CREATING CLARITY

Not a copycat: Why cats are not small dogs when it comes to chronic pancreatic disease

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Conflicts of Interest & Disclaimer

+ Stephanie Sorrell is an employee of IDEXX Laboratories UK

+ *The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions, and cautions. Diagnosis and treatment decisions are the ultimate responsibility of the primary care veterinarian.*

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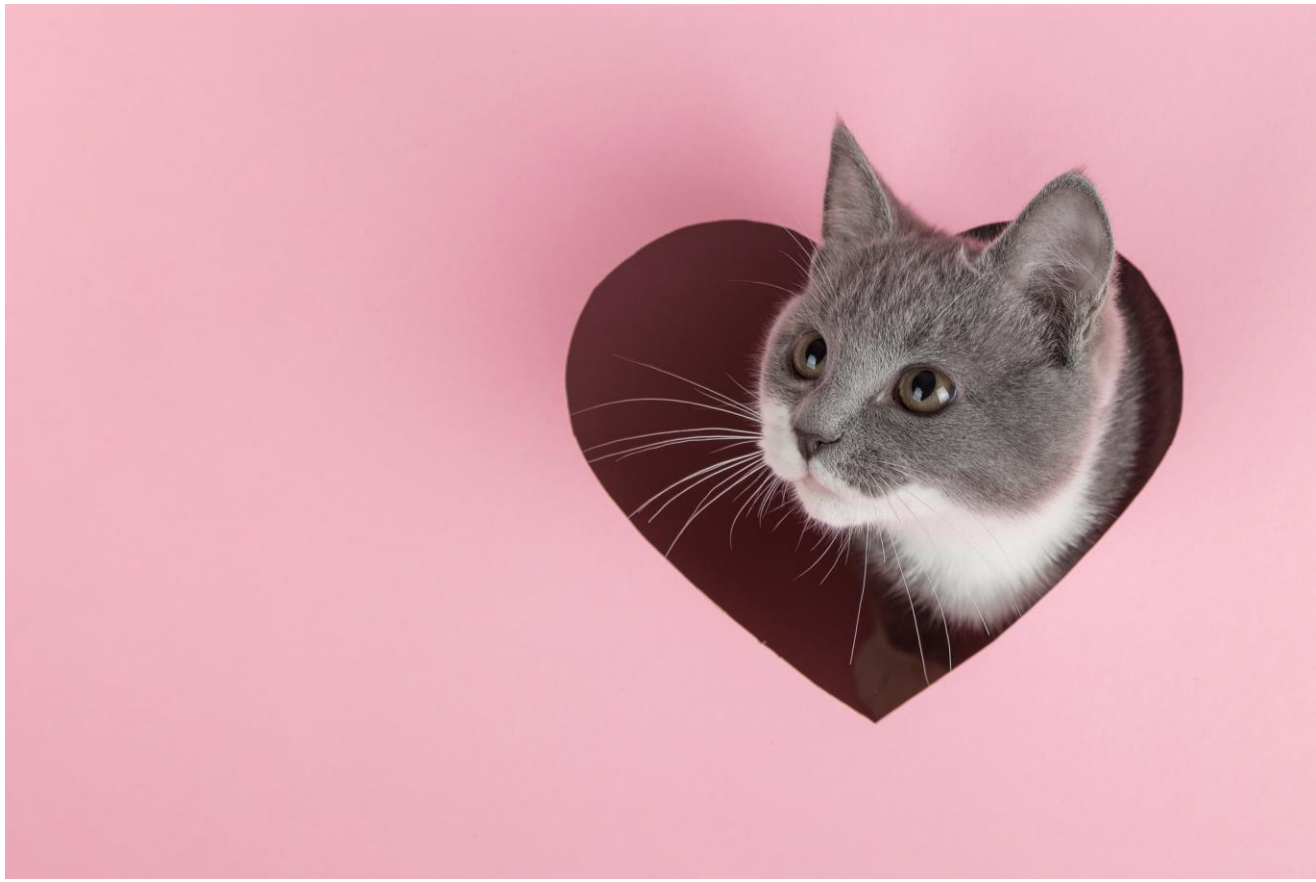
Agenda

+ Aetiology of pancreatitis
+ Risk factors
+ Diagnostic approach to case
+ Treatment plan
+ Case Study



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What is pancreatitis?

- Inflammatory disease of the exocrine pancreatitis tissue
- Chronic pancreatitis is characterised by lymphocytic inflammation, fibrosis and acinar atrophy.
- Chronic pancreatitis is characterised by irreversible histopathological changes whereas acute pancreatitis is reversible once inviting cause has been removed

