Feline pancreatitis is a relatively common disorder causing non-localizing clinical signs of inappetence, lethargy, vomiting, weight loss and less commonly, diarrhea and physical examination findings of dehydration, hypothermia, and icterus. Biochemical abnormalities are common including increased liver enzyme activities, hyperbilirubinemia, hypercholesterolemia, hypoglycemia, ionized hypocalcemia, and hypoalbuminemia but are also non-specific to the pancreas. Despite these non-localizing and non-specific abnormalities, the frequency of diagnosis of pancreatitis in cats has increased with advances in pancreatic serology and imaging. Multiple generations of serologic tests for pancreatitis have been developed and evaluated with the sensitivity, negative predicative value, specificity and positive predicative value established for a majority of these tests (see Table 1). Additionally, multiple pancreatic imaging techniques have also been evaluated (see Table 1) including advanced imaging of the pancreas with computed tomography and endosonography. This lecture will review feline pancreatic serology and imaging including abdominal ultrasound. Lastly, a clinical classification scheme will be proposed as a tool in establishing the likelihood of feline pancreatitis.

Pancreatic Serology
Amylase and lipase enzyme levels were the first broadly utilized serologic tests for feline pancreatitis. However research determined amylase lacked specificity and sensitivity and while lipase was specific, it lacked sensitivity. Trypsin-Like Immunoreactivity (TLI) was developed and has improved specificity (75%) but also lacked sensitivity (28%) for feline pancreatitis, however has remained the gold standard testing for Exocrine Pancreatic Insufficiency (EPI).

The next generation of pancreatic serology testing, following the serum TLI, was 2 similar but technically different feline pancreas-specific lipase assays. The feline pancreatic lipase immunoreactivity assay (fPLI) is a polyclonal sandwich radioimmunoassay. Sensitivity and specificity was established utilizing histopathology as the gold standard and for a measure of pancreatitis severity. The reference interval for fPLI was 2.0–6.8 µg/L, with concentrations >10 µg/L considered consistent with pancreatitis. The assay was both sensitive in cats with moderate to severe pancreatitis (100%), and specific in the healthy cats (100%), however a lower sensitivity (54%) was noted in cats with mild pancreatitis and poor specificity (33%) in ill cats without pancreatitis.

IDEXX Laboratories, in conjunction with Texas A&M University Gastrointestinal Laboratory then developed a monoclonal sandwich enzyme-linked immunosorbent assay (ELISA) to measure feline pancreas-specific lipase (Spec fPL® Test). A correlation study with known fPLI (range 2.0–128 µg/L) revealed a high correlation with Spec fPL (R² = 0.938). This assay’s sensitivity and specificity was established utilizing a pancreatitis likelihood classification scheme as a gold standard incorporating pancreatic cytohistopathologic evidence in select cases. The reference interval for Spec fPL was 0.7–3.5 µg/L, with concentrations >5.4 µg/L considered consistent with pancreatitis. Using a Spec fPL concentration of 5.4 µg/L as the diagnostic cut
off, and excluding cats with indeterminate pancreatitis, the sensitivity and specificity was 79.4 and 79.7, respectively.

A patient side (in hospital use) feline pancreas-specific lipase (SNAP fPL® Test) was then developed and released. The SNAP fPL is a serum based, semi-quantitative, monoclonal antibody test that is reported by IDEXX laboratories to be optimized to match the performance of the Spec fPL test. Two result options are displayed, normal or abnormal. A normal result correlates directly with the normal reference interval for the Spec fPL (0.7–3.5 µg/L), however an abnormal result correlates with both the grey zone (3.6 – 5.3 µg/L) and the interval considered consistent with pancreatitis (>5.4 µg/L). The grey zone was included to permit the SNAP fPL to be utilized as a screening test (higher negative predicative value, a patient tested negative is unlikely to have the disease), however at the expense of a lower positive predicative value.

