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Update in Feline Gastroenteric Syndromes

Top Practice Tips For Cats

Therapeutic Implications of Renal Insufficiency: New Thoughts

Untangling the Complexities of the Flutd Complex
11. DRA. SHERCK MARGIE

11.1 UPDATE IN FELINE GASTROENTERIC SYNDROMES

Overview: This discussion will include pancreatitis, triaditis, the use of rectal cytology in large bowel diarrheas, *Tritrichomonas foetus*, *Cryptosporidium parvum*, esophagitis and megacolon.

Pancreatitis

For years, feline pancreatitis has been assumed to be a similar disease to that in dogs. Currently, as with so many other disorders, it would appear that this group of disorders is different in the cat. Remembering that the term "pancreatitis" implies nothing more than inflammation of that organ, it is not surprising that each species may have a variety of etiologies.

The incidence of pancreatitis is higher than previously believed. In fact, in a German retrospective study, the prevalence of pathologically significant lesions in dogs was found to be 1.5% and in cats, 1.3% of the specimens submitted. Indeed, there are papers reporting the incidence as high as 2.9 and 3.5% of necropsied cats.

Drs. Joerg Steiner and David Williams classify feline pancreatitis as acute or as chronic. Acute pancreatitis is a short term, completely reversible and without fibrosis on biopsy evaluation. Chronic pancreatitis is a long-term inflammation of the pancreas associated with irreversible histopathological changes, primarily fibrosis. Most of what we see in cats is the latter which is unfortunate in that it isn't curable; however, it can generally be controlled and is less fatal than severe necrotizing pancreatitis.

Both acute and chronic pancreatitis can be mild or severe, but most commonly acute cases tend to be more severe, and chronic cases mild. Mild pancreatitis generally results in minimal clinical signs, minimal necrosis, and low mortality.

In severe pancreatitis, (necrotizing, hemorrhagic) extensive pancreatic necrosis and multiple organ involvement +/- organ failure are seen. Fortunately, because in cats this form is rare, severe multi-system complications are uncommon. The prognosis for severe pancreatitis is poor.

Pancreatic complications may or may not be present including fluid accumulation around the pancreas, infection of necrotic areas, pseudocysts, and abscesses.

*It is conceivable that we will have histopathological classification schemes in the not too distant future (e.g. focal*
suppurative, diffuse fibrosing, lymphocytic/plasmacytic, eosinophilic pancreatitis, etc.). This should help in designing appropriate therapeutic protocols for our patients. In order to achieve this goal, pancreatic biopsies are required for histopathological evaluation in our patients. In fact, if you submit pancreatic biopsies (which I hope you will all start doing in your pancreatitis kitties), be sure you get a good description from your pathologist.

**Etiology**

1. More than > 90% of the cases of feline pancreatitis are idiopathic.
2. Anything causing ischemia to the organ. “The most pivotal determinant in the development and progression of pancreatitis is likely the maintenance of local blood flow. Ischemia favours progression to an auto-digestive state; impairment of the microcirculation results in retention of activated enzymes, depletion of anti-proteolytic proteins, and reduced removal of toxic products. Necrosis of the gland follows pancreatic ischemia, leading to a self-perpetuating cycle of damage.” (Center SA, Proceedings of AAFP 2000 Fall Meeting)
3. Traumatic pancreatitis has been reported in a few cats associated with motor vehicle accidents or high-rise syndrome.
4. Several infectious agents have been implicated including feline parvovirus, Toxoplasma organisms (of 45 pancreata examined in 100 cats infected with Toxoplasma, 38 had lesions), feline herpesvirus I, Eurytrema procyonis (a fluke), feline infectious peritonitis (FIP), and, rarely, Amphimerus pseudofelineus. Look for toxoplasmosis.
5. Feline pancreatitis was reported in 2 cats following topical fenthion administration (organophosphate intoxication is a common cause of pancreatitis in children in underdeveloped countries).
6. Experimentally, hypercalcemia induced by calcium gluconate IV; and pancreatic duct infusion of oleic acids or infected fluids have induced pancreatitis in experimental models but probably aren’t significant causes of spontaneous pancreatitis.
7. Drugs have been implicated as causing pancreatitis in humans and dogs but not yet in cats. Drugs associated with pancreatitis in humans include azathioprine, chlorothiazide, hydrochlorothiazide, estrogens, furosemide, tetracycline, sulfonamides, L-asparaginase, 6-mercaptopurine, methylidopa, pentamidine, nitrofurantoin, dideoxynosine, valproic acid, and procainamide. Bear these in mind when selecting medications for patients with suspected pancreatitis.
8. NOTE. There is no evidence for glucocorticoids causing acute pancreatitis in dogs and nor in cats!
9. There is also no evidence that dietary fat induces or exacerbates pancreatitis in the cat.

**Pathogenesis**

It is believed that various noxious stimuli can cause the exocrine pancreas to decrease the secretion of pancreatic enzymes, followed by the formation of cytoplasmic vacuoles with the co-localization of proenzymes of digestive enzymes and lysosomal enzymes. Normally the lysosomal enzymes are strictly segregated from proenzymes to prevent premature activation of the proenzymes. A decreased pH along with the loss of segregation of the lysosomal enzymes and proenzymes cause abnormal intrapancreatic activation of trypsinogen which when activated to trypsin activates other proenzymes resulting in a local and systemic inflammatory response.

**Clinical findings**

Pancreatitis should be included in a diagnostic rule-out list whenever there is a history of lethargy, anorexia, dehydration, hypothermia, vomiting (in only 35% in one paper), abdominal mass effect, dyspnea, diarrhea and ataxia. Concurrent problems may include hepatic lipidosis, cholangitis/cholangiohepatitis, idiopathic inflammatory bowel disease, enteritis, diabetes mellitus, and vitamin K1 responsive coagulopathy. As such, the clinical findings on examination may be vague.

Statistically, 38% of cats diagnosed with hepatic lipidosis had concurrent acute pancreatitis and these patients were more likely to be cachectic and have coagulation abnormalities. **This is very important, as these lipidotic cats have a worse prognosis.**

**Diagnostics**

The classical signs of abdominal tenderness or mass in the right anterior quadrant along with haziness in this region and displacement of abdominal viscera on abdominal radiographs and/or visualization of a (nodular) hyperechogenicity or peripancreatic fluid or a pancreatic abscess or mass on ultrasound examination support the presumptive diagnosis of pancreatitis.

1) Radiographic findings reportedly include reduced contrast in the cranial abdomen, localized dilatation of small intestinal loops, displacement of abdominal organs with the duodenum often moved dorsally and laterally, the stomach moved to the left, and the transverse colon caudally.

2) Ultrasonographic findings may include the following changes in the pancreas -- swelling, increased echogenicity, mass effects, and fluid
accumulation around the pancreas or there may be no ultrasonographic changes.

3) Contrast-enhanced computed tomography (CT) is used in humans to diagnose and stage the severity of pancreatitis with its ability to detect and delineate areas of necrosis.

 Practically speaking, ultrasound is the most sensitive, commonly available, non-invasive evaluative tool that we have at this time.

Biochemically and hematologically, changes are most commonly mild and nonspecific. There may be mild, non-regenerative anemia in chronic pancreatitis or a severe anemia terminally in acute, necrotizing pancreatitis. An inflammatory or stress leukon may be present, and in the case of a pancreatic abscess or a suppurative pancreatitis, a left shift may be seen.

Concurrent elevations of sap and alt are not uncommon and reflect inflammatory or lipidotic involvement of adjacent tissue. Nonspecific changes, such as hyperglycemia (stress or concurrent diabetes), hypocalcemia, hypokalemia (inappetance), hypercholesterolemia, azotemia (prerenal and/or renal), and hyperbilirubinemia have all been reported.

The lack of sensitivity and specificity of amylase and lipase is a source of frustration in diagnosing feline pancreatitis. The lack of hyperlipasemia cannot be depended on to rule-out pancreatitis. Elevations in serum amylase may occur not only with pancreatitis, but more commonly from other gastrointestinal diseases, as well as from decreased renal clearance of this enzyme.

TLI has been shown to be diagnostic for severe acute pancreatitis. However, this does NOT detect the more common, chronic and milder forms of pancreatitis. Trypsinogen and trypsin are pancreas-specific in origin, and both are detected by the trypsin-like immunoreactivity (TLI) assay. TLI test is very specific but NOT sensitive. Even though published normals are 17-48 micrograms/dl values under 150-200 are equivocal. TLI seems most reliable in identifying acute pancreatitis. Later in the course of disease it may not be elevated because either the sick pancreas has leaked all of the enzymes that it had made and isn’t capable of producing more (after several days of inflammation) or the pancreatic blood flow has decreased following the worst phase of the inflammatory response. Mild inflammation may also just not stimulate much leakage of enzyme. So, early on in pancreatitis you are most likely to get an abnormally high test result.

More recently, feline PLI has been developed and is available though the Texas A&M GI Lab for clinical use. While it appears to be a more
useful test than fTLI, more work needs to be done to correlate its results with type and severity of clinical disease. It is essential to request the *feline* PLI when ordering the test and submit a fasting serum sample.

Ultimately, surgical biopsy is required to make the histopathological diagnosis. Whilst dogma was that biopsying the pancreas is a pathophysiologically dangerous undertaking, in the cat, this does not appear to be the case. *I routinely biopsy the pancreas in all of my exploratory patients.*

Gently isolate the pancreas from the surrounding viscera and pack it off with a few gauze swabs prior to selecting either a gross lesion or routine selection of both poles for biopsy using fine iris scissors. Submit a small piece in a culture medium as well as formalin preserved samples, in case the lesion is reported as suppurative.

**Therapy**

- Depends on type of pancreatitis.
- Fluid therapy and pain relief are the cornerstones in supportive care.
- Concurrent problems (such as lipidosis or enteritis) need to be addressed.
- Feed, do not fast unless they are vomiting.

Therapy for pancreatitis is best designed about the form/class of pancreatitis. Fluid therapy and pain relief are the cornerstones in supportive care. Sustain blood and plasma volume, correct acid-base and electrolyte disorders. Concurrent problems (such as lipidosis or enteritis) should be addressed as well. A noteworthy difference between the dog and cat is the recommendation to feed, rather than fast, those patients suspected of (or confirmed as) having pancreatitis unless they are vomiting. Even with the vomiting cat, designing a nutritionally supportive protocol is of great importance due to this species ease of developing lipidosis. Thus, I fast cats for no longer than 48 hours utilizing anti-emetics as necessary. In these few intractably vomiting cats, total parenteral nutrition or jejunostomy tube feeding may be advisable for 7-10 days.

Discussion of tube feeding (nasogastric, esophageal, gastrotomy, jejunostomy) may be found in numerous texts, and therefore won’t be discussed here. An excellent resource is Hill R: Enteral and Parenteral Nutrition, 1999.

Complications of ACUTE pancreatitis that may arise include DIC, thromboembolism, cardiac arrhythmia, sepsis, acute tubular necrosis, pulmonary edema, and pleural effusion. It has been suggested that a
low dose of dopamine (5 mcg/kg/min) diminishes the severity of the disease. To prevent bacterial translocation, cover these patients with broad-spectrum antibiotics.

When the use of anti-emetics is being considered, bear in mind that as these agents are metabolized by the liver their clearance rates may be decreased. Doses should be reduced accordingly. Anti-emetics commonly used in the cat include metaclopramide (Reglan™) and chlorpromazine (Largactil™). Each of these drugs also has its own, inherent side effects, such as the central nervous system (CNS) sedation or frenzied behaviour or disorientation of Reglan™ in the cat or the hypotensive effect of the Largactil™. Zofran™ while costly, is very beneficial in the intractably vomiting patient. (Please refer to Washabau R: The Vomiting Cat, 1997 for a discussion on the rational for using different antiemetics and their mechanisms of action.)

