter to

accentuate to sac. When performing the deep dissection of the sac wall care is taken to make certain the dissection does not go deep to the sac wall. This is the location of the caudal rectal nerve fibers. Dissection is continued until the sac is completely disected free and removed from its surrounding tissue.

Closure consists of suturing together any cut fibers of the external anal sphincter muscle with 3-0 Maxon and the skin closed with 4-0 Biosyn using an intradermal technique. This is the authors preferred technique for anal sacculectomy.

This technique is illustrated on the Anal Sacculectomy video located in the GI Surgery I DVD. Check it out at www.videovet.org.

SPLENECTOMY

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INDICATIONS

Splenectomy is indicated for removal of splenic neoplasm, rupture, torsion, infarct, abscess and hypersplenism.

PATIENT POSITIONING

The patient is placed in dorsal recumbency for routine celiotomy.

RECOMMENDED INSTRUMENTS

A Balfour self-retaining abdominal retractor is essential to maintain adequate exposure allowing complete exploration of the abdominal cavity as well as visualization of the splenic blood supply. When large amounts of blood or fluid are present in the abdominal cavity suction is helpful. It is best to have a variety of sizes of hemostats available. The author recommends a minimum of 4 medium to large hemostatic forceps (Crile, Kelly or Carmalt) and 4 – 5 small hemostatic forceps (mosquito).

Ligation of individual blood vessels or clusters of vessels is performed using 3-0 or 4-0 synthetic absorbable suture material. Common sutures include Biosyn, Monocryl, Dexon, Vicryl, Polysorb, PDS or Maxon.

SURGICAL TECHNIQUE

A ventral midline incision from xyphoid to pubis is made to allow adequate exposure of all abdomen organs. The spleen is located in the cranial left quadrant of the abdominal cavity just caudal to the greater curvature and fundus of the stomach. A Balfour self-retaining retractor is positioned to provide exposure of the abdominal cavity.

The spleen is identified, and gently elevated through the abdominal incision. If the surgeon is dealing with a bleeding spleen (e.g., hemangiosarcoma) the exteriorized spleen is placed across the body wall to help place pressure on the splenic blood vessels. In addition, a dry laparotomy pad can be placed directly on the point of hemorrhage and gentle pressure applied.

Several structures should be identified. The greater curvature of the stomach, dorsal and ventral layers of the greater omentum, the gastrosplenic ligament and the left limb of the pancreas. Trace the splenic artery and vein as they course from the dorsal layer of the greater omentum into the gastrosplenic ligament. Identify the left gastroepiploic artery and vein, the many splenic arterial and venous branches into the hilus of the spleen, the short gastric vessels and the vessels continuing into the greater omentum.

The spleen receives its blood supply from 3 major sources. Three to five short gastric vessels supply the cranial aspect of the spleen. The central portion of the spleen is supplied by the major splenic artery and vein and the caudal pole of the spleen by 4-5 small omental tributaries.

The spleen can safely be removed using a technique requiring only 3 to 4 ligatures. Visualization of these vessels is accomplished by first elevating the spleen from the abdominal cavity. When attempting to exteriorize the spleen it is noted that the cranial pole is tethered by the 3 to 4 short gastric vessels. These vessels are identified and cluster ligated with two encircling ligatures. The vessels are transected between ligatures thus releasing the tethering effect. The spleen can now be further mobilized from the abdominal cavity allowing easy exposure of all remaining vessels.

Next the major splenic artery and vein is located and ligated prior to its bifurcation. Care should be taken to visualize the left limb of the pancreas and make certain it is a safe distance from the proposed ligature site. This splenic artery and vein are generally double ligated and depending upon size the artery can be transfixed. Finally the remaining vessels supplying the caudal pole of the spleen are cluster ligated using one or two ligatures.

During the procedure, several points should be remembered:

1) identify the location of the pancreas and do not occlude its blood supply
2) double ligate all major vessels
3) carefully inspect all ligated vessels for evidence of hemorrhage

CLOSURE

The Balfour retractor is removed and the abdominal incision is closed in a routine fashion.

POSTOPERATIVE CONSIDERATIONS

Postoperative care involves monitoring the patient for blood loss that may be encountered should a ligature slip from the ligated vessels.