

Update on Testing for Pancreatitis and Leptospirosis

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Update on Testing for Pancreatitis and Leptospirosis

Interpretation of Results to Aid in Diagnosis

A Case Based Approach

WARNING!
LEPTOSPIROSIS
HEALTH HAZARD

FRESH WATER STREAMS AND MUD
POSSIBLY POLLUTED WITH BACTERIA

EXERCISE CAUTION










Marnin Forman DVM, DACVIM


Cut to the Chase!

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'Simba'


16 year old MC DSH


History

- 1 week vomiting & inappetence
- 3 days lethargy & diarrhea
- Treated for CKD for 6 years (IRIS stage III, hypertensive non-proteinuric)
- Chronic occasional vomiting

Medications

Amlodipine, Amphogel, Hill's K/D, Gastric feeding tube intermittently used

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Physical Examination

- Quiet, alert, responsive
- Mildly painful abdomen
- Kidneys small & irregular
- Possible painful
- Retinal hemorrhage
- Grade III/VI Systolic Heart Murmur, left base
- MicKey Gastrostomy Tube, no discharge


Body Weight
7.9 lbs (3.6 kg)

Body Condition
Score 5/9

Temperature
102.6°F (39.2°C)

Heart Rate
210 bpm


Respiratory Rate
40 bpm


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Simba: Problem List

- Vomiting and inappetence
- Apparent abdominal pain
- Retinal hemorrhage
- Chronic kidney disease
- Heart murmur
- Diarrhea

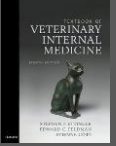
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Vomiting: Differentials

Primary vs. Secondary GI causes

- Acute on chronic kidney disease
 - Pyelonephritis
 - Ureteroliths
- Pancreatitis
- Cholangitis or hepatic disease
- Hyperthyroidism
- IBD
- Gastrostomy tube complication
- GI Neoplasia



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Workup

CBC

HCT 24.9%

WBC 8,500 / μ L

↓ Lymphs 170 / μ L

Platelets 203,000 / μ L

Biochemical panel

↑ BUN 40 mg/dL (14.3 mmol/L)

↑ Crea 3.2 mg/dL (282.9 mmol/L)

P 3.8 mg/dL (1.23 mmol/L)

Lipase 78 IU/L (UL)

↑ Amylase 1775 IU/L (UL)

T4 = 1.4 ug/dL

Urinalysis

USG 1.015

Glucose neg.

Bilirubin neg.


WBC None

RBC None


Bacteria None

Blood pressure

204 mm Hg

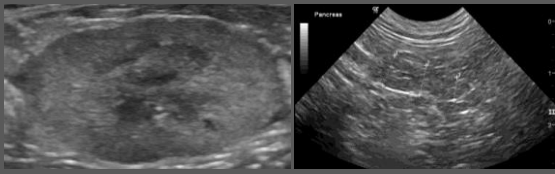


Thoracoabdominal Radiographs




Small irregular kidneys
Microcardia

Abdominal Ultrasound



Small, irregular kidneys
Normal pancreas



How Can We Diagnose Pancreatitis?

Clinical signs & Physical Examination


Laboratory tests

- CBC, Biochemistry profile (amylase, lipase)
- TLI, PLI, Spec fPL, Precision PSL, TAPs

Imaging

- Radiography, Computed tomography, MRI
- Pancreas Endosonography
- Ultrasonography


Cytology & histopathology



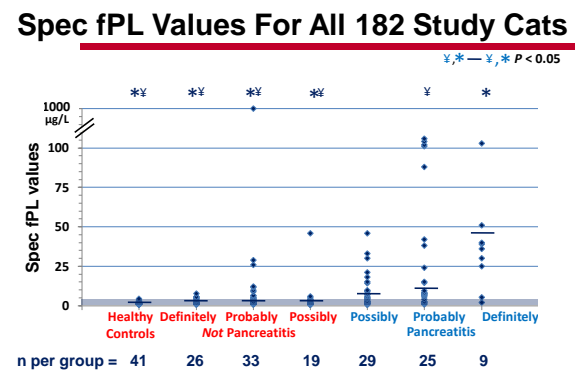
The OLD? Amylase and Lipase Story For Diagnosing Feline Pancreatitis

- Amylase decreased in experimentally induced pancreatitis¹
- Amylase failed to increase in any cat in a study evaluating spontaneous pancreatitis²
- Amylase lacks specificity and sensitivity³

- Lipase increased early in experimentally induced pancreatitis¹
- Lipase failed to increase in any cat in one study evaluating spontaneous pancreatitis²
- Lipase is specific but lacks sensitivity³



1. Kitchell B et al., *AJVR*, 1986, n=6 with induced pancreatitis.
2. Parent C et al., *JWIM* (abstr), 1995, n=12 cats with pancreatitis.
3. IDEXX internal data, 2008, n=39 sick cats with and without pancreatitis.