**Select Anti-emetics for use in the Cat**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Product™</th>
<th>Dose (feline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>Thorazine, Largactil</td>
<td>0.5 mg/kg q8h IM</td>
</tr>
<tr>
<td>Prochlorpromazine</td>
<td>Compazine</td>
<td>0.1 mg/kg q6h IM</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl</td>
<td>2.0-4.0 mg/kg q8h PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0 mg/kg q8h IM</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>Dramamine</td>
<td>8.0 mg/kg q8h PO</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Reglan</td>
<td>1-2 mg/kg constant rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>infusion IV over 24 hours</td>
</tr>
<tr>
<td>Ondansentron</td>
<td>Zofran</td>
<td>0.1-0.15 mg/kg slow push IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>q6-12 hours prn</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>Anzemet</td>
<td>0.6 mg/kg IV, SC, PO q24h</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Remeron</td>
<td>3-4 mg/cat PO q72h</td>
</tr>
<tr>
<td>Maropitant</td>
<td>Cerenia</td>
<td>1 mg/kg SC q 24 hr x up to 5 days</td>
</tr>
</tbody>
</table>

Cats, being obligate carnivores, don’t normally utilize carbohydrates well. Feed a balanced, non protein-restricted diet.

Modification of gastric acidity is advised. An H2 blocker, such as famotidine (0.5 mg/kg PO, IV q24h) or a proton pump inhibitor, such as omeprazole (0.5-1.0 mg/kg PO q24h) may be used. Symptomatic treatment using antimicrobials against anaerobic and gram-negative enteric opportunists is recommended. If specific pathogens are identified from a pancreatic abscess or other samples, the antimicrobial drugs can be chosen based on gram stain, initially, and, ultimately, the sensitivity pattern.

While pancreatic enzymes are not indicated other than in the rare case of feline exocrine pancreatic insufficiency, David Williams has mentioned that they are used in human pancreatitis patients with the
thought that they may reduce pain through feedback to the pancreas inhibiting further enzyme release (and leakage). Whether this is the case in cats (or dogs) isn’t known.

Analgesia is of critical importance in the comfort of the patient, but also in the progression of the disease/inflammation through the negative physiological effects of pain. PAIN CAUSES DISEASE AND PREVENTS HEALING. Even if obvious abdominal pain isn’t present, I recommend a test dose of 0.1-0.2-mg/kg oxymorphone IV or buprenorphine IV, SC to see if the patient improves over the approximately 6 hour effective period. If that is the case, then constant rate infusion of a narcotic may be considered or a transdermal fentanyl patch (Duragesic™) for continuous relief. Torbugesic™ is not as effective for visceral pain as the opioid agonists are.

NSAIDs may be selected for their usefulness both as anti-inflammatory agents as well as their analgesic component. As always, adequate hydration of a patient, knowledge of appropriate renal function and the lack of gastrointestinal bleeding are important before choosing this class of drugs. Use of COX-2 inhibitors minimizes the risk to feline patients as does appropriate dosing and dosing intervals.

Antibiotics are only indicated if the diagnosis of a suppurative pancreatitis has been made. In this case, antimicrobial selection is best made with the knowledge of a sensitivity spectrum. Note that a suppurative pattern may be seen on histology in a sterile pancreatitis caused by enzyme damage. Corticosteroids are indicated if a lymphocytic/plasmacytic form is reported or in an acute shock presentation. No benefits have been seen with the use of anticholinergics, GI hormones (somatostatin, glucagon), or calcitonin. Dopamine has been useful in acute experimental feline pancreatitis.

Fresh frozen plasma may be considered in cats with severe pancreatitis to replace plasma proteases, albumin and alpha 2 macroglobulins. Selenium was shown to be useful in dogs, however, to date; no study has been done to assess the role of selenium in therapy of pancreatitis in cats.

**Prognosis**

Prognosis depends on the type of pancreatitis as well as the degree of duration and severity. Many cats have chronic, low-grade smoldering pancreatitis and live long lives, but do better with diagnosis and appropriate therapy.
**Triaditis vs. “IBD”**

The clinical signs of IBD vary with location of the inflammatory process: duodenal and gastric lesions usually present as vomiting and weight loss while small intestinal or colonic lesions present as diarrhea +/- weight loss (if small intestinal). However, some colonic IBD may cause vomiting as well. There are also cats in whom the inflammatory process extends beyond the gastrointestinal tract and affects the liver (+/- the gallbladder) and pancreas. This is fondly termed "triaditis". These cats may present with signs attributable to these organs, which may or may not include vomiting and diarrhea.

Anatomically and pathophysiologically, it is “logical” to understand why this may occur. If there is pathology in the distal common bile duct, either ascending from the duodenum or originating in the duct itself, (such as infection or cholelithiasis), this could predispose to pancreatitis because of the functional relationship between the major pancreatic and common bile duct sphincters in the cat. Experimentally, it has been shown that when the major pancreatic duct is perfused with bile acids, marked structural changes occur not only within the pancreatic duct, but also in the pancreas itself. This is why feline pancreatic disease is a common cause of extrahepatic biliary obstruction.


In approximately 80% of cats, the accessory pancreatic duct is absent. The pancreatic duct enters the common bile duct before the latter opens into the duodenum at the major duodenal papilla.
Exocrine Pancreatic Insufficiency (EPI)
EPI is a syndrome caused by insufficient synthesis of pancreatic digestive enzymes by the exocrine portion of the pancreas. The clinical signs most commonly reported are weight loss, loose and voluminous stools and greasy soiling of the hair coat. Serum fTLI is subnormal in affected cats. Treatment of cats with EPI consists of enzyme supplementation with powdered pancreatic extracts or raw beef pancreas. Many cats with EPI have concurrent small intestinal disease. Most cats with EPI also have severely decreased serum cobalamin concentrations and may require parenteral cobalamin supplementation.

Pancreatic Neoplasia
Pancreatic adenocarcinoma is the most common neoplastic condition of the exocrine pancreas in the cat. At the time of diagnosis, the tumor has already metastasized in most cases, and the prognosis is poor. Pancreatic pseudocyst, pancreatic abscess, pancreatic parasites, pancreatic bladder, and nodular hyperplasia are other exocrine pancreatic disorders that are less commonly seen in cats. Pancreatic neoplasia characteristically has a dermatologic paraneoplastic syndrome of thin, friable alopecic skin.

CHOLECYSTITIS
Cholecystitis generally presents as a vague malaise with inappetance and dehydration, (pretty much like everything else in the cat). Vomiting may be present. While this too may involve a lymphocytic-plasmacytic inflammatory infiltrate of the gall bladder wall, it more often is suppurative. If surgical evaluation occurs, and the gall bladder looks inflamed or if it does not compress and empty normally, or if ultrasound is suggestive of cholecystitis, bile aspiration and culture (aerobic and anaerobic) should be performed. This technique, while uncommonly performed in North America, is used in some European countries.

❖ Percutaneous ultrasound-guided cholecystocentesis in healthy cats

Abstract
Percutaneous ultrasound-guided cholecystocentesis (PUC) is a minimally invasive technique for bile collection that is used successfully in human patients with cholecystitis. Its use in veterinary medicine for evaluation of hepatobiliary disorders has been limited because of the perceived unacceptable risk of bile peritonitis. An experimental study was conducted to evaluate the safety and efficacy
of PUC, to collect data on bile cytology and bacteriologic culture, and to attempt to isolate Helicobacter spp. from the bile of healthy cats. In fasted and sedated cats, PUC was performed with a 22-gauge 1.5-in. (3.81 cm) needle with an attached 12-mL syringe via a right-sided transhepatic approach (n = 1) or into the fundus of the gallbladder (n = 11) via a right ventral abdominal approach. An attempt was made to completely empty the gallbladder. A small amount of abdominal effusion, consistent with bile or blood, was seen ultrasonographically immediately after aspiration in the 1st cat. Ultrasonographic complications with the 2nd technique were not observed in the remaining 11 cats. Decreased appetite and evidence of mild abdominal pain were detected in 4 cats within 2 days after PUC. The mean neutrophil count increased 2 days after PUC (P < .01) but remained within the reference range. The bile was acellular in 11 of 12 cats, and aerobic, anaerobic, and Helicobacter spp. cultures yielded no growth in 12 of 12 cats. There were no remarkable gross or histologic lesions of abdominal organs at the postmortem examination (8 cats) performed 7-8 days after the procedure. PUC appears to be a safe and technically simple procedure. Further studies are warranted to determine the use and safety of PUC in cats with hepatobiliary diseases.

The surgical treatment of cholelithiasis in cats: a study of nine cases

Abstract
Nine cats that had surgical treatment for obstructive cholelithiasis were reviewed to evaluate clinical signs, diagnostic test results, and outcome after surgery. Common clinical signs included progressive vomiting (9/9), dehydration (9/9), anorexia (6/9), icterus (5/9), and lethargy (4/9). Five cats had a cholecystectomy performed, one cat had a cholecystotomy, and three cats had a biliary diversion procedure. Four of the cats that had a cholecystectomy had no recurrence of vomiting or anorexia. The majority of cats (7/9) had multiple choleliths, which were radiopaque and most commonly composed of calcium carbonate. Seven cats were diagnosed with cholangiohepatitis, and four of these cats did not need long-term medical therapy. Most cats (7/9) survived long term postsurgery (mean, 21 months; median, 24 months) without additional medical therapy, while the two cats with concurrent hepatic lipidosis died. Cholecystectomy appeared to have low morbidity with good clinical success.

EXTRA HEPATIC BILE DUCT OBSTRUCTION (EHBDO)
This is a cause for acute onset of vomiting and malaise in a patient. Plain radiographs may show a radiodensity in the region of the gallwort...
bladder; ultrasound confirms that the location is the bile duct as well will detect inspirations that are not radiodense. A urinalysis will detect this problem early, as there will be the presence of bilirubin but a lack of urobilinogen in the sample. Blood work will show a marked increase in bilirubin and eventually cholestasis (increased SAP) and some hepatocellular injury (increased ALT). This constitutes an emergency constitution and requires surgical correction. Inflammation of the biliary tree distal to the gall bladder may cause functional obstruction, which, if not decompressible, may need surgical relief as well.

**Pathogenesis and outcome of extrahepatic biliary obstruction in cats**

**Abstract**
Extrahepatic biliary obstruction (EHBO) was confirmed at surgery or necropsy in 22 cats. Biliary or pancreatic adenocarcinoma was diagnosed by histopathology in six cats and one cat had an undiagnosed mass in the common bile duct. The remaining 15 cats had at least one of a complex of inflammatory diseases including pancreatitis, cholangiohepatitis, cholelithiasis and cholecystitis. The most common clinical signs were jaundice, anorexia, lethargy, weight loss and vomiting. Hyperbilirubinaemia was present in all cases. Distension of the common bile duct and gall bladder was the most commonly observed finding on abdominal ultrasound. Nineteen cats underwent exploratory laparotomy for biliary decompression and diversion. Mortality in cats with underlying neoplasia was 100 per cent and, in those with non-neoplastic lesions, was 40 per cent. Long-term complications, in those that survived, included recurrence of cholangiohepatitis, chronic weight loss and recurrence of obstruction. Based on these findings, the prognosis for EHBO in cats must be considered guarded.