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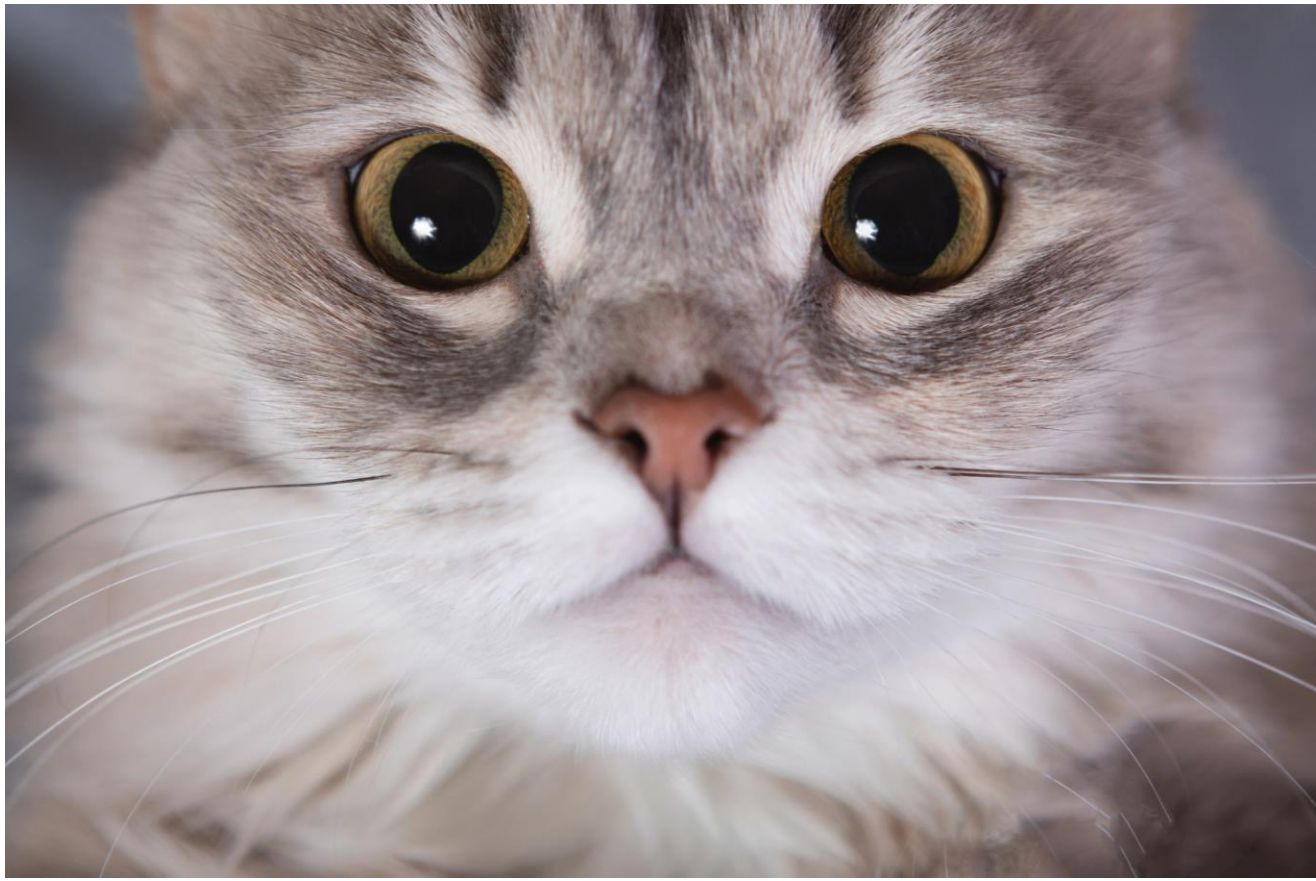
Chronic pancreatitis

- Most often idiopathic
- Need histopathology to differentiate acute vs chronic Based on histopathological changes
- Difficult to differentiate based on clinical signs



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Aetiology of pancreatitis

- Pancreatic insult results in inflammation primarily lead by cytokine production and premature activation of digestive enzymes and this results in pancreatitis

- Can result in further systemic inflammation

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Risk factors in cats vs dogs

- Most often idiopathic in both cats and dogs
- Breed- no predisposition in cats
- Medications- no known association in cats
- Dietary factors- no association in cats
- Infectious disease – rare
- Blunt trauma, hypotension, neoplasia

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Canine vs Feline Risk Factors

Idiopathic in both

Others in both: Blunt trauma, hypotension, neoplasia, immune mediated

Infectious in both

Certain breeds in dogs only

Certain medications in dogs only

Dietary factors in dogs only

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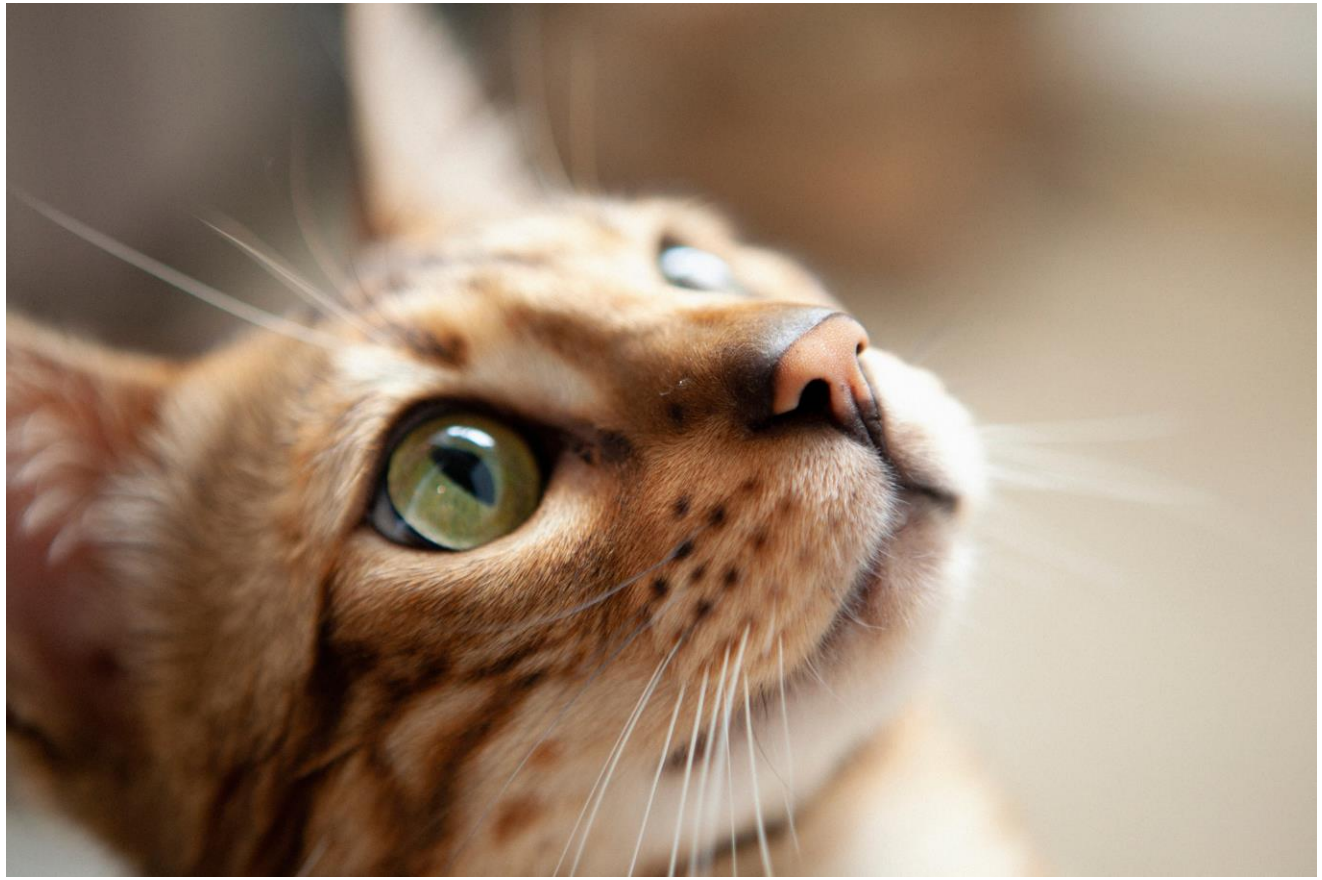
Concurrent disease