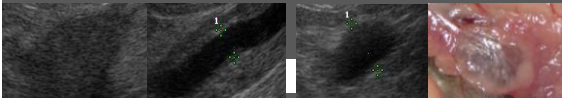
Pancreas Ultrasound Findings with Pancreatitis and in Older Cats

Consistent With Pancreatitis

- ✓ Enlarged & irregular pancreas
- ✓ Hypoechoic parenchyma
- ✓ Hyperechoic peripancreatic fat
- ✓ Dilated pancreatic or bile duct
- ✓ Peripancreatic fluid
- ✓ Corrugated thickened bowel wall
- ? Pancreatic pseudocyst

Incidental / Age Related Changes

- ✓ Pancreatic duct ↑ with age
- ? Panc. hyperechogenicity
- ✓ Pancreatic nodules
- ✓ Peripancreatic fluid
- ✓ Corrugated thickened bowel wall
- ? Pancreatic pseudocyst



Reported Diagnostic Utility of Non-Invasive Tests in Feline Pancreatitis

Test	Sensitivity	NPV	Specificity	PPV
Amylase, Lipase 1,2-diglyceride assay	Not Useful	Not Useful	Not Useful	Not Useful
Abd. Ultrasound ¹	24-67 ¹ %	57%	73%	80%
Endosonography	Not Useful	Not Useful	Not Useful	Not Useful
CT	Not Useful	Not Useful	Not Useful	Not Useful
TLI ¹ / TAPs	28%	41%	75%	71%
PLI ¹	67%	62%	91%	92%
Spec fPL ²	65 ³ -79 ² %	87%	63 ³ -80 ² %	69%
Precision PSL ³ DGGR-lipase activity	?	?	?	?

NPV, PPV= Negative & Positive Predictive Value, respectively

¹N=29 (21 ill & 8 healthy cats), ²N=182 (141 ill & 41 healthy cats), ³N=31 (all ill)

Precision PSL

- ANTECH Diagnostics
- **NOT** 'traditional' catalytic lipase assay
- Novel catalytic assay for DGGR-lipase activity
 - Poor correlation 1,2-diglyceride assay with the DGGR-lipase
- Reference range 8–26 U/L from 80 healthy cats
- Incorporated into routine biochemistry panel
 - Lower cost, increased availability
- Agreement studies were published in cats* & dogs^Δ

*J Vet Intern Med 2013;27:1077–1082

^ΔJ Vet Intern Med 2014;28:863–870

Feline PSL Agreement Study n=31

SUMMARY

- ✓ High precision and linearity
- ✓ Substantial agreement of the DGGR-lipase with Spec fPL

Table 2. Contingency table.

	Spec fPL			Total
	<3.5 µg/L	3.6–5.3 µg/L	≥5.4 µg/L	
DGGR-lipase ≤26 U/L	91	21	13	125
>26 U/L	16	11	99	126
Total	107	32	112	251

Table 3. Sensitivity and specificity (95% confidence interval).

	DGGR	Spec fPL ≥3.5 µg/L	Spec fPL ≥5.4 µg/L
Sensitivity			
Pancreatitis (n = 23)	48% (27–69%)	65% (43–83%)	57% (35–76%)
Acute pancreatitis (n = 4)	100% (40–100%)	100% (40–100%)	100% (40–100%)
Chronic pancreatitis (n = 19)	37% (17–61%)	58% (34–79%)	47% (25–71%)
Specificity (n = 8)	63% (26–90%)	63% (26–90%)	63% (26–90%)

“...impact of concurrent azotemia cannot be conclusively assessed...”

“...currently not known which assay yields more accurate results...”

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Spec fPL ²	65 ³ -79 ² %	87%	63 ³ -80 ² %	69%
Precision PSL ³ DGGR-lipase activity	48% Ac 100% Ch 37%	?	63%	?

NPV, PPV=Negative & Positive Predictive Value; Ac=Acute, Ch=Chronic

¹N=29 (21 ill & 8 healthy cats), ²N=182 (141 ill & 41 healthy cats), ³N=31 (all ill)



Simba's FINAL Results

Pancreatitis testing

↑ fPL 31 µg/L

↑ PLI 80 µg/L

↑ Precision PSL 40 U/L ☺

+ SNAP fPL (>3.6 µg/L)

He had Pancreatitis!
Recovered completely

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'Ike'



10 year old FS Poodle

History 5 days of
lethargy, vomiting,
inappetence
No toxin history

PE T 102.7° F, Wt. 25.9kg
5% dehydrated
Mild icterus
Liver enlarged

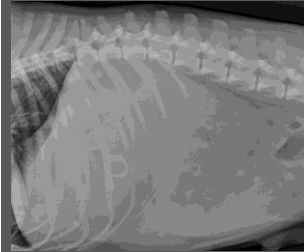
Laboratory Testing

CBC WNL
Chem ↑ ALP 1165 U/L
↑ ALT 1050, AST 472,
↑ GGT 310, Tbili 2.9
UA USG 1.009
Spec cPL Wnl, 198
Leptospirosis Pending