Questions have been raised about the significance of elevated Spec fPL concentrations concurrently with a potentially more significant disorder (for example inflammatory bowel disease (IBD)) or persistent increases despite resolution of clinical signs attributed to pancreatitis. The former may be explained by the high frequency of reported concurrent disorders (up to 2/3rd) in cats with pancreatitis. Concurrent disorders include, but at not limited to, IBD, hepatic lipidosis, cholangitis, diabetes mellitus however the clinical challenge is avoiding a diagnostic delay for a disorder that is ultimately causing the patient’s clinical signs (as with an obstructive intestinal foreign). Ultimately additional research is necessary to make strong clinical recommendations in this situation, however the author recommends screening for concurrent disorders or complications of pancreatitis when cats are being treated for pancreatitis and fail to improve. The explanation for the latter question is one part of recently completed study (data being evaluated at the time of this writing) involving serial serologic (Spec fPL) and ultrasonographic monitoring of cats with pancreatitis. This will be discussed during the lecture portion and is potentially explained by subclinical elevated pancreatic concentrations associated with chronic pancreatitis.

Pancreatic Imaging

Unlike submitting serologic tests, performing transabdominal ultrasound to screen for pancreatitis is considered challenging and operator, equipment and patient compliance dependent. However, it also provides the opportunity to detect non-pancreatic disorders, screening for causes of pancreatitis and obtain ultrasound guided fine needle aspiration cytology of abdominal organs (including the pancreas) and fluid accumulations. For the normal feline pancreas, the majority of the pancreas can be visualized with smooth pancreatic borders, relatively isoechoic pancreas parenchyma compared to liver and no pancreatomegaly, pancreatic duct enlargement, peripancreatic fluid accumulation, pancreatic nodules or cysts, or enlarged peripancreatic lymph nodes. Pancreatomegaly is defined as left limb larger than 9.5 mm in thickness, body greater than 8.5 mm in thickness or the right limb larger than 6 mm in thickness. The pancreatic duct is considered enlarged if greater than 2.5 mm in diameter. Ultrasonographic changes associated with pancreatitis include pancreatomegaly, hypoechoic pancreatic parenchyma, hyperechoic peripancreatic fat / mesentery, dilated pancreatic or bile duct(s), dilation of the gall bladder, thickened gastric wall and corrugated and thickened duodenal wall.

It is important to note, the minimum requirements for the ultrasonographic diagnosis of pancreatitis in cats has not been determined, and it has been shown cats can have severe pancreatitis with no ultrasonographic abnormalities. Further adding to the complexity of diagnosing pancreatitis via ultrasound is the finding of certain abnormalities, often associated
with pancreatitis, such as enlargement of pancreatic duct and pancreatic parenchyma hyperechogenicity, may be potentially seen in aged cats without pancreatitis. Additionally, certain abnormalities, pancreatic pseudocysts, nodules or duct dilation may suggest recent, but currently inactive pancreatitis while a non-pancreatic disorder is causing the current clinical signs. Wide and conflicting sensitivities for the diagnosis of pancreatitis by abdominal ultrasound have reported from 20-35% to 62% with a specificity of 73% based on limited numbers cats. Advances in ultrasonographic equipment, ultrasonographer training and study methodology may have contributed to wide range of sensitivities.

In a manner similar to pancreatic serologic testing, questions have been raised on the significance and/or presence of persistent ultrasound pancreatic abnormalities following an episode of pancreatitis. This was evaluated in recently completed study (data being evaluated at the time of this writing) involving serial serologic (Spec fPL) and ultrasonographic monitoring of cats with pancreatitis. This will be discussed during the lecture portion.

Table 1: Reported Diagnostic Utility of Non-Invasive Tests in Feline Pancreatitis

<table>
<thead>
<tr>
<th>TEST</th>
<th>Sensitivity</th>
<th>Negative Predicative Value</th>
<th>Specificity</th>
<th>Positive Predicative Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase, Lipase</td>
<td>Not Useful</td>
<td>Not Useful</td>
<td>Not Useful</td>
<td>Not Useful</td>
</tr>
<tr>
<td>Abdominal Ultrasound*</td>
<td>24-67*%</td>
<td>57%</td>
<td>73%</td>
<td>80%</td>
</tr>
<tr>
<td>Endosonography</td>
<td>Not Useful</td>
<td>Not Useful</td>
<td>Not Useful</td>
<td>Not Useful</td>
</tr>
<tr>
<td>Computed tomography</td>
<td>20%</td>
<td>Not Useful</td>
<td>Not Useful</td>
<td>Not Useful</td>
</tr>
<tr>
<td>TLI*</td>
<td>28%</td>
<td>41%</td>
<td>75%</td>
<td>71%</td>
</tr>
<tr>
<td>PLI*</td>
<td>67%</td>
<td>62%</td>
<td>91%</td>
<td>92%</td>
</tr>
<tr>
<td>Spec fPL^</td>
<td>79.4%</td>
<td>87%</td>
<td>79.7%</td>
<td>69%</td>
</tr>
</tbody>
</table>