**TRITRICHOMONAS FOETUS**
*Tritrichomonas foetus* has recently been recognized as a common cause for recurrent large bowel diarrhea. In a study of 117 cats at a cat show, the prevalence of *T. foetus* was 31%, of *Giardia lambia*, 31% and of coinfections with both protozoal parasites, 12%. The conclusion was made that *T. foetus* infected catteries are common and contain a significantly larger number of cats with diarrhea. Evidence did not exist for transmission of *T. foetus* by
water, food or contact with other species. In contrast, *Giardia* sp. infection was significantly associated with source of water and direct contact with other indoor-outdoor species. There is no known effective anti-microbial treatment and dietary manipulations are ineffective long-term. In a follow-up study, it was found that most cats experienced spontaneous resolution of diarrhea within 2yrs (with a median of six months) after the diagnosis, despite persistent infection on the basis of fecal PCR. Changes in diet, administration of medication or other stressors resulted in recurrences of diarrhea in approximately 50% of the cats. By 2-5 years after diagnosis, infection was no longer detectable in 50% of the cats by PCR so the conclusion was made that the long-term prognosis for resolution and cure is good for cats infected with *T. foetus*.

Over this past two years (2006-7), a paper reported on the prevalence of *T. foetus* infection in cats with diarrhea in the United Kingdom (Gunn Moore) showing that this problem is world-wide.

Ronidazole and tinidazole have been evaluated for efficacy both clinically as well as for their ability to eliminate infection based on PCR testing. In the first study (Gookin JVIM 2006), experimentally infected cats were treated with ronidazole (10 mg/kg PO BID X 14 days). For relapsing infection, the dose was increased to either 30-50 mg/kg PO BID X 14 days. At the higher dose regime, all cats remained free from infection for periods of 21-30 weeks follow-up based on direct microscopic examination, culture and weekly PCR. The later study evaluated the efficacy of tinidazole by treatment with 30 mg/kg PO BID X 14 days. At the end of this therapeutic course, amoxicillin was administered to induce diarrhea successfully resulting in recrudescence of *T foetus* in some of the cats. The magnitude of shedding was lower in cats treated previously with tinidazole than in those who hadn’t been. (Gookin AJVR 2007) The conclusion at this time is that ronidazole remains more efficacious for the treatment and elimination of *T foetus* in cats. Caution should be practiced to avoid possible neurotoxicity from this agent by not administering > 30 mg/kg PO BID.

Fecal culture may be considered when specific pathogens are to be investigated. Routine culturing will give results that are difficult to interpret and is not recommended. Growth of *Salmonella*, *Campylobacter* sp., or *Clostridium* sp. may be attempted on specific culture media when these agents are suspected, such as in an acute (or recurrent) outbreak of diarrhea after showing or in multiple cats in a household.

For large bowel diarrhea, cytology from rectal scrapings (see below) and gram stain of prepared slides may be very useful in identifying inflammatory cells, fungal hyphae, and *Cryptosporidium* sp. The
presence of clostridial spores must be interpreted carefully and a fecal enterotoxin assay should be performed to determine if disease causing clostridial enterotoxin is present or not.

Cryptosporidium parvum

*Cryptosporidium parvum* is a tiny coccidia (approximately 5 microns) that commonly infects people and may cause severe gastrointestinal disease. Cryptosporidial oocysts are directly infectious when passed with feces. The presence of oocysts or antigen has been documented in the feces of many cats with or without diarrhea. The prevalence of infection with this organism is equal to or greater than with *Giardia* spp. in two recent studies in New York state and Colorado. While infection with this organism in people is usually from contaminated water, zoonotic spread from infected cats is possible. Fortunately, the organism is shed in small numbers and intermittently in the feces. Unfortunately, this makes it difficult to diagnose. Diagnosis may be pursued using modified Ziehl-Neelsen or Kinyoun acid-fast staining techniques, immunofluorescence detection (more sensitive and specific) or the Alexon ProSpecT® *Cryptosporidium* Microplate enzyme immunoassay. The "Rapid" version of this (and the *Giardia* test) is not as sensitive.

**Rectal Cytology/Scraping**

This technique is extremely helpful in definitive diagnosis in many cases of large bowel diarrhea. Insert a sterile culture swab 2-3 cm into the rectum of the cat and rotate it gently. Roll this swab gently and thoroughly on two microscope slides and store the swab in the culturette medium. Submit the slides for cytology plus gram stain and follow with the swab as indicated by the cytology results. Rectal swabs may diagnose bacterial suppurative colitis, cryptosporidium, giardia, campylobacter infections.

From Dr. Lappin, WSAVA 2002: **Update of infectious causes of vomiting or diarrhea in cats:**

“There are many infectious agents associated with vomiting or diarrhea in cats. Primary clinical signs associated with infectious causes of gastrointestinal tract diseases are abbreviated as follows: S = small bowel; M = mixed bowel; L = large bowel; V = vomiting. Any of the agents that induce diarrhea potentially can induce vomiting as well. The primary bacteria associated with gastrointestinal tract disease in cats include *Salmonella* spp. (S,M,L), *Campylobacter jejuni* (M,L), *Clostridium perfringens* (L,rare), *Helicobacter* spp.(V), bacterial overgrowth syndrome (S), bacterial peritonitis (S), and bacterial cholangiohepatitis (S). The primary viral agents include feline coronaviruses (S), feline leukemia virus (FeLV; V,S,M,L), feline immunodeficiency virus (FIV; V,S,M,L), and feline panleukopenia virus (V only frequently, S). The primary helminths are
Ancylostoma/Uncinaria (S,M), Strongyloides cati (S,M, rare), Dirofilaria immitis (V), Toxocara cati (V), Toxascaris leonina (V), Ollulanus tricuspis (V), and Physaloptera spp. (V). Enteric protozoans include Giardia spp. (S,M), Cystoisospora spp. (Isospora; M,L), Cryptosporidium spp. (S,M), Entamoeba histolytica (L, rare), and Tritrichomonas foetus (L, rare). The cestodes Taenia, Dipylidium, and Echinococcus generally cause subclinical infection.”

Esophagitis

Consideration should be given to this condition in a patient in whom vomiting or inappetance occur as a post operative complication. Diagnosis is by barium paste contrast radiography or endoscopy. Therapy should include an H2 blocker and sucralfate along with analgesia. It is critical to administer the sucralfate at least 30 minutes before the H2 blocker as it requires an acid environment to be effective.

Megacolon

"Many cats have one or two episodes of constipation without further recurrence, while others progress to complete colonic failure. Middle-aged, male cats are particularly at risk for the clinical continuum of constipation, obstipation and dilated megacolon. Pelvic canal stenosis and nerve injury are (numerically) minor causes in the development of this syndrome. In most affected cats, the underlying pathogenesis appears to involve colonic smooth muscle dysfunction. In the latter group of cats, it is not clear whether this disorder represents a primary or secondary (resulting from long-standing constipation and colonic distension) abnormality. Many cats with mild to moderate constipation will respond to conservative medical management, e.g., (rehydration), dietary fiber supplementation, emollient or hyperosmotic laxatives, colonic prokinetic agents. Indeed, early use of colonic prokinetic agents is likely to prevent the progression of constipation to obstipation and dilated megacolon in many cats. Some cats may become refractory to these therapies, however, as they progress through moderate or recurrent of constipation to obstipation and dilated megacolon. These cats will eventually require colectomy. Cats have a generally favorable prognosis for recovery following colectomy, although mild to moderate diarrhea may persist for 4 to 6 weeks postoperatively in some cases." (excerpted from Dr. Bob Washabau’s notes, Fall AAFP Meeting Proceedings, 1998).

Dr. Washabau recommends using cisapride (Prepulsid™ 2.5-5.0 mg/cat po q8-12h) in conjunction with ranitidine (Zantac™, 1-2 mg/kg po q12h) or nizatidine (Axid™, 2.5-5.0 mg/kg po q12h) as these latter two agents inhibit acetylcholine-esterase thus favouring...
smooth muscle contraction. Cimetidine and famotidine are not effective.

**Referentes**


11.2 TOP PRACTICE TIPS FOR CATS

INTRODUCTION

What is a cat? What characteristics are different for this species than we are or dogs are? Only by better understanding our patients can we provide better nursing care.

Cats are obligate carnivores. They diverged from canids approximately 30 million years ago, evolving metabolically into carnivores with unique strategies for the utilization of protein and amino acids, fats and vitamins. This concept must be at the centre of trying to understand the nutritional needs of cats and planning dietary therapies for health disorders.

Working with a species that has not evolved with a social structure similar to ours provides interesting challenges to the practitioner of veterinary science working with cats. Cats are able to function completely efficiently as a solitary creature. Cats do have complex and changing social interactions which make for a changing structure, much more intricate than that of a herd or pack species. Cats are also small predators. This has affected their anatomic and physiologic development, which has remained unchanged over several million years. While being predators, their size also makes them prey to other species. This aspect affects how they respond to us in a clinic setting and deserves to be discussed further in this presentation.

Relying on the “fight or flight” or epinephrine response, they escape situations viewed as dangerous. From the perspective of a cat, we are, and what we do is, dangerous. Accordingly, one of the great challenges we see on a daily basis is the frightened and assertive cat. It is essential to remember at all times that this small creature feels more threatened than we do so that we do not become frightened
ourselves. Because cats are small, they try to avoid physical confrontation at all costs and attempt to intimidate using sounds and posture as much as possible.

1. Handling the uncooperative cat: a comprehensive physical examination can usually be done using a towel as a protective barrier. Facing the cat away from you is less threatening for him/her. Confining the cat between your legs as you sit on the floor provides adequate persistent firm restraint that is reassuring rather than frightening.

2. Collection of blood and urine can be done by bundling a difficult cat’s forelimbs, torso and head in a towel and using the medial saphenous vein and a lateral approach for cystocentesis. This vein is also a superb choice for catheter placement and administration of intravenous medications.

3. Blood pressure evaluation may also be done recognizing that a persistently elevated systolic value of greater than 170 or 180 mm Hg is probably represents true hypertension rather than the stress response. If in doubt, repeat the value later on during the visit.

4. Elevated blood glucose and glucosuria may be a result of persistent stress. The diagnosis of diabetes, therefore, is dependent on finding and elevated serum fructosamine or glycated hemoglobin.

Domestic cats have evolved from the wild cat model remarkably little. (They display a much narrower diversity of phenotype than dogs.) They are anatomically and physiologically adapted to eating 10-20 small meals throughout the day and night. This allows them to hunt and eat when their prey are active. Small rodents make up the majority of their diet, with rabbits, birds, insects, frogs and reptiles making up a smaller proportion. The average mouse provides 30 kcal of energy, which is about 8% of an average feral (i.e. active) cat’s requirements. Repeated hunting behaviours throughout the 24 hour period are needed to meet this need; this has evolved into the normal grazing feeding behaviour of domestic cats. Under stressful situations, cats will refuse a novel food; under other circumstances, the same cat may be very adventuresome and chose a new diet over their familiar food.

A critical difference in cats is that, while other species are able to rest their metabolic pathways from the efforts of glucose (energy) synthesis when they have been fed cats must continue gluconeogenesis in both the fed and fasted states. When cats are anorectic, they catabolize body proteins. Protein supplementation during fasting will slow hepatic lipid accumulation. Urea cycle enzymes in the liver of cats are always „turned on“. This does not, however, imply that cats cannot use carbohydrates as they are capable over the longterm to adapt to lower protein diets. Adult cats
have a much higher requirement for protein than dogs or humans. Expressed as a percentage of diet, adult cats need 29% vs. the adult canine requirement of 12% or the human need for 8%.

