Acute Canine Pancreatitis - Diagnosis and Treatment

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March 2025

Disclosures:

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Pancreatic Enzymes

- Secreted & stored as precursor molecules
  - Zymogens
- Activation of trypsinogen occurs in duodenum
  - Enterokinase
  - Trypsinogen → Trypsin
- Trypsin activates other zymogens
- Prevents autodigestion

Pancreatitis

- Intraductal/intracellular activation of pancreatic enzymes
- Destruction of pancreatic tissue
- Oedema
- Haemorrhage
- Necrosis

Two primary types of pancreatitis…

Acute **Chronic**

Acute Pancreatitis

- Neutrophilic inflammation
- Oedema and necrosis
- Peripancreatic fat saponification
- REVERSIBLE
- May lead to chronic pancreatitis
  - Acute necrotizing (cell death) pancreatitis is a life-threatening condition

Chronic Pancreatitis

- Lymphocytic inflammation
- Permanent progressive fibrosis
- Acinar atrophy
- IRREVERSIBLE
- Flare-ups may occur, resulting in acute pancreatitis
  - Often manageable with close monitoring and dietary discretion

DeCock, Forman et al. 2007

Prevalence of Acute Pancreatitis

- In 40 dogs with acute vomiting
  - 35.7% for primary AP
  - 64.3% for secondary AP
    - GI foreign body
    - Renal disorders
    - Hepatic tumours
- Common
- Probably underdiagnosed
- Diagnosis is challenging

Abhilaasha, C.M., Chandrasekaran, D., Kavitha, S. and Vairamuthu, S. (2020). Prevalence of acute pancreatitis in dogs. J. Anim. Res., 10(3): 453-458

Aetiology #1

- Most cases idiopathic
  - Risk factors in dogs not very clear
- Diet?
- Drugs
  - (L-asp, phenobarb, potassium bromide, azathioprine, meglumine antimonate)
- Toxins
  - Organophosphates
- Endocrine disease
  - HAC, DM, hypoT4
  - Maybe due to high trigs
  - Glucose toxicity may play a part in DM

Aetiology #2

- Hypertriglyceridaemia
  - XS trig broken down to FFA by pancreatic lipase
- Breed disposition
  - Schnauzer, Cavalier, Poodle, Cocker
  - SPINK gene mutation in Schnauzer
- Hypercalcaemia
- Miscellaneous
  - Ischaemia

Presenting Signs

+ Dehydration
+ Abdominal pain
+ Fever
+ Jaundice
+ Vomiting
+ Weakness
+ Abdominal pain
+ Diarrhoea
+ Haematemesis

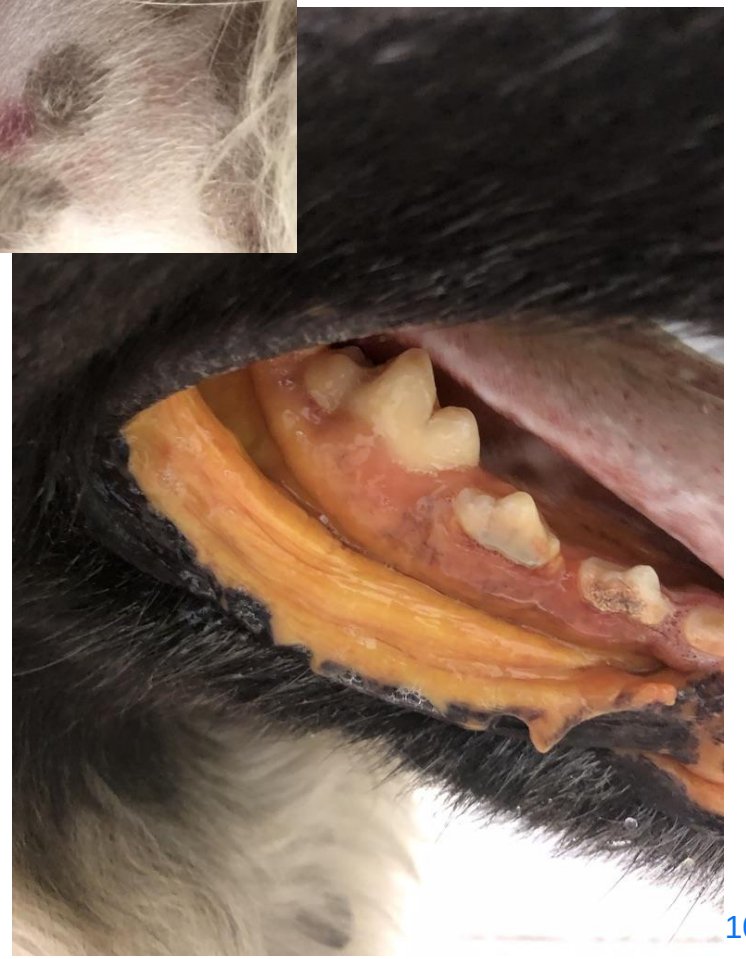
J Am Vet Med Assoc. 1998 Sep 1;213(5):665-70.

Clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in dogs with fatal acute pancreatitis: 70 cases (1986–1995)

R S Hess [1], H M Saunders, T J Van Winkle, F S Shofer, R J Washabau

Complications of Pancreatitis

- Local
  - Pancreatic necrosis
  - Peripancreatic fluid
  - EHBDO
  - Thromboembolic disease
  - GI stasis
- Systemic
  - Coagulopathy/DIC
  - Acute kidney injury
  - Aspiration pneumonia
  - Transient hyperglycaemia
  - Myocarditis
  - SIRS/MODS



Non-specific Clin Path Changes in Acute Pancreatitis

Haematology

+ Neutrophilia (+/- left shift)

+ Mild non regenerative anaemia

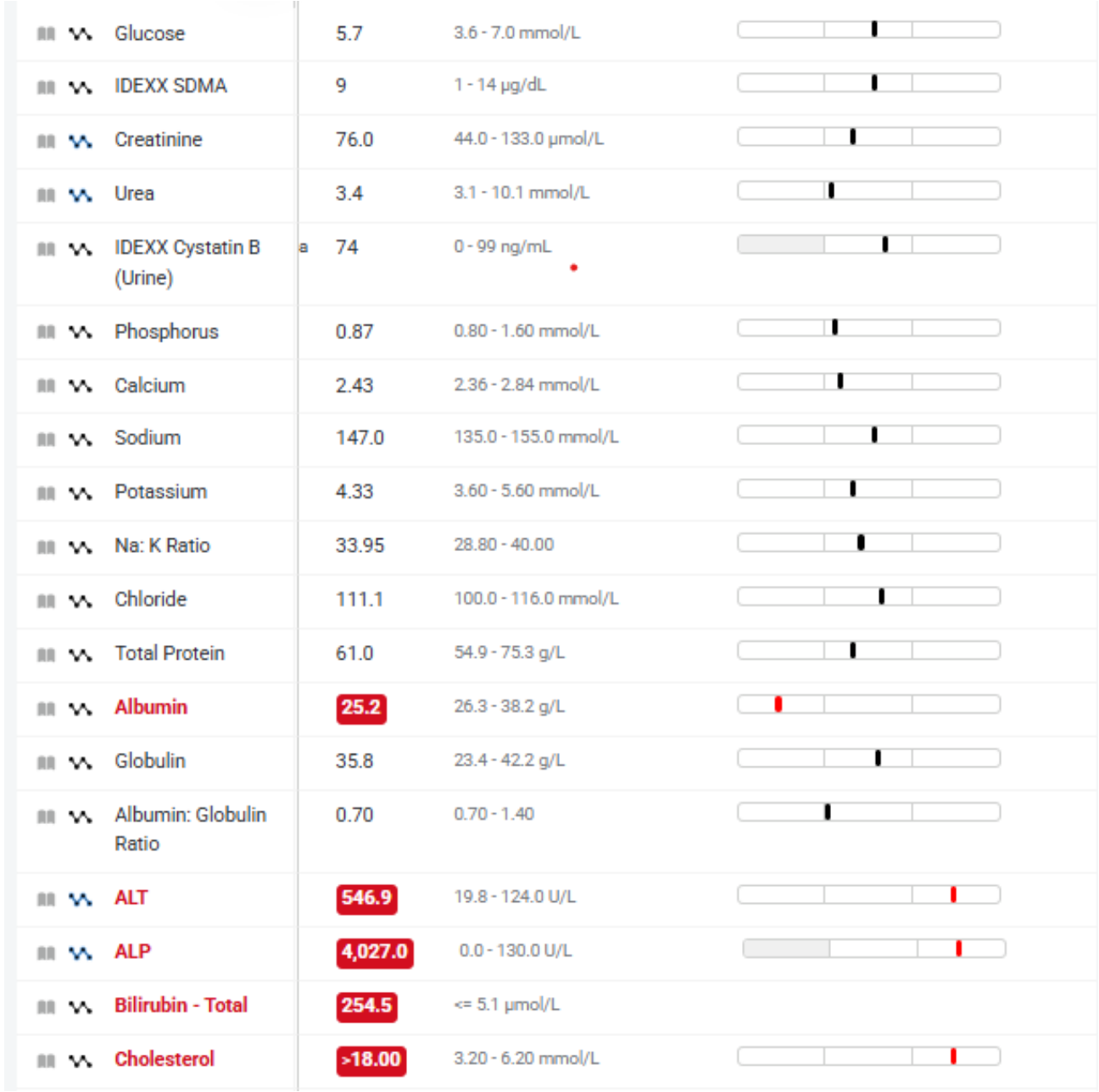
+ Mild thrombocytopenia

RBC	5.91	5.65 - 8.87 x10^12/L	
Haematocrit	0.369	0.373 - 0.617 L/L	