*N=29 (21 ill & 8 healthy cats), ^N=182 (141 ill & 41 healthy cats)

Classification scheme in the diagnosing the likelihood of feline pancreatitis

The ability to definitively include and exclude pancreatitis as a diagnosis in cats, dogs and humans is challenging. Intestinal and hepatic inflammation, commonly noted concurrently with pancreatitis, can cause similar clinical, physical examination, biochemical and hematologic abnormalities and confuse the diagnosis of pancreatitis. Histopathology, the gold standard for other gastrointestinal disorders including inflammatory bowel disease, has established limits with pancreatitis.

Pancreatitis can be multifocal and focally severe and therefore, pancreatic inflammation can be inadvertently not detected without serial sections of the pancreas, which is contraindicated in live clinical cats. Additionally the degree and type of pancreatic inflammation which correlates with the clinical signs of pancreatitis have not been definitively established.

A clinical classification scheme of six categories (see Table 2) was developed by which to classify each cat as to the likelihood that the cat had pancreatitis. Within each category several criteria were evaluated including: cytohistopathologic (if available), ultrasound and clinicopathologic findings and the presence or absence of another convincing disease.
**Table 2: Feline pancreatitis classification scheme**

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pancreatitis</strong></td>
<td></td>
</tr>
<tr>
<td>Strong (definite)</td>
<td>Clinicopathologic and cytohistopathologic evidence of pancreatitis independent of ultrasonographic findings.</td>
</tr>
<tr>
<td>Moderate (probable)</td>
<td>Compatible clinicopathologic with convincing ultrasonographic evidence of pancreatitis and no available cytohistopathologic evidence.</td>
</tr>
<tr>
<td>Weak (possible)</td>
<td>Compatible clinical signs with weak or no ultrasonographic or laboratory evidence and no available cytohistopathologic evidence. A clinical suspicion of pancreatitis without alternative disease.</td>
</tr>
<tr>
<td><strong>Not Pancreatitis</strong></td>
<td></td>
</tr>
<tr>
<td>Weak (possible not)</td>
<td>Compatible clinical signs with weak or no ultrasonographic or laboratory evidence and no available cytohistopathologic evidence. A clinical suspicion of pancreatitis is present; however a convincing alternative disease is diagnosed.</td>
</tr>
<tr>
<td>Moderate (probably not)</td>
<td>Weak or inconsistent clinicopathologic and/or ultrasonographic evidence of pancreatitis and no available histopathologic evidence.</td>
</tr>
<tr>
<td>Strong (definitely not)</td>
<td>Histopathologic evidence of the absence of pancreatitis; or normal ultrasound of pancreas with alternative disease, not known to be associated with pancreatitis.</td>
</tr>
</tbody>
</table>

**Conclusion**

The expanded utilization of pancreatic serology and imaging is changing the dogma of the challenging nature of antemortem diagnosis of feline pancreatitis. The next diagnostic challenge with feline pancreatitis is accurate interpretation and correlation to the pet’s clinical signs of elevated pancreatic serologic concentrations and abnormal pancreatic ultrasonographic findings.

**References**

PCR-Based Testing for Enteropathogens and Parasites

PCR based fecal tests for enteropathogens and parasites are now readily available for use in veterinary medicine. These tests are fast (1 to 3 days), highly sensitive and highly specific. They are available as bundled tests for broad screening of multiple organisms. How will they change the way we work up cases?

Optimal management of GI disease always begins with the basics, complete history, physical exam, and screening diagnostics based on a rational differential list. For most GI cases this means fecal flotation, fecal cytology and specific ELISA testing as indicated.