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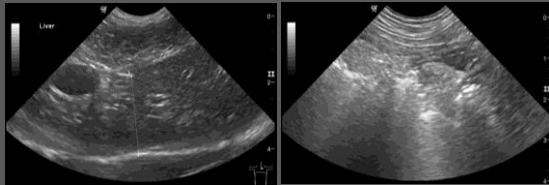


Abdominal Radiographs



Mild hepatomegaly, Gastric foreign body

Abdominal Ultrasound



Mild hepatomegaly, Normal echotexture
Gastric Foreign body

Acute Liver Injury Differentials



- Infectious hepatopathies
 - Bacterial: Leptospira, Bartonella
- Neoplasia
- Inflammatory hepatopathies
- Copper storage hepatopathy
- Hepatotoxin exposure
- Adverse drug reactions

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'Ike' Treatment & Update



Treatment

Initially

- Norm + 20mEq KCl @ 120 ml/hr
- Maropitant 25 mg SQ Sid
- Ampicillin 20mg/kg IV Tid
- Pepcid 0.5mg/kg IV Bid

Repeat Liver panel

- ↑ ALP 1165 to 1500
- ↑ ALT 1050 to 2100
- ↑ AST 472 to 810
- ↑ GGT 310 to 690
- ↑ Tbili 0.9 to 2.1

Update

- Vomiting resolved
- Persistently inappetent
- Marked lethargy

'Ike' Treatment & Update



Treatment

Initially

- Norm + 20mEq KCl @ 120 ml/hr
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Update

- Vomiting resolved
- Persistent inappetent
- Marked lethargy

➔ WHAT WOULD YOU DO?

Leptospirosis

- After exposure & infection leptospire multiple in bloodstream for ~4-10 days → **kidneys, liver, etc.**
- THEN urine shedding within 10-14 days
- Antibodies
 - IgM ↑ in 3-10 days then ↓ by ~14 days
 - IgG ↑ by 14-21 days then ↓ slowly
- Testing is influenced by this AND
 - Leptospirosis vaccinations (timing & brand)
 - Antibiotics against Leptospirosis

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How Can We Diagnose Leptospirosis?

Clinical signs & PE, Vaccination?

Laboratory tests

- CBC, Biochemistry profile, Urinalysis
- ID *Leptospira* → PCR, culture
- Detect immunologic response → Microscopic agglutination test (MAT), ELISA

Imaging

- Radiography, Ultrasonography
- Cytology & histopathology

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Leptospirosis Specific Tests

TEST	Affect Results		Sample needed?	Comments
	Vaccines?	Antibiotics?		
MAT	+++	+	Serum	Titers may be low if <7-10days ≥4x ↑ paired titers ideal Serovar cross-reactivity occur
ELISA	+++*	+	Blood, plasma, serum	Rapid results, for some tests can run in house, ability to test relatively early in disease
PCR	No	+++	Blood, urine, body fluids (i.e. CSF)	Can be run early in disease Submit blood/urine to ↑ diagnostic reliability
Culture	No	+++	Urine, blood, tissue	Rarely done, requires special medium to maintain growth

* Depends on the test submitted

Point Of Care Assays & ELISA Tests

Detect IgG and/or IgM antibodies to leptospire
 → **WITNESS Lepto** (Zoetis®): Detects IgM, ~4 days
 → **SNAP Lepto test** (Idexx®) or **Canine Leptospira spp. Antibody**: Detects IgG, outer surface protein

SUMMARY* n=460 samples
 SNAP and MAT (≥ 1:800)
 % Positive agreement 83%
 % Negative agreement 82%

Peak MAT Titer	# Samples	# Rapid ELISA Positive	% ELISA Positive
100	8	5	62.5%
200	20	11	55.0%
400	29	21	72.4%
800	53	37	69.8%
1600	34	25	73.5%
3200	13	10	76.9%
6400	19	16	84.2%
12800	32	29	90.6%
25600	14	14	100.0%
51200	18	18	100.0%
≥102400	19	19	100.0%
Total	289	205	70.9%

*Vol. 13, No.3, 2015, IJARVM

Ike's story - Laparoscopy



Mild cobblestone appearance, Rounded margins

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Ike's FINAL Results



Biopsy

Moderate subacute
 hepatocellular necrosis

Leptospirosis titer

L. Autumnalis 1:800
 Convalesce 1:3200

Copper level

340 PPM (normal)

Hepatic culture

Negative



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Summary



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CAUTION

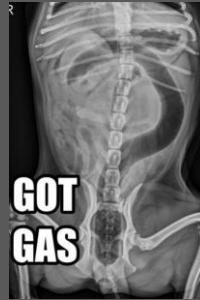
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Questions

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