Haemoglobin	123	131 - 205 g/L	
MCV	62.4	61.6 - 73.5 fL	
MCH	20.8	21.2 - 25.9 pg	
MCHC	333	320 - 379 g/L	
RDW	17.8	13.6 - 21.7 %	
% Reticulocytes	1.8	%	
Reticulocytes	104.0	10.0 - 110.0 K/µL	
Reticulocyte Haemoglobin	24.1	22.3 - 29.6 pg	
WBC	19.90	5.05 - 16.76 x10^9/L	
% Neutrophils	79.5	%	
% Lymphocytes	5.4	%	
% Monocytes	11.3	%	
% Eosinophils	3.6	%	
% Basophils	0.2	%	
Neutrophils	15.84	2.95 - 11.64 x10^9/L	
Lymphocytes	1.07	1.05 - 5.10 x10^9/L	
Monocytes	2.25	0.16 - 1.12 x10^9/L	
Eosinophils	0.71	0.06 - 1.23 x10^9/L	
Basophils	0.03	0.00 - 0.10 x10^9/L	

Biochemistry

+ Increased liver enzymes
+ Increased bilirubin
+ Increased triglycerides/cholesterol
+ Hypoalbuminaemia
+ Hyperglycaemia/hypoglycaemia
+ Azotaemia (prerenal vs renal)
+ Hypokalaemia