+ Triaditis
+ Hepatic lipidosis
+ Cholangitis/cholangiopathies
+ Chronic enteropathy
+ Diabetes mellitus

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Clinical Presentation

- Vague clinical signs including weight loss, lethargy and anorexia.
  - Dogs more commonly present with vomiting, abdominal pain and lethargy
- Cats more likely to be underweight cf dogs often obese
- Vomiting and abdominal pain less common in cats
- Temperature
  - 25% pancreatitis cases pyrexic and 50% hypothermic

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Investigations

- Full haematology, serum biochemistry
- SNAP fPLi, Quantitative fPLi or DGGR lipase measurement
- Folate/B12 assessment
- Abdominal imaging
  - Radiographs have low sensitivity
  - Ultrasound is superior
- For a definitive diagnosis, biopsies are required but very rarely done

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Blood work

- Non specific changes on routine blood work.
  - No significant difference between chronic and acute pancreatitis cases
- May see non regenerative anaemia and leukocytosis
- Liver parameters often increased
- Hyperglycaemia common
- Hypertriglyceridemia rare

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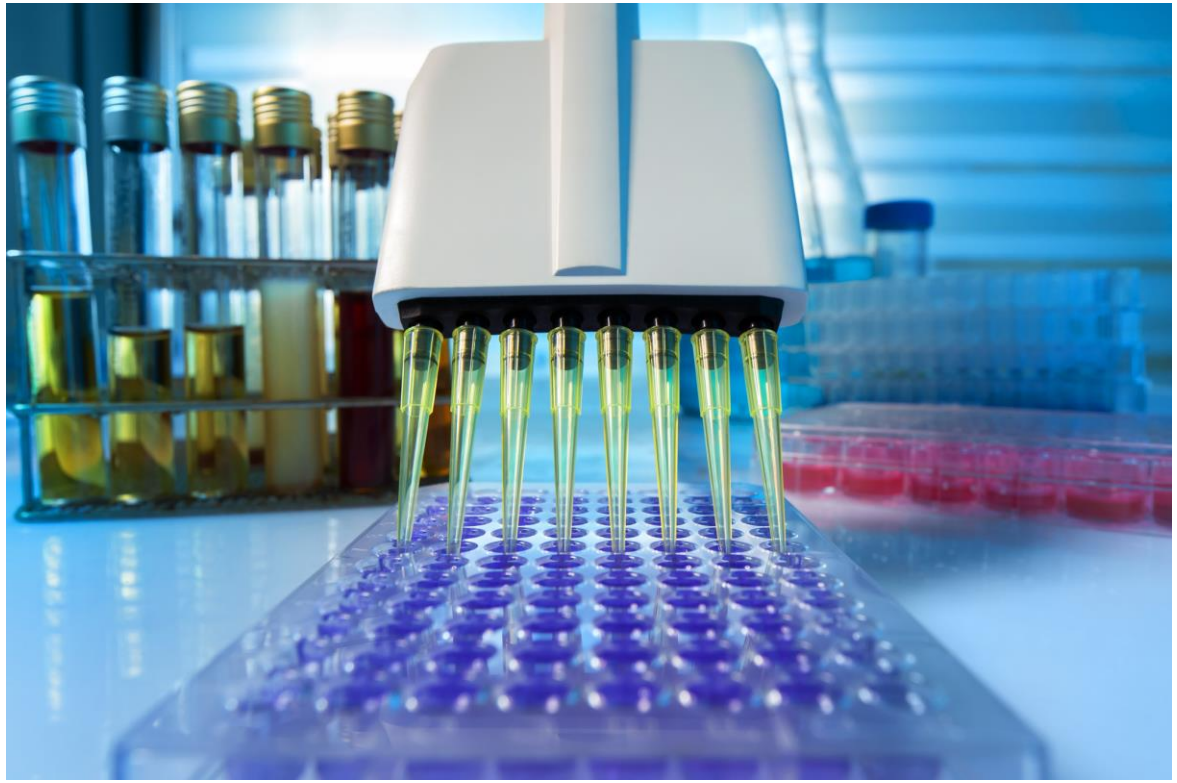
Pancreatic tests