Esophagostomy tubes are easy to place in under 10 minutes of anaesthesia. Feeding can be started within 2 hours after recovery. Using a syringable food such as Hill’s a/d or Royal Canin Recovery (1.3 kcal/ml) or Eukanuba Maximum Calorie (2.1 kcal/ml) is ideal. Should they need diluting, use a liquid feline diet, such as Clinicare (1 kcal/ml) rather than water in order to avoid loss of caloric density. These tubes are easy to maintain and can be removed as soon as the patient is eating on his/her own enough to prevent weight loss without nutritional support over a one week period. Should they clog, infusion of 10 ml of a cola drink or meat tenderizer in solution will unplug the tube if left for 10 –15 minutes. Gradually increase the volume of each meal reducing the number of feedings needed to meet the daily caloric requirements, the goal being to have 4 feedings/day, as this is a reasonable number that clients can cope with at home. If, in so doing, vomiting recurs even with a small volume of food (e.g. 10 ml) then “trickle feeding” can be instituted. This consists of fill an empty IV bag with either of the aforementioned diets, Clinicare or another liquid diet, attach it to an IV line, and run the line as a drip throughout the day attached to the feeding tube. Either gravity flow or IV pump are suitable. Use a fresh bag and new solution every 12 hours to prevent bacterial or yeast growth.

Successful management of a cat with diabetes mellitus requires a committed healthcare team. The client needs to know that they will see improvement, that this will take several months and that they have their veterinary team behind them. Confirming the diagnosis using a serum fructosamine, we book a counselling appointment. At this time, we listen to the client’s concerns and beliefs about diabetes and help them understand the pathophysiology. The client is taught to handle insulin and syringes properly, nutrition is discussed and they are taught how to use the diary. The first blood glucose curve (hourly measurements for 12 hours) is booked for two weeks hence; at this time, the insulin dose most likely is adjusted and the client is taught how to perform glucose measurements at home before administration of insulin. Thereafter, curves are performed every 2 weeks until the cat’s condition is stable. These are initially performed in clinic. After one month on insulin, a fructosamine is evaluated again. Once the client is comfortable enough with monitoring blood glucose, curves are performed at home and reported by email, phone or fax to the doctor for recommendations.

Being largely self-dependent, cats mask illness and pain extremely well. The signals of problems are often subtle. Listening carefully to clients when interviewing them for the history and their concerns is
extremely important. Often clients detect changes intuitively that represent real problems. This is more common, in the author’s experience, than the client who is blissfully unaware of significant health problems. By asking open-ended questions, one elicits a more detailed history than using only specific questions. For example: starting with: “Have you noticed any changes in the contents of the litter box?”, results in a yes/no answer. Asking: “What does his stool look like?” Provides a useful answer.

One simple technique for detecting subtle changes is measuring body weight at every visit and calculating the percentage change in body weight. By 12 –15 months of age, a cat should reach their adult weight. By noting slight changes in weight, either increases or decreases, one can follow trends and hopefully avert significant problems such as lipidosis or obesity and detect malabsorption of nutrients or catabolism of cancer in the earlier stages.

\[
\text{% change} = \frac{\text{previous weight} - \text{current weight}}{\text{previous weight}}
\]

Monitoring body weight in hospitalized cats is invaluable in helping to assess the success of rehydration efforts as well as the adequacy of feeding. Weight gain in the face of fluid therapy without voiding could be an indicator of third space fluid accumulation. Thus, cats in clinic on IV fluids should be weighed at least twice a day; cats boarding or otherwise in the hospital should be weighed daily. The “grumpy” cat can be weighed in towel and, by subtracting the weight of the towel, we get the body weight with being minimally intrusive. Other uses for scales are to evaluate volume of urine produced by knowing the weight of the unused litter box and comparing it to the used box; a postage scale may be used to determine volume of blood in surgical swabs.

Urine collection: Agitation of the bladder just before collection of urine by cystocentesis provides a better sediment yield. Because sediment is heavier than urine and is gravity dependent, resuspension of the sediment within the bladder is diagnostically beneficial. A low number of white blood cells, trace protein or the absence of bacteria should be interpreted with suspicion in dilute urine. A culture and sensitivity may be warranted when the specific gravity is < 1.025 in this situation. Conversely, when high numbers of bacteria are seen in a highly concentrated urine (e.g. usg > 1.050), collection induced contamination should be expected, especially when a mixture of rods and cocci are reported.

Blood pressure evaluation should be performed in every cat over the age of eight years and in any ill or anaesthetized patient. Hypertension is common in cats with renal insufficiency or with hyperthyroidism. Hypotension in an ill cat may signal hypovolemia or
sepsis. During anaesthesia, hypotension precedes alterations in pulse oximetry and, if remedied promptly, can prevent hypoxemia from developing.

Hematocrit tubes provide vital information. Not only should the PCV and total solid (TS) be noted, but also the percentage buffy coat, as an estimate of massive white cell number changes and the character/colour of the serum. Icterus may be noted in the serum (or in the urine) before serum bilirubin rises or before it becomes evident in the pre-auricular skin, the conjunctive or the soft palate. Calculation of fluid rates for patients requires knowledge of the TS along with the PCV. These measurements should be taken minimally once a day; in more anemic and volume fragile patients, more frequent measurements are indicated. Like blood glucose measurement, blood for hematocrits may be collected by ear pricking with minimal annoyance for the patient.

Assessment of degree of dehydration should take all of the following parameters into consideration: skin turgour, eye position, mucous membrane moisture and TS. Replacement of volume deficit plus maintenance requirements of 60 ml/kg/day should be calculated using the normal, hydrated weight not the ill weight. When prescribing subcutaneous fluid therapy as part of home care for a patient (for constipation, renal insufficiency, etc.), assuming the patient is adequately rehydrated, the volume to be given at home should be 60 ml/kg/day, not an arbitrarily assigned 50, 100, 150 ml/day based on the size of the cat.

Intubation of cats can be easily accomplished without the use of a laryngoscope, which can be cumbersome. With the assistant holding the cat’s mouth open with one hand (hand over head, fingers at angle of jaw), she/he pulls the skin over the larynx rostrally. Simultaneously, the person intubating pulls the tongue forward and down, exposing the laryngeal folds. These are numbed with a drop of lidocaine and then the lubricated cuffed endotracheal tube is easily slid into the clearly visualized opening.

Bronchopulmonary disease diagnostics requires the harvesting of airway secretions for cytologic and microbiologic evaluation analysis for differentiation and diagnosis of the various causes of coughing and/or wheezing in the cat. Tracheal wash is readily available to all practitioners and samples the contents of the larger airways. Using a sterile endotracheal tube is less stressful than the traditional trans-tracheal technique. Pass a 3-5 Fr. red rubber feeding tube through an opening made in the end of its packaging, through the endotracheal tube until slight resistance is met. Flush two 6 ml aliquots of nonbacteriostatic physiologic sterile saline and aspirate the wash back into a sterile collection syringe. Repeat this procedure until 6-12 mls
of saline have flushed the airways. Submit some of the collected sample on air-dried slides, in an EDTA tube as well as in a sterile red top tube for culture, should the fluid cytology show significant organisms. The presence of Simonsiella bacteria or squamous cells indicates oropharyngeal contamination.

Transfusions are an underutilized therapeutic modality. They are simple and life-saving as whole blood provides not only oxygen carrying capability of the red blood cells, but also platelets to initiate clotting, coagulation factors, oncotic properties of albumin to raise blood pressure, electrolytes, nutrients and white blood cells to fight infection.

It is important not only to blood type the recipient and use a suitably typed donor, but also to cross-match the potential donor to the recipient. There are too many type B cats in the population to not blood type and because of numerous alloantibodies as well as antibodies to things a cat has been exposed to, we mustn’t err by not cross-matching. Either small blood bags can be used or 12 or 20ml syringes with CPDA1 added. The PCV and TS of both the donor and recipient are needed. With this information, the ideal amount of blood to be given may be calculated. Mostly one collects 40-50ml from the donor and gives the entire unit. An 18G needle and extension set (rinsed with CPDA1) or butterfly catheter can be used for collection from a sedated donor. A three way stop cock or one way valve is helpful for changing syringes during collection. An in-line pediatric filter is needed for the administration of the blood. The most important thing (other than typing and cross matching) is that the human team are all relaxed. This is not a difficult procedure!

Donor requirements:
• Retrovirus and mycoplasma negative
• Good health, good body weight, well hydrated
• High PCV with normal TS

Care of donor after collection:
• Subcutaneous or IV fluid therapy
• Iron orally or by IM injection
• Good nutrition…and a treat!
• LOTS OF TLC

Care of the recipient after transfusion:
• Administer the transfusion over 1-2 hours and monitor body temperature, RR and attitude closely during transfusion.
• Check a PCV and TS after 24 hours
Bone marrow taps are another procedure that may intimidate some practitioners in the relatively smaller feline patient. The author uses 16G needles rather than a Jamshedi needle and readily harvests both a bone corer as well as marrow for evaluation of marrow diseases. Sites that may be used for collection are the femur, medial to the greater trochanter, the wing of the ilium or the humerus. After surgical prep the samples collected should be placed into EDTA tubes, at least 6 slides should be made and air-dried and the bone core placed into formalin in a red top tube. Be sure to collect a blood sample for a CBC at the same time to evaluate how the cells are being released into the periphery.

Analgesia has thankfully come of age in veterinary medicine. We now have numerous types of agents that we can use safely in cats. The American Animal Hospital Association (AAHA) and the American Association of Feline Practitioners (AAFP) have jointly created Pain Management Guidelines in 2006. Whether we chose opioids, NSAIDs, antidepressants, antiseizure meds or acupuncture, we must be pre-emptive wherever possible and proactive. Conditions that would be painful for us are likely painful for our patients. Pain is an experience that varies greatly between individuals. It is not only unpleasant but also deleterious to health, interfering with recovery and possibly resulting in death. If clients believe their cat is suffering, they are more inclined to consider euthanasia. If recovery is delayed, hospitalization costs increase, which may also influence the client’s frame of mind.

Conditions commonly seen in feline patients for which we may not routinely provide analgesics include lower urinary tract disease (LUTD), pancreatitis, and arthritis. In LUTD, antispasmodics may be beneficial and humane along with an anti-inflammatory agent. Arthritis requires the use of agents that can be given long-term, such as judiciously dosed NSAIDS, glucosamine and chondroitan sulphate and acupuncture if available and tolerated. A wonderful resource for learning about the recognition and alleviation of pain is: Pain H.U.R.T.S. available through www.jonkar.ca/RPain/.

Recently aerosol inhalers (for both steroids and bronchodilators) have been recommended and used with success clinically in small animal medicine. Fluticasone is an inhaled steroid, which comes in 3 dose strengths (44, 110, 220 mcg/dose). Beta₂-adrenergic agonists come in a selection of albuterol, salmeterol or terbutaline. These may be delivered with the use of an Aerokat (www.aerokat.com) or an Optichamber (Respironics: www.respironics.com) held over the cat’s muzzle for 30 seconds. Drug delivery remains a significant question, both getting effective drug concentrations into the affected airways as...
well as avoiding excess drug/the potential of overdosing these small animals.