In acute GI disease PCR testing may be most useful as an alternative to bacterial cultures for enteropathogenic bacteria. PCR is faster, more specific and potentially more sensitive than culture. However, there is significant potential for over diagnosis as clinically normal animals are often asymptomatic carriers of these organisms. PCR may also be useful as a secondary, perhaps more sensitive, test when initial diagnostics, such as ELISA, culture or cytology, are negative or inconclusive.

The work up of chronic GI disease usually involves a series of diagnoses of exclusion. First we rule out acute disease based on history, then systemic disease based on physical exam and a minimum diagnostic database. Prior to moving up the chain of assessment to dietary intolerance, allergies, neoplasia and finally chronic inflammatory disease we must address GI pathogens and parasites.

For most adult otherwise healthy patients, GI pathogens and parasites are a relatively uncommon cause of significant chronic disease. Broad PCR testing is as likely to lead you astray as to nail the diagnosis. Positive tests must be assessed critically, based on the clinical presentation of the patient, other more clinically relevant diagnostics and therapeutic trials. In patients that are young, or immune compromised, the potential for enteropathogenic, or parasitic chronic disease is much greater. PCR panels are more likely to be helpful in these patients, but they must be interpreted with care.

PCR panels can be a very helpful diagnostic tool, or a diagnostic obstacle depending on how they are used.

Advantages and Limitations of PCR Testing for GI Disease

Advantages
1. Very high sensitivity and specificity
2. Fast turn around time compared to cultures (1-3 days)
3. Bundled tests offer cost savings compared to individual tests
4. Surveillance tool for dog or cat populations (shelters, or breeding facilities)
5. Screening tool to identify and minimize human exposure to zoonotic pathogens
Limitations
1. Positive results may not correlate with clinical significance due to high sensitivity. (This applies to both the clinical diagnosis of disease, and surveillance)
2. PCR is not a substitute for basic screening tests (fecal flotation, cytology and ELISA).
3. PCR tests may not detect silent carriers (when not shedding).
4. Concurrent treatment may result in negative results.
5. Organism numbers below limit of detection may result in negative results.
6. Strain variation (especially with parvovirus) may lead to negative results due to high specificity.
7. Tests may remain positive for weeks after treatment (with or without clinical resolution of disease).
8. Modified live vaccines may lead to positive test results for several weeks.

Note: For an excellent review of testing for enteropathogenic bacteria (including PCR and FISH) see the ACVIM Consensus Statement: Enteropathogenic Bacteria in Dogs and Cats: Diagnosis, Epidemiology, Treatment, and Control

Fluorescence In Situ Hybridization (FISH)
Fluorescence in situ hybridization (FISH) is a tissue staining technique which uses ribosomal rRNA probes to locate and identify bacteria within formalin fixed tissues. Simpson Laboratory at the Cornell University College of Veterinary Medicine is currently using FISH to studying Boxer Colitis (Granulomatous Cholitis) and other chronic GI diseases associated with intra-mucosal and intracellular bacterial colonization. The laboratory is accepting tissue for assessment in two ongoing studies of Boxer Colitis and Yorkie PLE. FISH may also be helpful in clinical cases where bacterial involvement is suspected based on clinical or histological evidence. Examples include chronic granulomatous disease, cholangiohepatitis, endocarditis, suppurative pancreatitis, pyelonephritis, lymphadenitis, chronic cystitis. See the website of the Simpson Lab for further information: www.vet.cornell.edu/labs/simpson/
Bundled GI PCR Tests

**Idexx Canine Diarrhea RealPCR™**
- Salmonella spp.
- C. perfringens enterotoxin A gene
- Cryptosporidium spp.
- Giardia spp.
- Canine parvovirus 2
- Canine enteric coronavirus
- Canine distemper virus

**Idexx Feline Diarrhea RealPCR™ - Comprehensive**
- Salmonella spp.
- C. perfringens enterotoxin A gene
- Cryptosporidium spp.
- Giardia spp.
- Toxoplasma gondii
- Tritrichomonas foetus
- Feline coronavirus (FeCoV)
- Feline panleukopenia virus

Specimen req: 5 g fresh feces (1 g min); keep refrigerated
Turn around time: 1 to 3 working days