- In house
  - Lipase
  - Amylase
  - fPLi- SNAP
  - Catalyst Pancreatic lipase
- At lab
  - Quantitative Spec® fPL™
  - DGGR lipase
  - fTLI



- fPLi SNAP good to rule out
- fTLI, lipase, amylase not useful to confirm pancreatitis

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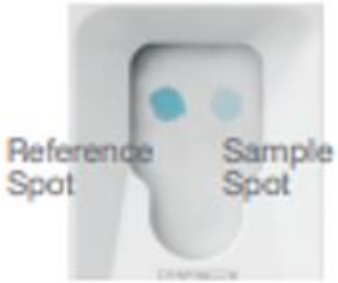
SNAP vs fPL

Spec fPL (cats)	≤4.4 U/L	≥4.5 U/L	
SNAP	Normal	Abnormal*	
	 Sample spot is lighter than reference spot.	Sample spot is the same as reference spot.	Sample spot is darker than reference spot.

***an abnormal SNAP PL should be followed-up with SPEC PL**

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Activity vs Immunossays

ACTIVITY ASSAYS

e.g Catalyst Pancreatic Lipase Test

1. Chemical reagent that mimics fat
2. Measures amount of reagent breakdown over time
3. Various substrates available
4. Specificity for pancreatic lipase varies among available assays
5. Measured in U/L

IMMUNOASSAYS

e.g SNAP fPL, Spec fPL

1. Specific antibodies against feline pancreatic lipase
2. Measures amount of antibody binding to pancreatic lipase
3. High specificity for pancreatic lipase
4. Measured in ug/L

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Catalyst® Pancreatic Lipase Test

- Activity assay cf Spec® fPL™ which is an immunoassay
- Catalyst® Pancreatic Lipase Test aligns well with Spec® cPL™ and Spec® fPL™ tests
- One test validated for both dogs and cats
- Real-time diagnoses with results in less than 10 minutes

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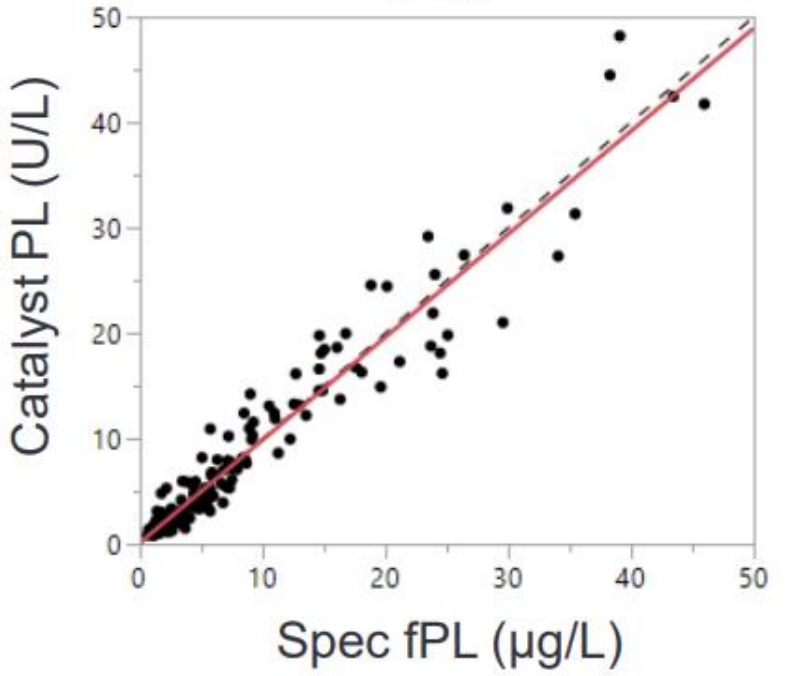
Catalyst Pancreatic Lipase Test alignment with Spec Fpl test



$r = 0.96$
Slope = 0.97
n = 216

Line of best fit
x = y

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Comparison of lipase tests

- To rule out can consider
  - SNAP fPL or Catalyst PL and Spec fPL
- To rule in and monitor known pancreatitis
  - Catalyst PL and Spec fPL
  - TAT for catalyst PL is quicker
- Catalyst PL and Spec fPL qil quantitatively measure pancreatic lipase cf SNAP fPL which will semi quantitatively measure pancreatic lipase.

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Diagnostic imaging

- Ultrasound is superior to radiographs
- In pancreatitis often see thick left limb of the pancreas, severely irregular pancreatic margins, and hyperechoic peripancreatic fat
- Overlap between changes seen with chronic and acute disease
- Care re: age related changes
- Cytology can be performed on FNA samples and safe even in face of pancreatitis
  - False negatives more common in chronic pancreatitis

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Treatment

- Depends on severity of signs
- Need investigate/treat comorbidities
- Supportive treatment often required
  - Fluid therapy
  - Analgesia
  - Anti emetics
  - Feeding tube placement

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Treatment

- Analgesia
- Anti-emetics
- Lack of evidence regarding low fat diets
- Consider placement of feeding tube
  - NO vs O tube
  - Start at 1/3 RER divided into several meals
- Treat any concurrent disease

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Analgesia

- Opioids
  - Methadone or buprenorphine in hospital
  - Transmucosal buprenorphine at home
- Gabapentin for longer term
- Maropitant
  - May provide some visceral analgesia