Tips on aerosol use:
- Acclimate kitty to device over several days, letting him/her investigate it.
- Reward fearless approaches to device and start placing it near kitty’s face. (Praise, food, catnip, stroking?)
- Practice with the mask over the cats face without anything in the chamber
- Pre-load the chamber with a puff of albuterol (in addition to the dose required)
- Make sure the mask is over the muzzle for 4-6 breaths
- Administer bronchodilator (albuterol) first, to allow better delivery of corticosteroid

In the patient who is nauseous and swallowing frequently, esophagitis or gastritis may be suspected. Administration of famotidine SC along with an oral bolus of sucralfate suspension will make the kitty much more comfortable for examination.

As well as medical therapy for pruritis, the cat with itchy skin will benefit if SoftPaws™ (www.softpaws.com/) are applied to the nails of their back (+/- front) feet.

As cats age, they tolerate less time in the clinic. Siamese cats are especially prone to depression. Three days is about as long as a cat can stand the indignities of hospitalization, even with daily visits from his/her person. Because cats “see” the world in overlapping clouds of smells, we must provide familiar smells and aim to reduce foreign, medicinal smells wherever possible. Client worn shirts are helpful in their cages/beds. Because their sense of hearing is tuned more finely than ours, we must keep as quiet and reassuring environment as possible. They should not be exposed to the sounds of predators, namely barking dogs. Certain induction agents enhance their sense of hearing, e.g., ketamine, so a safe sounding environment should be achieved. Changing diet while hospitalized is likely to result in inappetance and the development of an aversion, thus if a change in diet is required therapeutically, try to make that change at home, in a gradual fashion.

Client care, i.e. care of the client, is essential to providing complete patient care. It is only through hearing and working with the client that we are able to offer the very best veterinary care.

Remember, in order to provide compassionate and effective care for cats, try to think like a cat. Imagine what their experience might be like. When we reach into a carrier or kennel, we are huge creatures,
blocking the light. We smell wrong and don’t sound familiar. Shushing reassuringly sounds like a hiss in cat. Remember that the less is more when restraint is required. Always leaving as much contact with the floor as possible; if collecting from a jugular in sternal position, have the forefeet touch the table; procedures requiring lateral recumbency are less frightening when the front end is sternal. Allow the client to be with the kitty as much and whenever possible. And don’t forget that hissing, spitting, growling and posturing are all attempts to not have to strike or bite you. Cats avoid direct physical confrontation if possible.

11.3 THERAPEUTIC IMPLICATIONS OF RENAL INSUFFICIENCY: NEW THOUGHTS

Renal function declines with increasing age as a normal event. Consequently, renal insufficiency is very common in aging cats. The term chronic renal insufficiency is preferable to chronic renal failure because this condition is progressive, rather than imminently terminal, and can be managed.

Cats may live for many years after the initial detection of decreased urine specific gravity and elevated blood urea nitrogen (BUN) and serum creatinine levels, depending on the disease’s stage and cause. To grossly lump everything together as chronic renal failure is an oversimplification and a disservice to our patients and clients. Table 1 shows the criteria proposed by the International Renal Interest Society in 2006 to characterize renal disease. Staging allows for better communication among practitioners and offers guidelines for the initiation of different therapies. To provide high-quality patient care, practitioners must attempt to carefully define the stage of chronic renal disease as well as identify and manage any concurrent medical conditions.

HISTORY

Clinical signs of renal insufficiency may include anorexia or inappetence, vomiting, dehydration, weight loss, lethargy, oral ulceration, ptyalism, anemia, social apathy, and constipation. Polyuria and polydipsia are reported less commonly in cats than in dogs, perhaps because of the secretive nature of cats. In assessing the degree of illness, it should be kept in mind that both decreased muscle mass (wasting) of cats with chronic renal insufficiency and concurrent hyperthyroidism will mask the severity of renal insufficiency by lowering serum creatinine levels. Often cats with even moderate renal insufficiency are asymptomatic. Our goal should be to correct and maintain physiologic parameters that will enable them to enjoy a good quality of life.
Because these patients are older cats, they may have more than one clinical condition. It is not uncommon to have a patient with chronic renal insufficiency that also suffers from pyelonephritis, cardiac disease, or hypertension associated with renal or thyroid disease. Constipation is extremely common in elderly cats. There may be concurrent inflammatory bowel or small airway disease, diabetes mellitus, neoplasia, or osteoarthritis. These comorbid conditions may complicate our ability to untangle a diagnosis and balance treatments for a specific patient.

**DIAGNOSTICS**

Following a comprehensive physical examination and consultation (including a fundic examination and blood pressure determination), a minimum database for cats beyond middle age (8 years or older) consists of a complete blood count (CBC) with differential, serum chemistry profile (including baseline tetraiodothyronine (T4) and free T4), and a complete urinalysis. Cats with renal insufficiency classically have a urine specific gravity of less than 1.040, despite some degree of dehydration. Additionally, with progressive decline in function, BUN and creatinine will exceed normal reference values in rehydrated patients. As renal disease progresses, there will be varying changes in urinary protein and potassium levels as well as alterations in serum electrolytes (ionized calcium, phosphorus, and potassium). Anemia also develops due to several causes.

Urine should be collected by cystocentesis. Because pyelonephritis is often subclinical, urine culture and sensitivity testing should be considered in patients with dilute urine (urine specific gravity <1.020) and white blood cells or trace protein without adequate red blood cells to account for the protein. The method of urine collection (free catch vs. cystocentesis) affects the interpretation of bacterial colony counts. If the urine is collected by cystocentesis, any number of bacteria is significant. For a free-catch urine sample, bacterial colony counts need to be higher than 10,000/ml to be significant. Both dilute urine and glucosuria encourage bacterial growth. Additional tests, such as serum fructosamine, can be recommended depending on clinical concerns and diagnostic findings.

**MANAGING CHRONIC RENAL DISEASE**

**Hydration**

Rehydration is a key component of treatment in cats with chronic renal disease. Rehydration is critical in perfusing tissues with oxygen and nutrients and scavenging waste. Rehydration also aids in acid–base homeostasis. Because cats with renal insufficiency are usually in a state of metabolic acidosis, alkalinizing fluids are the preferred fluid type. In dehydrated patients, increased urea reabsorption due to decreased tubular flow rates may lead to an increase in BUN—even
before the glomerular filtration rate (GFR) is decreased—causing prerenal azotemia. This also causes serum BUN to appear higher than it actually is.

The patient should be rehydrated and blood work repeated before a prognosis is given. With an impaired ability to concentrate urine—despite polydipsia—exogenous fluids are required. Clients commonly administer subcutaneous fluids to cats at home. Increasing water intake can be encouraged by flavoring water and feeding more canned foods. Recirculating water fountains may appeal to some cats. For cats with a fragile cardiovascular system, maintaining hydration to optimize renal function yet not overload cardiovascular capabilities requires fine-tuning through ongoing client communication. This requires frequent reassessment of packed cell volume (PCV), total solids, BUN, and serum creatinine along with reassessment of body weight, skin elasticity, appetite, and energy.

For the most part, constipation is a clinical sign of dehydration. Cellular water content has priority over fecal water content; thus, primary treatment should address rehydration and the underlying cause of dehydration rather than stool passage (e.g., with laxatives). Promotility agents, laxatives, osmotic agents, and fiber-enriched diets should be used only after the patient is rehydrated.

Renally impaired cats with diarrhea from chronic small or large bowel disease have increased fluid losses above their maintenance replacement needs. The underlying cause of the diarrhea should be controlled as much as possible. Should corticosteroids be part of therapy (e.g., for inflammatory bowel disease or small airway disease), polyuria may worsen. Similarly, for cats with renal disease and diabetes mellitus, cellular water needs should be addressed.

Inappetence, Nausea, and Vomiting
Many cats with uremic gastritis show only signs of partial anorexia or nausea rather than outright vomiting. H₂-receptor antagonists are underutilized; they function by preventing gastric hydrochloric acid production. Famotidine (0.5 mg/kg PO every 24 to 48 hours) or ranitidine (2 to 3 mg/kg PO q12h) may be considered once serum creatinine is higher than 2.5 mg/dl (220 mmol/L), even if the cat seems nauseated.

Appetite stimulation should be attempted with cyproheptadine (1 mg PO q12h) or mirtazapine (3 mg PO q72h), which has the added benefit of antiemetic effects. Regardless of concurrent problems, adequate calories need to be ingested. For patients not ingesting adequate calories (as evidenced by weight loss, poor coat and muscle mass), placement of an esophagostomy or other large-bore feeding tube should be considered.
Hypertension
The incidence of hypertension in cats with renal insufficiency has been reported to be 60%, whereas, in cats with hyperthyroidism, the incidence reportedly ranges from 40% to 60%. Evaluation of blood pressure should be considered in all older cats and any ill cats. Cats with chronic renal insufficiency lose the normal autoregulatory capacity of the glomerular arterioles. This not only causes systemic hypertension but may also promote the progression of renal insufficiency through glomerular injury.

Treatment of hypertension should be considered in cats with systolic blood pressure consistently over 170 mm Hg. Amlodipine is the most efficacious agent (0.625 mg PO q12–24h, increase gradually over weeks as needed), as it has a direct effect on the peripheral vasculature calcium channels. Angiotensin-converting enzyme (ACE) inhibitors are not as efficacious in decreasing systemic blood pressure. β-blockers reduce renin secretion and are similarly unimpressive for treating feline hypertension.

Metabolic Acidosis
Cats with chronic renal diseases commonly have metabolic acidosis. This acid–base imbalance promotes severe catabolism of endogenous proteins, exacerbates azotemia regardless of diet, promotes wasting (degradation of protein), inhibits protein synthesis, causes a negative nitrogen balance, and enhances hypokalemia. Acidosis should be corrected aggressively with the use of alkalinizing fluid therapy and H2-receptor antagonists.

ADDITIONAL TREATMENT OPTIONS
ACE Inhibitors
A large, multi-institutional study (the BENRIC [BENazepril in Renal Insufficiency in Cats] Clinical Trial1) assessed the effects of benazepril on chronic renal insufficiency in cats. Results of this and other smaller studies2,3 showed no significant difference in survival time between benazepril and placebo administration. However, for cats with urinary protein loss (urine protein:creatinine ratio), benazepril treatment resulted in longer survival times and better appetite than placebo. Cats without protein-losing glomerulonephropathy may potentially be harmed by this agent because it diverts renal blood, causing a beneficially increased renal interstitial blood flow but a potentially deleterious reduction in GFR. Before diagnosing a protein-losing glomerulonephropathy, sequential urine protein:creatinine ratios should be checked (two over a 2-week period) to ensure that proteinuria is persistent rather than physiologic and transient. Cats with an increased urine protein:creatinine ratio (>0.4) that are started on benazepril (0.25 to 0.5 mg/kg/day PO) should be...
rechecked within 3 to 7 days and have their renal parameters, hydration, body weight, appetite, and overall health monitored. Stable patients should be reevaluated every 2 to 4 months.

**Erythropoietin**

Erythropoietin causes rapid correction of anemia by stimulating marrow progenitor cells. When PCV is less than 20%, erythropoietin (75 to 100 U/kg SC three times per week) should be considered until the PCV is in the low-normal range (35%); the dosage should then be reduced to 50 to 75 U/kg SC twice a week. It is important to monitor PCV for the first 60 to 90 days to detect development of anti-erythropoietin antibodies as noted by a decline in PCV rather than an increase (at comparable total solids). If this occurs, erythropoietin treatment should be discontinued immediately. The cat may be transfusion dependent for 2 to 4 months until anti-erythropoietin antibody levels decrease. It is also important to administer iron at the start of the regimen and until the cat’s appetite improves. While there is a risk that anti-erythropoietin antibodies may develop, most cats will enjoy the benefits of an increased PCV.