**Antech FastPanel© PCR Canine GI Profile**
- Salmonella spp. *
- Campylobacter coli *
- Campylobacter jejuni *
- C. difficile toxins A/B **
- C. perfringens enterotoxin **
- Cryptosporidium spp.
- Giardia spp.
- Canine parvovirus
- Canine enteric coronavirus

**Antech FastPanel© PCR Feline GI Profile**
- Salmonella spp. *
- Campylobacter coli *
- Campylobacter jejuni *
- C. difficile toxins A/B **
- C. perfringens enterotoxin **
- Cryptosporidium spp.
- Cryptosporidium felis
- Giardia spp.
- Tritrichomonas foetus
- Feline parvovirus (feline panleukopenia)

* Reflex culture and sensitivity
** Confirmatory enterotoxin ELISA

Specimen req: 0.5 to 1 g fresh feces, Plus 1 Copan fecal swab.
Turn around time: 1 to 3 days
# PCR Testing For GI Disease

<table>
<thead>
<tr>
<th>Organism</th>
<th>Clostridium perfringens enterotoxin A</th>
<th>Clostridium difficile toxins A/B</th>
<th>Salmonella spp</th>
<th>Campylobacter coli and jejuni</th>
<th>Cryptosporidium spp (+ falciparum)</th>
<th>Giardia spp</th>
<th>Trichomonas foetus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>Gram Positive Bacteria</td>
<td>Gram Positive Bacteria</td>
<td>Gram Negative Bacteria</td>
<td>Gram Negative Bacteria</td>
<td>Cocida</td>
<td>Protozoa</td>
<td>Protozoa</td>
</tr>
<tr>
<td>Lab</td>
<td>Idexx, Antech</td>
<td>Antech</td>
<td>Idexx, Antech</td>
<td>Antech, TAMU</td>
<td>Idexx, Antech</td>
<td>Idexx, Antech</td>
<td>Idexx, Antech, TAMU</td>
</tr>
<tr>
<td>Species Affected</td>
<td>Dogs, Cats</td>
<td>Dogs, Cats</td>
<td>Dogs, Cats</td>
<td>Dogs, Cats</td>
<td>Dogs, Cats</td>
<td>Cats</td>
<td>Cats</td>
</tr>
<tr>
<td>Clinical Signs</td>
<td>acute, chronic, intermittent</td>
<td>acute</td>
<td>fever, depression, vomiting, diarrhea (+/-hemorrhagic)</td>
<td>diarrhea, anorexia, vomiting, diarrhea (+/-hemorrhagic)</td>
<td>acute, chronic, intermittent, small or large bowel diarrhea</td>
<td>acute, chronic, intermittent, small or large bowel diarrhea</td>
<td>chronic or recurrent, small or large bowel diarrhea</td>
</tr>
<tr>
<td>Prevalence ^</td>
<td>7% - 14% <em>normal</em> dogs</td>
<td>non-diarrheic dogs</td>
<td>0% - 1.5% diarrheic animals</td>
<td>0% - 1.4% diarrheic animals</td>
<td>9% - 45% dogs (culture)</td>
<td>7.3% kittens</td>
<td>31% in PB cats</td>
</tr>
<tr>
<td></td>
<td>41% diarrheic dogs</td>
<td>non-diarrheic dogs</td>
<td>0% - 1.5% diarrheic animals</td>
<td>0% - 1.4% diarrheic animals</td>
<td>20% dogs (culture)</td>
<td>4.3% shelter cats</td>
<td>14.4% cats with diarrhea in UK</td>
</tr>
<tr>
<td>Prevalence **</td>
<td>39% dogs</td>
<td>0.8% dogs</td>
<td>0.1% dogs</td>
<td>0.2% dogs</td>
<td>2.9% dogs</td>
<td>6.0% dogs</td>
<td>8.3% dogs</td>
</tr>
<tr>
<td></td>
<td>37.8% cats</td>
<td>2.3% cats</td>
<td>0.4% cats</td>
<td>2.2% cats</td>
<td>5.4% cats</td>
<td>5.1% cats</td>
<td>9.2% cats</td>
</tr>
<tr>
<td>Clinical Significance</td>
<td>detection may be significant</td>
<td>detection may be significant</td>
<td>detection may be significant</td>
<td>detection may be significant</td>
<td>detection significant</td>
<td>detection significant</td>
<td>detection significant</td>
</tr>
<tr>
<td>Additional Diagnostics</td>
<td>enterotoxin ELISA</td>
<td>enterotoxin ELISA</td>
<td>culture and sensitivity</td>
<td>culture and sensitivity</td>
<td>acid fast fecal stains</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