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Antiemetics/Appetite stimulants

- Maropitant
  - May provide some visceral analgesia as well
- Ondansetron
- Mirtazapine
  - Transdermal licensed
- Capromorelin
  - Ghrelin receptor agonist
  - Available in USA currently

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Nutrition

- Enteral feeding is important
- Encourage nutrition
- No evidence for low fat diet in cats
  - Consider highly digestible diet
- Often concurrent disease and diet may need to be modified to treat this
- ?adding in pancreatic enzymes
  - PERT (pancreatic enzyme replacement therapy) used in humans with chronic pancreatitis
  - No scientific evidence in cats unless develop EPI

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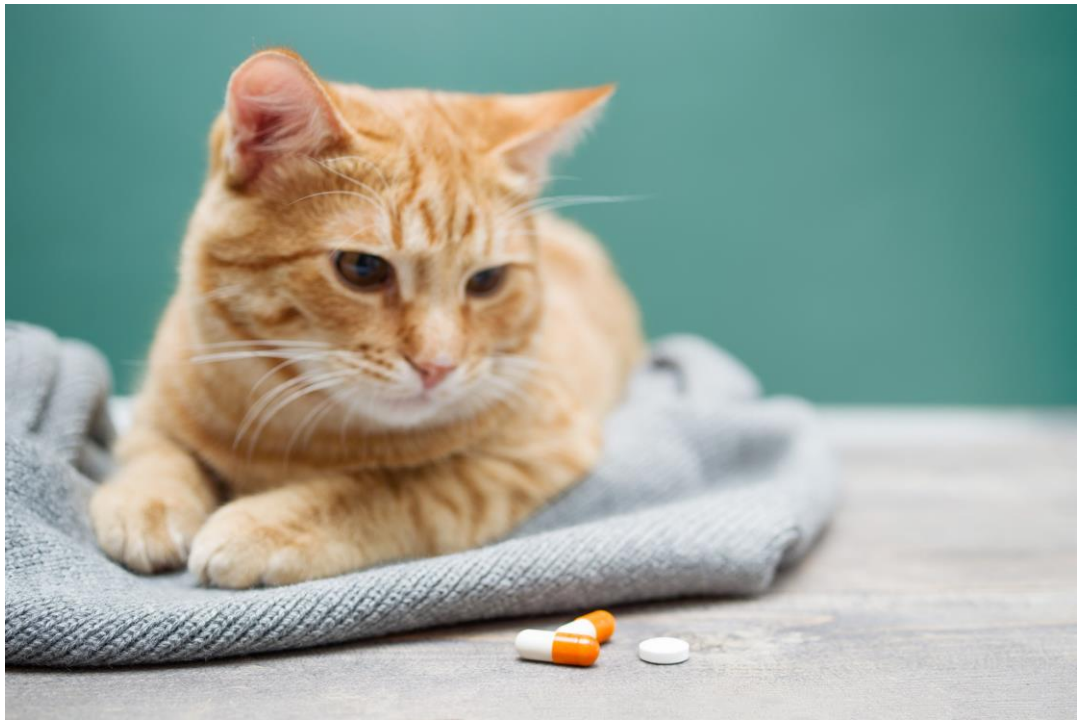
Immunomodulatory treatment

- ?steroids
  - If lymphocytic inflammation present may be indicated
  - If end stage and fibrosis, then no benefit
  - Most often used if concurrent disease is steroid responsive
- ?ciclosporin



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Immunomodulatory studies in feline pancreatitis

Article

Cyclosporine Treatment in Cats with Presumed Chronic Pancreatitis—A Retrospective Study

Nina Hoeyrup [1,†], Thomas Spillmann [2] and Linda Toresson [1,2,*]

STANDARD ARTICLE OPEN ACCESS

Small Animal Internal Medicine Gastroenterology

Randomized Open-Label Clinical Trial Comparing Prednisolone and Cyclosporine With a Nonrandomized Active Control for Treating Presumed Chronic Pancreatitis in Cats

Yu-An Wu[1,2] | Jonathan A. Lidbury[1] | Samiran Sinha[2] | Jörg M. Steiner[1]

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Alonzo – 9y MN DLH

+ 1 month history of weight loss (1Kg)
+ Otherwise no concerns
+ UTD vaccinations and flea treatment
+ No travel history
+ Indoor/outdoor access.
+ Not known to hunt

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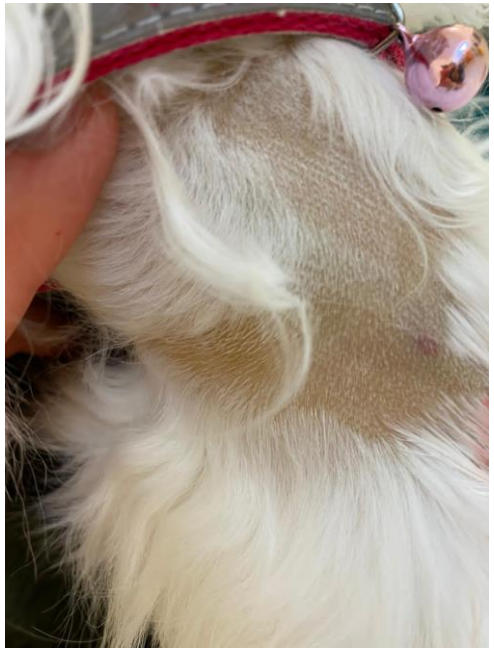
Physical examination

+ Bright, alert and responsive
+ Visibly icteric - skin, mucous membranes
+ TPR wnl
+ Thoracic and abdominal palpation unremarkable
+ LN wnl