Recently, darbepoetin has been receiving attention as an alternative to erythropoietin, and it may be less antigenic and can be given less frequently. The dose is 0.45 mg/kg/week, but it’s also possible to convert the current erythropoietin dose (Table 2).

**DRUG DOSE ADJUSTMENTS**

For a drug that relies on the kidneys for clearance, a loss in renal function will proportionately decrease drug excretion. Thus, a 75% loss in renal function results in a 75% loss in renal drug clearance. Dosage adjustments can be made from estimates in the loss of renal function. The most exact method of assessing renal function is to measure creatinine clearance as an estimate of GFR.

A less precise but more practical approach is to make a dose adjustment based on serum creatinine, as follows:

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\text{New dose} = \frac{\text{Old dose} \times \text{Normal serum creatinine level}}{\text{Patient’s serum creatinine level}}
\]

\[
\text{New interval} = \frac{\text{Old interval} \times \text{Patient’s serum creatinine level}}{\text{Normal serum creatinine level}}
\]

Remember that this type of dose adjustment estimate is risky in geriatric pets compared with younger pets because serum creatinine is affected by muscle mass. Therefore, a geriatric animal with decreased muscle mass and renal function may have a falsely low serum creatinine level.
DIETARY RESTRICTION OR SUPPLEMENTATION

Protein
Based on results in the feline remnant kidney model, dietary protein restriction does not ameliorate progression of renal insufficiency in cats. However, it is important to note that the remnant kidney model does not reflect or emulate natural disease.

The effectiveness of a therapeutic renal diet was examined in cats with stages 3 and 4 chronic kidney disease by a randomized, controlled clinical trial. This study examined the benefits of feeding a renal diet versus a standard feline maintenance diet. Cats were randomly assigned to either the renal or maintenance diet but were managed in an identical manner with respect to other treatment interventions. Cats fed the maintenance diet had significantly more uremic episodes (22%) than did cats fed the renal diet (0%). A significant reduction in renal-related mortality was observed in cats fed the renal diet. Importantly, significant adverse effects of feeding the renal diet were not detected in the study.

However, in acute renal failure and in mild to moderate chronic renal insufficiency, dietary protein restriction may limit the kidney’s compensatory response to injury. Protein restriction may lead to protein malnutrition, which impairs the immunologic response and decreases hemoglobin production, thus promoting anemia, decreasing plasma protein levels, and promoting muscle wasting. Inadequate protein also decreases urinary excretion of magnesium, which may result in calcium phosphate precipitation in the kidneys. Watching for evidence of protein–calorie malnutrition should include monitoring for weight loss, hypoalbuminemia, poor hair coat quality, and muscle wasting.

Dietary treatment of moderate to severe chronic renal insufficiency (serum creatinine >5 mg/dl, BUN >75 mg/dl in the rehydrated cat) is not controversial; restriction of both protein and phosphorus is required to avoid uremic complications. Benefits of protein restriction are related to nonrenal effects (toxins affect organs other than kidneys). Using protein sources of high biological value is important. Protein restriction may be especially harmful in renal patients who are inappetent because a sustained calorie deficit causes body proteins to be catabolized to supply calories and the nitrogenous end-products of this process will further accentuate uremic signs. Inappetence is an indication for avoiding protein-restricted diets.

Phosphorus
It is important to restrict phosphorus in moderately azotemic patients. Phosphorus restriction is more important than protein restriction to survival in the canine remnant kidney model and has
been shown to produce renal lesions that are less severe than those seen in the feline remnant kidney model. The dose of intestinal phosphate binders cited in the literature may be too low (e.g., aluminum hydroxide initially at 30 to 90 mg/kg/day but dosage must be individualized); the dose should be increased as needed to produce serum phosphorus levels that are consistently within the normal range. If calcium-based intestinal phosphate binders are used, serum calcium levels should be monitored carefully and switched to or combined with aluminium-based phosphate binders if necessary. For these agents to be effective, they must be given with food; they act by binding the phosphorus in the ingested food and making it unavailable for absorption.

**Potassium**

Because hypokalemia may induce a reversible, functional decline in GFR, potassium supplementation is warranted for cats with chronic renal insufficiency and hypokalemia, even in the absence of overt clinical signs. Polyuria results in increased urinary potassium loss as well. Dietary acidification causes intracellular potassium to shift to the extracellular space, raising serum potassium levels but not reflecting total body potassium levels. Thus, metabolic acidosis results in a shift of potassium into the extracellular fluid and should be rectified early in the management of hypokalemia. Potassium supplementation (potassium gluconate 2 to 4 mEq PO q12h) may be considered after acidosis is corrected.

**Calcitriol**

The use of calcitriol is still controversial in that some researchers feel that its use is more urgent than others. Calcitriol advocates suggest that it should be started at 2.5 to 3.5 ng/kg/day PO in early renal insufficiency when serum creatinine is 2 to 3 mg/dl, urine specific gravity is compatible with chronic renal insufficiency, and phosphorus is less than 6 mg/dl. In these patients, when parathyroid hormone levels are still normal, calcitriol is used to prevent PTH levels from increasing, thereby slowing progression of chronic renal insufficiency and preventing clinical signs related to parathyroid hormone toxicity. In patients with a serum creatinine level higher than 3 mg/dl and serum phosphorus level less than 6 mg/dl, the dose is 3.5 ng/kg/day PO. A baseline parathyroid hormone measurement is useful in these patients because the levels are commonly elevated and may require higher doses of calcitriol. It is imperative to have good client compliance—ionized calcium and parathyroid hormone levels should be monitored carefully. The Ca X P product must be less than 60.

**CONCLUSION**

Chronic renal insufficiency is progressive and can be treated. To provide high-quality care, veterinarians must carefully define the
stage of chronic renal disease by taking a thorough history, performing a comprehensive physical examination, and running indicated laboratory tests. With proper hydration and management of concurrent medical conditions, cats may live for many years after chronic renal insufficiency is detected.

REFERENCES

TABLE 1.
Staging Chronic Renal Disease in Cats*

<table>
<thead>
<tr>
<th>Stage</th>
<th>I: Non-azotemic Renal Disease</th>
<th>II: Mild Renal Azotemia</th>
<th>III: Moderate Renal Azotemia</th>
<th>IV: Severe Renal Azotemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine level</td>
<td>&lt;1.6 mg/dl (&lt;140 mmol/L)</td>
<td>1.6–2.8 mg/dl (140–250 mmol/L)</td>
<td>2.9–5.0 mg/dl (251–440 mmol/L)</td>
<td>&gt;5.0 mg/dl mg/dl (&gt;440 mmol/L)</td>
</tr>
<tr>
<td>Clinical signs</td>
<td>None</td>
<td>Possible inappetence, weight loss, polyuria, polydipsia</td>
<td>Usually inappetence, weight loss, polyuria, polydipsia</td>
<td>Uremia, clinically ill</td>
</tr>
<tr>
<td>Progression</td>
<td>Stable for long periods of time</td>
<td>Stable for long periods of time</td>
<td>May progress</td>
<td>Fragile</td>
</tr>
<tr>
<td>Therapeutic goals</td>
<td>Identify and treat specific primary kidney disease (e.g., acute pyelonephritis, nephrolithiasis)</td>
<td>Identify and treat specific primary kidney disease (e.g., acute pyelonephritis, nephrolithiasis)</td>
<td>Modify progression: phosphorus restriction, omega-3 fatty acids</td>
<td>Ameliorate uremic signs: protein restriction, antiemetics, fluid therapy, pyelonephritis, appetite stimulation, dialysis</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Classify*</td>
<td>Classify*</td>
<td>Classify*</td>
<td>Classify*</td>
</tr>
</tbody>
</table>
Table 1: Blood Pressure Classification

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Classifya</th>
<th>Classifyb</th>
<th>Classifyc</th>
<th>Classifyd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonhypertensive</td>
<td>&lt;150 mm Hg</td>
<td>no complications</td>
<td>&lt;150 mm Hg</td>
<td>no complications</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>&gt;150 mm Hg</td>
<td>with no complications</td>
<td>&gt;150 mm Hg</td>
<td>with no complications</td>
</tr>
<tr>
<td>Extradrenal complications</td>
<td>&gt;150 mm Hg</td>
<td>with clinical signs plus blood pressure &gt;150 mm Hg</td>
<td>&gt;150 mm Hg</td>
<td>with clinical signs plus blood pressure &gt;150 mm Hg</td>
</tr>
</tbody>
</table>

*aBased on International Renal Interest Society staging system.
*bProteinuria is determined by evaluating sequential urine protein:creatinine (UPC) ratios: nonproteinuric = UPC <0.2; borderline proteinuric = UPC 0.2 to 0.4 (reevaluate after 2 months); proteinuric = UPC > 0.4.
*cClassification of blood pressure (systolic): Nonhypertensive <150 mm Hg with no complications; borderline hypertensive = 150–160 mm Hg with no complications; hypertension with no complications = systolic blood pressure consistently >160 mm Hg; hypertension with extrarenal complications = clinical signs plus blood pressure >150 mm Hg.

Table 2: Equivalent Erythropoietin and Darbepoetin Doses

<table>
<thead>
<tr>
<th>Erythropoietin (U/wk)</th>
<th>Darbepoetin (mg/wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1,500</td>
<td>6.25</td>
</tr>
<tr>
<td>1,500–2,499</td>
<td>6.25</td>
</tr>
<tr>
<td>2,500–4,999</td>
<td>12.5</td>
</tr>
<tr>
<td>5,000–10,999</td>
<td>25</td>
</tr>
<tr>
<td>11,000–17,999</td>
<td>40</td>
</tr>
<tr>
<td>18,000–33,999</td>
<td>60</td>
</tr>
</tbody>
</table>

*aTotal weekly doses.

Concurrent osteoarthritis, degenerative joint disease, and other disorders

Degenerative joint disorders have been recognized in 90% of geriatric cats and are but one category of many potentially chronic, painful conditions that can occur in these cats. Bacterial cystitis and pyelonephritis are more common in older cats, while the incidence of interstitial, sterile cystitis or inflammatory bowel disease is not different than in younger cats. The likelihood of neoplasia increases with age.

Analgesic considerations in older cats

With increasing age come certain risk factors that need to be considered when planning analgesic protocols. Body composition changes in many elderly cats with a decline in interstitial water and possibly a concurrent decrease in muscle mass. Drug dose calculations should, therefore, be made based on an estimate of lean body weight rather than total weight in overweight cats. Attempts to rehydrate to optimize extracellular water components, tissue perfusion, and glomerular filtration should be made. A decrease in renal clearance, as well as any impairment of hepatic function, may alter the pharmacokinetics of therapeutic agents. When liver disease is present, a rough rule of thumb for drugs that require hepatic metabolism is to reduce their dose by 25%. For drugs requiring renal clearance, the frequency of administration should be
reduced or the dose used may be restricted. Cats with chronic renal disease may suffer from uremic gastritis, just as dehydrated cats with reduced gastric blood flow do; in both situations, the use of NSAIDs increases the risk of gastric ulceration with or without perforation.

**Making Analgesic Choices**

The advantages of pure opioid agonists in older cats are their safety, the lack of a ceiling effect allowing dosing to effect, and partial to complete reversibility, if needed. In older patients or those with impaired renal or hepatic function, additional doses of opioid prolong the analgesic effect. Opioids are suitable for use in moderate to severe acute pain or mild to severe chronic pain. Any opioid works in any patient at any age or stage—the dose should be started low and titrated up until the desired effect is seen.