2. [Antech diagnostic resources](http://www.antechdiagnostics.com/MainTestGuide.aspx)

* Based on multiple studies using different assays (see Idexx website for references)
** Idexx RealPCR prevalence data from 516 samples for dogs and 944 samples for cats collected over a 6-month time frame
## PCR Testing For GI Disease

<table>
<thead>
<tr>
<th>Organism</th>
<th>Toxoplasma gondii</th>
<th>Canine Enteric Coronavirus</th>
<th>Feline Coronavirus (FeCoV)</th>
<th>Canine Parvovirus 2</th>
<th>Feline Panleukopenia Virus</th>
<th>Canine Distemper Virus</th>
<th>Heterobabaria americana</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>Coccosis</td>
<td>RNA virus</td>
<td>RNA virus</td>
<td>DNA virus</td>
<td>DNA virus</td>
<td>RNA virus</td>
<td>Schubbilovia</td>
</tr>
<tr>
<td>Lab</td>
<td>Idexx</td>
<td>Idexx</td>
<td>Idexx</td>
<td>Idexx</td>
<td>Idexx</td>
<td>Idexx</td>
<td>TAMU</td>
</tr>
<tr>
<td>Species Effected</td>
<td>Cats</td>
<td>Dogs</td>
<td>Cats</td>
<td>Dogs</td>
<td>Cats</td>
<td>Dogs</td>
<td>Dogs</td>
</tr>
<tr>
<td>Clinical Signs</td>
<td>asymptomatic or self-limiting small bowel diarrhea</td>
<td>mild acute small bowel diarrhea + vomiting + fever</td>
<td>acute small bowel diarrhea or FIP</td>
<td>acute small bowel diarrhea + hemorrhagic vomiting, anorexia, fever, sepsis</td>
<td>acute anorexia, vomiting, dehydration, fever, sepsis</td>
<td>chronic liver disease</td>
<td>anorexia, vomiting, diarrhea and neurologic signs</td>
</tr>
<tr>
<td>Prevalence * (in literature)</td>
<td>0.9% of feline fecal samples</td>
<td>15% to 26% of family pets</td>
<td>up to 80% of cats from shelters, catteries or large multiunit homes</td>
<td>~25% of cats from 1-2 cat homes and 1-2 cat apartments</td>
<td>19.2% of diabetic cats presenting to veterinary teaching hospital in Germany</td>
<td>19% of diabetic cats</td>
<td>chronic liver disease + malabsorption</td>
</tr>
<tr>
<td>Prevalence ** (based on PCR)</td>
<td>0.5% cats</td>
<td>10.9% dogs</td>
<td>60.2% cats</td>
<td>3.5% dogs</td>
<td>3.2% cats</td>
<td>1.2% dogs</td>
<td></td>
</tr>
<tr>
<td>Clinical Significance</td>
<td>detection may not be significant</td>
<td>detection may not be significant</td>
<td>detection may not be significant</td>
<td>detection significant</td>
<td>detection significant</td>
<td>detection significant</td>
<td>detection significant</td>
</tr>
<tr>
<td>Additional Diagnostics</td>
<td>IgM and IgG if extraintestinal disease</td>
<td>If FIP signs FeCoV/PCR on effusions, tissue or blood</td>
<td>CBC leucopenia</td>
<td>CBC leucopenia</td>
<td>CBC leucopenia</td>
<td>CBC leucopenia</td>
<td>CBC leucopenia</td>
</tr>
</tbody>
</table>

* Based on multiple studies using different assays (see Idexx website for references)
** Idexx FeCoV prevalence data from 568 samples for dogs and 594 samples for cats collected over a 6-month time-frame