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Haematology

	*RBC	9.33	10^12/L	7.12 - 11.46	
	*Haematocrit	0.415	l/L	0.282 - 0.527	
	*Haemoglobin	12.5	g/dL	10.3 - 16.2	
	*MCV	44.5	fL	39.0 - 56.0	
	*MCH	13.4	pg	12.6 - 16.5	
	*MCHC	30.1	g/dL	28.5 - 37.8	
	*Reticulocytes	8.4	10^9/L	<=50.0	
Low	***Reticulocyte Haemoglobin**	**14.1**	**pg**	**15.3 - 22.9**	
	*WBC	11.8	10^9/L	3.9 - 19.0	
	*% Neutrophils	71.0	%		
	*% Bands	2.0	%		
	*% Lymphocytes	17.0	%		
	*% Monocytes	9.0	%		
	*% Eosinophils	1.0	%		
	*% Basophils	0.0	%		
	*Neutrophils	8.38	10^9/L	2.62 - 15.17	
	*Bands	0.24	10^9/L	0.00 - 0.30	
	*Lymphocytes	2.01	10^9/L	0.85 - 5.85	
High	***Monocytes**	**1.06**	**10^9/L**	**0.04 - 0.53**	
	*Eosinophils	0.12	10^9/L	0.09 - 2.18	
	*Basophils	0.00	10^9/L	0.00 - 0.10	
	*Platelets	302	10^9/L	155 - 641	

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Biochemistry

	Glucose	5.1	mmol/L	3.9 - 8.0	
	IDEXX SDMA	8	ug/dL	1 - 14	
	Creatinine	130.0	umol/L	80.0 - 203.0	
High	**Urea**	**11.4**	**mmol/L**	**2.5 - 9.9**	
	Phosphorus	1.51	mmol/L	0.90 - 2.20	
	Calcium	2.70	mmol/L	2.05 - 2.95	
	Magnesium	0.90	mmol/L	0.80 - 1.00	
	Sodium	155.0	mmol/L	145.0 - 157.0	
	Potassium	4.55	mmol/L	3.50 - 5.50	
	Na: K Ratio	34.07		28.00 - 40.00	
	Chloride	119.7	mmol/L	100.0 - 124.0	
High	**Total Protein**	**83.4**	**g/L**	**60.0 - 80.0**	
	Albumin	34.4	g/L	25.0 - 45.0	
High	**Globulin**	**49.0**	**g/L**	**25.0 - 45.0**	
	Albumin: Globulin Ratio	0.70		0.60 - 1.50	
High	**ALT**	**441.8**	**U/L**	**5.0 - 60.0**	
High	**AST**	**207.0**	**U/L**	**10.0 - 50.0**	
High	**ALP**	**145.0**	**U/L**	**<=60.0**	
High	**GGT**	**5.3**	**U/L**	**2.0 - 5.0**	
High	**Bilirubin - Total**	**81.0**	**umol/L**	**<=5.1**	
High	**Cholesterol**	**7.10**	**mmol/L**	**2.20 - 4.00**	

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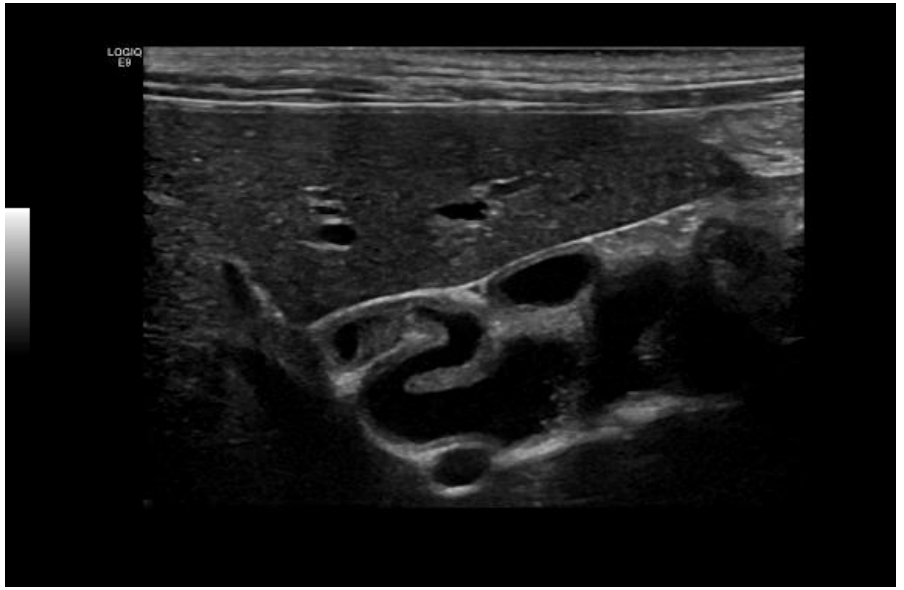
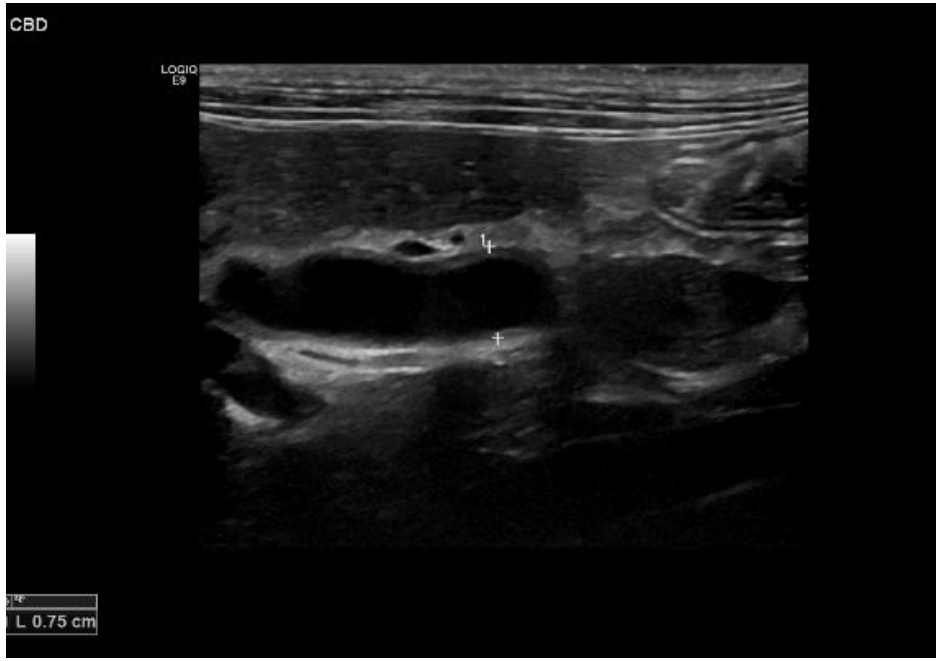
Abdominal ultrasound