Cats with joint pain are often older patients with concurrent problems. Of most concern are the possible consequences of using NSAIDs in patients predisposed to dehydration, with deleterious effects on their gastric mucosal health or renal function. Additionally, certain NSAIDs may negatively affect proteoglycan synthesis by cartilage. According to in vitro studies, some NSAIDs, including meloxicam and carprofen, do not have this negative effect when used at recommended doses.²

Pharmacokinetic and safety data are lacking for long-term NSAID use in cats. The carprofen half-life varies from 9 to 40 hours in cats.³,⁴ As most NSAIDs have long half-lives in cats when compared with other species, the frequency of administration should be reduced to avoid toxicity. It is important to remember that individual patients respond differently to the same agent and dose; the lowest effective dose should be used. Long-term dosing for meloxicam should be based on lean, hydrated weight (day 1: 0.1–0.2 mg/kg SC or PO once; days 2 to 4: 0.1 mg/kg/day PO; long-term: 0.025 mg/kg PO q48–72h).⁵

NSAIDs must be used carefully and with renal, hepatic, and coagulation status in mind. While it would be ideal to avoid NSAID use unless renal function is normal, you can enhance quality of life in patients with concurrent renal disease and chronic pain by ensuring hydration and dosing conservatively. Informing the client of possible side effects is important.

There will never be medical practices that are 100% risk-free; good veterinary medicine aims to minimize risks and maximize quality of life for the individual patient.
References


11.4 UNTANGLING THE COMPLEXITIES OF THE FLUTD COMPLEX

The name continues to change but the definition remains the same. Feline Lower Urinary Tract Disease (FLUTD, LUTD, FUS, etc.) is a group of disorders, a syndrome, characterized by hematuria, stranguria and pollakiuria. There are many causes for these signs. The purpose of this presentation is to look at the problem from a logical pathological perspective to try to shed light on causes, diagnostics and therapeutics. We will look at the entity called Interstitial Cystitis (or Idiopathic Cystitis) in depth.

"More mistakes are made from want of a proper (work-up) than for any other reason."
(Russell J Howard)

ETIOLOGIES

While most of us have been prone to think first of nutritional causes, it is very important to approach and assess each stranguric cat in an unbiased and thorough manner.

<table>
<thead>
<tr>
<th>Etiologies of feline lower urinary tract disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic</td>
</tr>
<tr>
<td>Inflammatory</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Neurogenic</td>
</tr>
<tr>
<td>Iatrogenic</td>
</tr>
<tr>
<td>Anatomic abnormalities</td>
</tr>
<tr>
<td>Neoplastic</td>
</tr>
<tr>
<td>Idiopathic</td>
</tr>
</tbody>
</table>
**Metabolic:** Uroliths and urethral plugs

Uroliths are best analyzed quantitatively by polarizing light microscopy and X-ray diffraction...this gives the most accurate answers as it looks at all layers of the stone or plug. The following is a list of the composition of these structures as of 1997 (Minnesota Urolith Center).

**UROLITHS:** 47% Mg ammonium phosphate  
Ca oxalates: 40% most were monohydrate, a few were mixed mono and dihydrate and rest were dihydrate  
Uric acid and urates: 6%  
7% various, single crystal types, compounds or matrix.

**URETHRAL PLUGS:** 76% were Mg ammonium phosphate, 16% were matrix, 4% were mixed, 2% were Ca phosphates, 1.4% were Ca oxalates and the rest a variety.

**Clinical relevance:**

1) When we measure urine pH on a stick, the value is very inaccurate relative to the value determined with a pH meter.

2) The pH of the urine at the time of sampling is a reflection of many factors summated over the past hours during which the urine was being produced. Factors such as fear and stress tend to raise the urine pH; this may be misleading. During the postprandial period the total body pH rises because of HCl acid secretion into the stomach, resulting in a temporarily higher urine pH.

3) While we associate Ca oxalate crystals with an acidic pH, in fact they can occur at any urine pH. Monohydrate crystals at a low specific gravity reflect toxicosis such as from ethylene glycol; monohydrate crystals at a normal or high urine specific gravity (usg) reflect dietary cause or normal physiologic mechanisms. A few Ca oxalate crystals may be completely normal and may have just precipitated out over time.

4) The presence of a few Mg ammonium phosphate crystals may be completely normal in a cat and either not associated with disease or not the cause of the current episode of LUTD. These crystals occur in neutral to alkaline pH.

5) Agitation of the bladder during cystocentesis greatly improves sediment yield. Free catch collection may result in falsely negative urine sediment as the mechanics of voiding predispose to the dorsal contents being expressed and the heavier sediment settling to the bottom of the bladder.

6) Incidence of type of LUTD changes with age: struvite crystalluria is more prevalent in younger cats and generally tapers off after 3-5 years.
of age while Ca oxalate crystalluria incidence increases from about 3 years of age onwards.

7) Bacterial urinary tract infections are most common in cats with low usg (e.g. renal insufficiency) or glucosuria (e.g. diabetes mellitus).

8) Urethral plugs: how do they form, what are they made of? Think of fruit Jell-O.

Let's say we start with inflammation (infectious/noninfectious) group of causes of LUTD: These may cause inflammatory reactants and Tamm-Horsfall (TH) proteins in the urine, making matrix (Jell-O) for crystals (fruit) to get caught in. Alternately the TH proteins and inflammatory reactants cause hematuria and dysuria on their own. Of course, the crystals, even without the Jell-O can either cause hematuria and dysuria or urethral obstruction.

9) Concept: functional vs. mechanical obstruction.

**Improving Success with CaOx Uroliths**

1) Removal of calcium oxalate uroliths may be done by voiding urohydropropulsion, catheter retrieval, lithotripsy or surgery. **Be sure to remove all uroliths at the time of surgery!** Flush urethroliths back into the urinary bladder by retrograde urohydropropulsion PRIOR to surgery and leave urethral catheter in urethra throughout the cystotomy, leave the tip just proximal to the tip of the penis, occlude the distal urethra digitally and flush copious volumes (50-60 cc) of fluid back into the bladder intra-operatively, using suction to empty the bladder during the procedure. Flushing through the catheter or urethra from the bladder, may allow stones to lodge in the distal urethra. Radiograph immediately post-operatively to verify that all uroliths have been removed so that future evaluations will be accurate with regards to the presence of new stone formation.

2) **Ensure adequate fluid intake!!!** Much controversy has occurred over dietary therapy. With the increasing number of cats suffering from CaOx stones, new diets have been developed over the last decade to try to prevent the formation of these stones. As the frequency of CaOx stones has increased, attention has been turned to the role of acidification of urine and other alterations to diets in the previous decade to reduce the occurrence of struvite uroliths.

Let us look for a moment at some of the concepts. If urine has fewer minerals in it, there will be less chance of crystal or stone formation. If urine is dilute, then minerals of any sort are unlikely to crystallize. Avoid supersaturation of the urine. If urine stays in situ for a shorter period, then we should also have less risk of crystal formation. In fact, if all of the preceding occur, then we should have less irritation.
to the delicate mucosal lining of the cat with sterile/idiopathic cystitis as well.

How do we do this? Canned diets contain significantly more water than dry diets do. Canned diets are 70-80% water; dry are 9-12% water. In addition, cats fed canned diets, produce more metabolized water and have a more dilute urine than cats eating a dry diet, yet who drink more water than their canned diet eating counterparts. (Osborne ref.)

Pet water fountains, full water bowls and water glasses in multiple locations throughout the home encourage a cat to drink more. Flavouring water with chicken broth, turkey stock, tuna juice may also make drinking more appealing to some cats. Adding water to the canned diet will also be beneficial to reduction of urine specific gravity chance of supersaturation. It is also important to minimize stress associated with feeding time by making feeding rituals consistent and sticking with the same good diet for cats diagnosed with sterile/idiopathic cystitis. (Buffington ref.)

Finally, clean and appealing litter boxes and opportunities to void are essential so that urine isn’t stored in the bladder for excessive periods of time.

3) **ALWAYS submit stones for quantitative analysis** to ensure appropriate preventative protocol planning. When compound uroliths occur (nucleus of one mineral and shell of another) of, for example, a calcium oxalate core with a struvite shell, the preventative strategies may be diametrically opposed. The goal may best be served by preventing reoccurrence of the core nucleus mineral deposition. Struvite uroliths can be medically dissolved and recurrence prevented through appropriate eradication and prevention of infection with urease producing bacteria.

4) **Obtain a full urinalysis, serum calcium and creatinine levels.** Monitor serum calcium levels. Approximately one third of cats with CaOx uroliths are hypercalcemic. Hypercalcemia promotes increased urine calcium excretion and is therefore, a significant risk for calcium oxalate urolithiasis. Attempts should be made to determine the cause for the hypercalcemia in the individual patient. In hypercalcemic cats whose serum concentrations of parathyroid hormone and 25-Vit D are normal, feeding Hill’s Prescription Diet Feline w/d and potassium citrate (40-75mg/kg PO BID) has been felt to be helpful by the Minnesota urolith group (Osborne, Lulich et al). Recently new diets have become available (Hill's c/d O, Eukanuba Nutritional Urinary Formula Moderate pH/O) or studies have been
done with existing diets (Waltham pH Control dry) to help prevent recurrence of CaOx stones. Time will tell how well these strategies work.

5) **Monitor urinalyses (and serum calcium and creatinine if previously abnormal) every 2-4 weeks.** If CaOx crystals persist, supplement the diet with water and consider vitamin B6 (2-4 mg/kg q24-48h). If aciduria persists (4-6 hours post-prandially), consider additional potassium citrate. After 3-6 months, re-evaluate the patient via dietary and general history, physical examination, full urinalysis, abdominal radiography and serum calcium and creatinine if previously abnormal. If no uroliths are present, re-evaluate every 3-6 months. If uroliths have recurred, consider non-surgical urolith removal; if unsuccessful, surgery may be considered if clinical signs warrant it, otherwise, continue therapy to minimize urolith growth.

6) **As a last resort, consider urethrostomy.** In some male, hypercalcemic cats, despite diligent medical and dietary attempts to prevent urolith recurrence, stones may reform frequently. In these cats, the formation of a wider urethra may be life saving. Bear in mind that the risk of bacteria urinary tract infections increases, thus, frequent urinalysis monitoring is necessary.

**A few more factors in the CaOx story.**

1) Potassium citrate helps inhibit CaOx uroliths by a) citrate competing with oxalate to combine with Ca to form soluble Ca salts in the urine...and b) by promoting systemic alkalinization, resulting in increased urine and blood pH.
2) Magnesium is believed to have some inhibitory role in the formation of CaOx stones.
3) Supersaturation of the urine with anything (other than water), is risky business, thus feeding tinned diets, or increasing water intake by whatever means, would likely be beneficial in cats prone to crystal/stone formation (of any sort);
4) in *humans*, Vit B12 deficient diets predispose to CaOx stones;
5) in *humans* and *dogs* high levels of dietary Na may enhance hypercalcuria;
6) in *humans* and *dogs* feeding increased amounts of animal protein significantly increases urine Ca and oxalate;
7) Thiazide diuretics may be beneficial to prevent CaOx stones in *humans* and *dogs*;
8) Vit D toxicosis or inability to breakdown Vit D has been reported to cause CaOx urolithiasis in *humans*.
**Inflammatory:** Infectious and non-infectious:

**INFECTIOUS:** Bacterial: (E. coli, Staph spp, Strep spp, Pasteurella, Proteus, Pseudomonas, Klebsiella, Enterobacter, and others)  
Fungal agents: (Candida spp, Aspergillus spp, Trichosporon spp, Cephalosporium spp)  
Parasites: (Capillaria feliscati)  
Potentially: Viral (calicivirus, cell-associated herpes, synctic forming virus)  
Mycoplasma and ureaplasma (M felis, M gateae, U spp)  
NON INFECTIOUS: Immune mediated?

**Clinical relevance:**

The feline urinary tract generally resists infection better than those of other species because of numerous features do. Cats are able to produce highly concentrated acidic urine with a high urea concentration. In addition, they possess the characteristics of other species for bacterial resistance, namely complete and frequent unidirectional voiding, mucosal defence barriers and acquired resistance factors from previous encounters with microbes. (Table 1)

It is also important to interpret the results of a urine culture and sensitivity in light of the other urinalysis parameters and the method of collection.

1) If the urine is collected by cystocentesis, any number of bacteria is significant. If a urine sample was by free catch, bacterial colony counts > 10,000/ml are significant.
2) Pay attention to the gram stain as well. If organisms are seen but not grown on culture, then perhaps the wrong type of culture was run. Occasionally anaerobic or L-form cultures may be necessary.
3) The urine specific gravity is critical in interpretation of the significance of many parameters including white blood cell numbers, protein levels and the absence of bacteria. With a low usg (<1.030 in cats), bacteria may be present with only a few wbc in the sediment despite their apparent absence on microscopic exam, thus culturing is indicated in the symptomatic cat.
4) Remember that urine specific gravity, nitrate and leukocyte pads on the stix are inaccurate in animals.
**Trauma**

**Neurogenic reflexes:** Reflex dysenergia
- Urethral spasm
- Hypotonic or atonic bladder (primary, secondary)
- Interstitial Cystitis

There is an excellent review of the neurophysiology of micturition in Current Vet Therapy VIII, p 1122-1127 by Drs. John Oliver and Carl Osborne. A concise reference discussing Sacrocaudal Fractures (occurring by tail pulling or automobile trauma) is found in August: Consultations in Feline Internal Medicine, (1st volume), by John Flanders entitled Sacrocaudal Fractures, p 493-5.

**Iatrogenic**
This thankfully uncommonly encountered group of causes includes the use of some reverse flushing solutions as well as urethral catheters, which may negatively alter the natural and acquired host defences of the lower urinary tract. Urethral catheters should be selected for being least irritative/reactive. It is strongly recommended to use only closed collection systems. Complications occasionally occur after removal of urethral catheters or post urethrostomy causing urethral stenosis.

**Anatomic abnormalities**
Rarely one may find a cat with a congenital urethrorectal fistula, a persistent uterus masculinus, phimosis or, more commonly, urachal diverticulum.

**Neoplastic**
While the frequency of feline lower urinary tract neoplasia is rare (over a ten year period, the Veterinary Medical Data Base recorded only 69 urinary bladder tumours), it may be helpful to have a list of recognized conditions. Transitional cell carcinoma is the most common urinary bladder tumour in the cat.

> **Benign:** papilloma, adenoma, hemangioma, rhabdomyoma, myxoma, neurofibroma, cystadenoma, leiomyoma, fibroma
> **Malignant:** transitional cell carcinoma, squamous cell carcinoma, adenocarcinoma, undifferentiated carcinoma, fibrosarcoma, leiomyosarcoma, hemangiosarcoma, lymphosarcoma (primary and metastatic), osteosarcoma, myxosarcoma, prostatic adenocarcinoma, rhabdomyosarcoma, endometrial adenocarcinoma

**Idiopathic**
As usual, this is a vague and disturbing category. In the case of FLUTD, this may include a large number of cases. The recently coined: “feline idiopathic cystitis” (FIC) or chronic interstitial cystitis (CIC) may represent more than Feline “Interstitial Cystitis”. FIC is discussed in depth further on in these notes.
**DIAGNOSTICS**

Determining the cause of the hematuria, stranguria and pollakiuria all hinge on the urinalysis. As previously mentioned, all urinalyses should include biochemical determinations by chemistry stick (recognizing that nitrates, leukocytes and specific gravity are not accurate in our patients), a urine specific gravity determination as well as a complete and carefully read microscopic sediment examination. The pH determination on the strip is inaccurate at best and should not be over-interpreted; ideally a laboratory pH meter reading should be obtained. The condition of the urine is important as several parameters (pH, glucose, crystals, wbcs and bacteria) are altered by storage (duration and temperature). Best is examination of a fresh, room temperature sample collected by cystocentesis into a sterile closed tube within 2 hours of collection. *Remember to agitate the bladder immediately before performing cystocentesis.*

**Interpretation of blood and rbcs:**

Blood may reflect older bleeding vs. rbcs, which may be from collection if the sample is read in a fresh state.  
*Blood and rbcs*----> iatrogenic? collection? (no wbcs, no crystals)---> confirm accuracy by collecting a free catch sample. If rbcs still present, then hematuria is real and further evaluation is warranted by ultrasound or plain and contrast urography.  
----> crystals? determine type and quantity and interpret in light of pH by pH meter, as well as presence of reactive cells (wbcs) and protein, then treat accordingly. Note the role of urine specific gravity: in a very dilute sample, a small number of anything in the sediment may be more important than you first think.  
----> wbcs reflect inflammation or infection, therefore culture and treat according to the culture and sensitivity results for 3-5 weeks, reculturing after one week into therapy to determine that therapy is effective. *Remember that a low usg may mask a bacteruria.* As concentrated urine is inhospitable to bacteria and wbcs, culturing urine with a usg > 1.050 is unlikely to be rewarding and contracted epithelial cells may look like wbcs. Below 1.040, culture is indicated if wbcs are seen. Below 1.025 low numbers of wbcs (or even none) may be significant and culture may in fact be indicated. Reculture one week after cessation of therapy to confirm that there is no recurrence.

Prepayment and advance scheduling of these repeat cultures are a good way to ensure compliance with recommendations. Recurrence of infection warrants further diagnostics to assess the possibility of urolith, anatomic anomaly or neoplasia. *Acute pyelonephritis is an underdiagnosed condition in the cat and should be included in the differentials for the cat with vague signs of "ain't doing right" without obvious signs of perirenal pain.*

The first step in visualization requires plain radiographic films be taken to assess the presence of radiodense stones. The lateral view will be more helpful than the VD; at Minnesota, the preliminary work-up for a cat with LUTD includes the exam, a urinalysis and a plain lateral radiograph. Contrast films or ultrasound are helpful in identifying all uroliths, urachal diverticulae, and bladder wall thickening (focal or generalized). Contrast material can be administered via a urethral catheter, of course, but can also be administered by cystocentesis. Also IVP/IVU are techniques for assessing renal and ureteral anatomy as well as bladder anatomy and contents. In order to assess the proximal urethra and distal ureters, compressing the bladder gently with a wooden spoon during radiography is helpful.

The advantages of ultrasound are that there is no upstream damage to the urethra, no risk of introducing infection of disrupting the natural antimicrobial capabilities of the urinary tract, no trauma by the radiographic material, and no anaesthetic is required. If one proceeds to introduce a double contrast medium (CO2 or N2O) one does not put the cat at further risk, however, if we use room air or O2, we could potentially cause fatal air embolism.

In addition, one can, with ultrasound determine whether a lucent mass is an air bubble, whether a mass is perhaps sediment by rolling the cat during the procedure, and one can better visualize smaller particulate matter, including inflammatory debris and blood clots.

**THERAPEUTICS**

**Analgesia**
FLUTD is very **painful**. Analgesia is often overlooked. There are several mechanisms we can utilize.

**Antispasmodics** are most commonly used.
flavoxate (Urispas™)
50 mg PO q12h for cats < 10lb BW,
100 mg PO q12h if > 10lb BW.

My favourite antispasmodic agent is Renazone, which I have prepared by the compounding pharmacist I work with. Any compounding pharmacist could make this for you.
General formula to prepare 100 capsules of Renazone substitute:

- Hyoscyamine HBr USP 9.00 mg
- * Atropine SO4 USP 0.75 mg
- ** Scopolamine HBr USP 0.24 mg
- Ammonium CI USP 4.0g

Package in #4 gel capsules, each capsule net weight 150 mg

Prepare separate dilutions for both atropine and scopolamine. For each, dilute 10 mg to 10 g with lactose.
- * Atropine: 0.75 mg in 750 mg of lactose mix
- ** Scopolamine: 0.24 mg in 240 mg of lactose mix

Dose in cats: 1 capsule PO BID X 5 days, then SID X 5 days
* Note: Renazone is acidifying

**Muscle relaxants**  Diazepam or phenoxybenzamine are commonly used. Remember that they work on different muscle types. Diazepam affects striated muscle; phenoxybenzamine affects smooth muscle. The urethra contains both types of muscle, so it may work better to use both agents simultaneously.

**Narcotics**
If a “test dose” of oxymorphone or buprenorphine appears to make a significant difference in the level of comfort of the patient, then application of a transdermal fentanyl patch (Duragesic™) may be warranted. I use them routinely in cats post-obstruction or in CaOx cystotomy patients.

**Antiinflammatory agents.**
Despite their common use, a study reported in the Vet Clinics of North America, Disorders of the Feline Lower Urinary Tract I & II, March and May 1996, shows that the use of corticosteroids is unsubstantiated and that there is no statistically significant benefit which could not be explained by spontaneous resolution of clinical signs or by placebo effect. Because of the risks of bleeding due to platelet function inhibition, use of agents such as ASA or newer NSAIDs is not recommended.

**INTERSTITIAL CYSTITIS**
This non-malignant inflammatory disorder of unknown etiology occurs in humans of any age, race or gender, but seen most frequently in middle aged, white women. It causes intense stranguria and dysuria, the pain of which is relieved by voiding. There may be pyuria, hematuria +/- proteinuria at varying times. Diagnosis is ultimately achieved by performing cystoscopy and dilating the bladder to increase the pressure in the walls, which results in typical hemorrhagic mucosal lesions called glomerulations. These do not occur in normal bladders at these lower pressures. The proposed causes include:
Chronic recurrent LUTD or Interstitial Cystitis may cause bladder wall scarring, which perpetuates the pollakiuria. A technique, which may be tried, is called hydrodistension, which depletes sensory neuroreceptors and helps to break down fibrosis, which can impair emptying. Under general anaesthesia, pass a urethral catheter and infuse LRS or physiological saline via gravity flow from 80cm/32 inches above cat; leave in for 3-5 minutes, release pressure, drain then repeat one more time. Follow-up care consists of administering 3-5 days of antibiotics prophylactically and starting amitriptyline 5 mg PO qpm after a few days to try to keep the nerve fibers quiescent and substance P release minimized.
RESULTS: During the first 6 months of treatment, 11 of the 15 cats had no owner-observed signs of lower urinary tract disease. During the next 6 months, 9 of 15 cats remained free of signs of cystitis. Despite clinical improvement, cystoscopic abnormalities persisted in all cats at the 6- and 12-month evaluations. Hematuria and proteinuria were decreased at the 12-month evaluation compared with the initial evaluation. Two of 15 cats initially appeared somnolent after amitriptyline treatment. Of 9 cats completing the study, 7 had increased body weight and 8 had decreased coat quality compared with the initial evaluations. Four cats developed small cystic calculi during the first 6 months of the study. Serum biochemical or hematologic abnormalities were not detected during the study.

CLINICAL IMPLICATIONS: Amitriptyline treatment successfully decreased clinical signs of severe recurrent IC in 9 of 15 cats treated. Somnolence, weight gain decreased grooming, and transient cystic calculi were observed during treatment in some cats.