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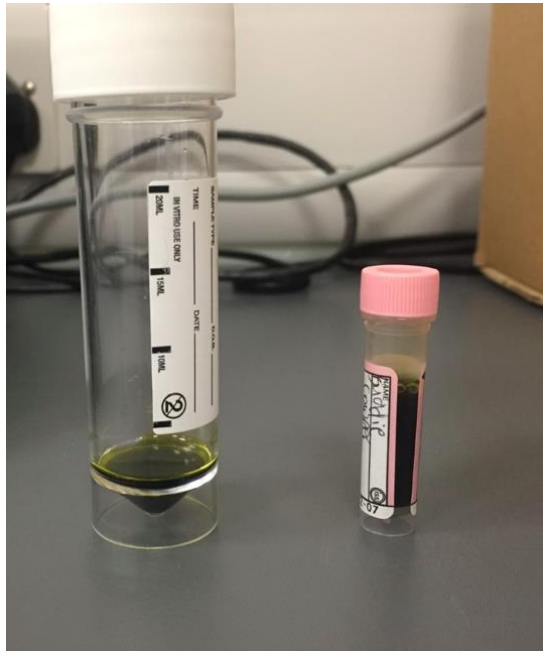
Further investigations

- Coagulation profile
  - PT 14.2 seconds (9-14)
  - APTT 44 seconds (28-44)
- Liver FNA
- Bile aspirate
- Bile cytology and culture

- No significant abnormalities
  - ?false negative result



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Screening for concurrent diseases

+ Folate wnl
+ Cobalamin 255ng/L (ref >400)
+ Spec® fPL™ 9 (ref <4)

+ Suggestive of possible triaditis

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Next step

- Trial treatment
  - Treatment for suspected enteropathy and pancreatitis
  - Treatment for liver disease ?inflammatory ?infectious ?other
- Pursue definitive diagnosis
  - Exploratory laparotomy with biopsies

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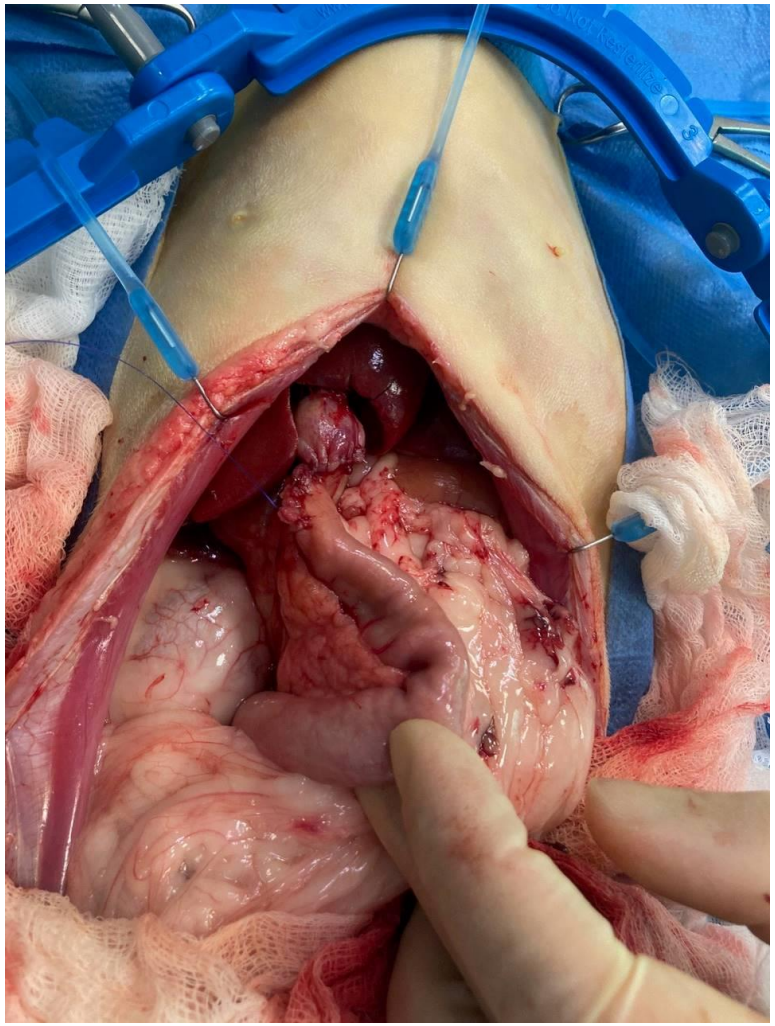
Exploratory laparotomy



Images courtesy of Professor Donald Yool

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Histopathology results

+ Lymphocytic cholangitis
+ Stomach – nad
+ Duodenum, ileum and jejunum – lymphoplasmacytic enteritis
+ Bile and liver culture – negative
+ Pancreas inflamed at time of surgery. Biopsy not taken

    + Results suggestive of triaditis

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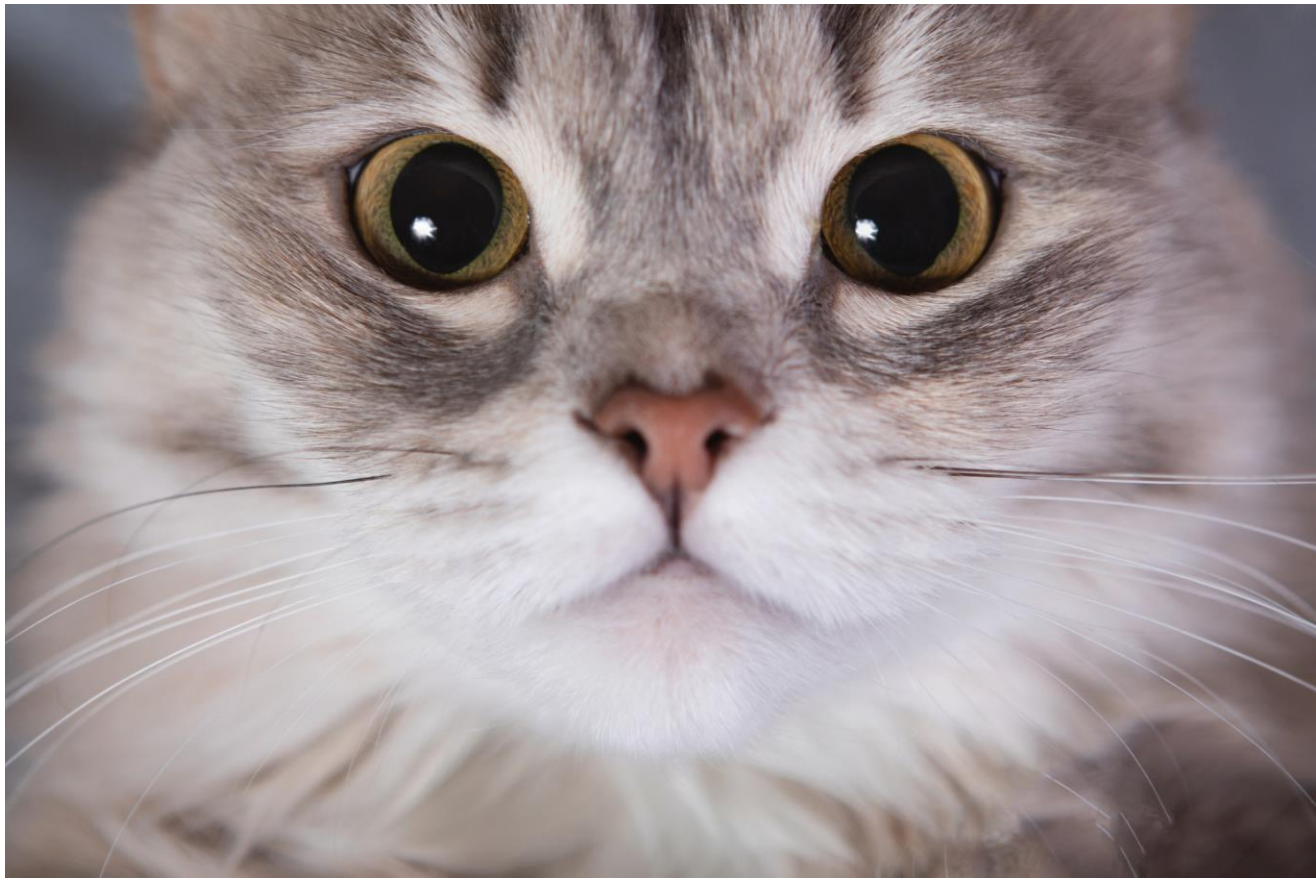
Aetiology of triaditis

+ Poorly understood
+ ?infectious
+ ?autoimmune
+ ?duct obstruction
+ ? different diseases in each organ or if the disease process in each organ has the same aetiology



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*ESVE Alive definition

Treatment

+ B12 supplementation
+
+ SAMe

+ Hydrolysed diet

+ Prednisolone therapy

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Outcome

+ Prolonged recovery post surgery

+ Once steroids started responded well to treatment

+ Transitioned to chlorambucil due to concern regarding DM

+ Long term dietary management and close monitoring

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Summary

- Signs are vague and non-specific
- Common canine risk factors often not present in cats
- Diagnosis ideally based on combination of clinical signs, blood work and imaging
- Need to investigate concurrent disease
- Treatment often aimed at concurrent disease

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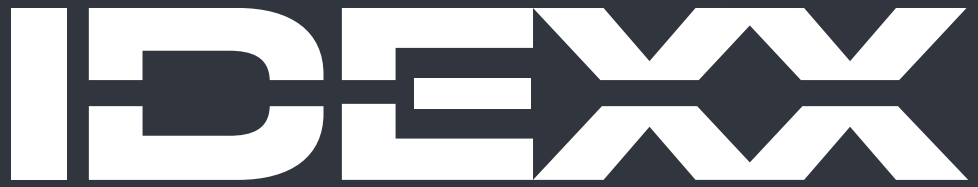
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