+ Hypertriglyceridemia
+ Hypercholesterolaemia
+ Hyperlactataemia



Glucose		5.7	3.6 - 7.0 mmol/L
IDEXX SDMA		9	1 - 14 µg/dL
Creatinine		76.0	44.0 - 133.0 µmol/L
Urea		3.4	3.1 - 10.1 mmol/L
IDEXX Cystatin B (Urine)	a	74	0 - 99 ng/mL
Phosphorus		0.87	0.80 - 1.60 mmol/L
Calcium		2.43	2.36 - 2.84 mmol/L
Sodium		147.0	135.0 - 155.0 mmol/L
Potassium		4.33	3.60 - 5.60 mmol/L
Na: K Ratio		33.95	28.80 - 40.00
Chloride		111.1	100.0 - 116.0 mmol/L
Total Protein		61.0	54.9 - 75.3 g/L
Albumin		25.2	26.3 - 38.2 g/L
Globulin		35.8	23.4 - 42.2 g/L
Albumin: Globulin Ratio		0.70	0.70 - 1.40
ALT		546.9	19.8 - 124.0 U/L
ALP		4,027.0	0.0 - 130.0 U/L
Bilirubin - Total		254.5	<= 5.1 µmol/L
Cholesterol		>18.00	3.20 - 6.20 mmol/L

C Reactive Protein (CRP)

+ Increased in 90% of dogs with AP
+ May be used to monitor response to treatment
+ CRP for non-survivors significantly higher than for survivors
+ Persistent elevation associate with poor prognosis

J Vet Intern Med. 2021 Sep;35(5):2187-2195. doi: 10.1111/jvim.16218. Epub 2021 Jul 11.

Serum concentrations of canine pancreatic lipase immunoreactivity and C-reactive protein for monitoring disease progression in dogs with acute pancreatitis

Kirstin M Keany [1], Geoffrey T Fosgate [2], Sean M Perry [3], Shannon T Stroup [1], Joerg M Steiner [4]

Prognostic value of C-reactive protein in dogs with elevated serum pancreatic lipase immunoreactivity concentrations

Sydney M. Oberholtzer DVM, Audrey K. Cook BVM&S, MSc Vet Ed, DACVIM, DECVIM, DABVP, Robynne Gomez MS, and Jörg M. Steiner MedVet, DrMedVet, PhD, DACVIM, DECVIM

DOI: https://doi.org/10.2460/javma.23.09.0533
Volume/Issue: Volume 262: Issue 3

Received: 26 Sep 2023 | Accepted: 03 Nov 2023 | Online Publication Date: 01 Dec 2023

J Vet Med Sci. 2016 Sep 23;79(1):35–40. doi: 10.1292/jvms.16-0009

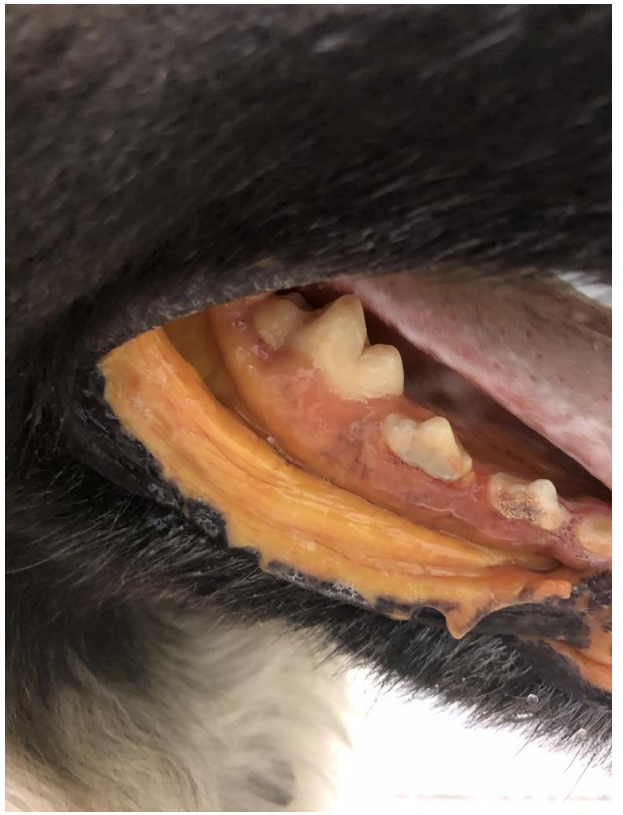
Assessment of severity and changes in C-reactive protein concentration and various biomarkers in dogs with pancreatitis

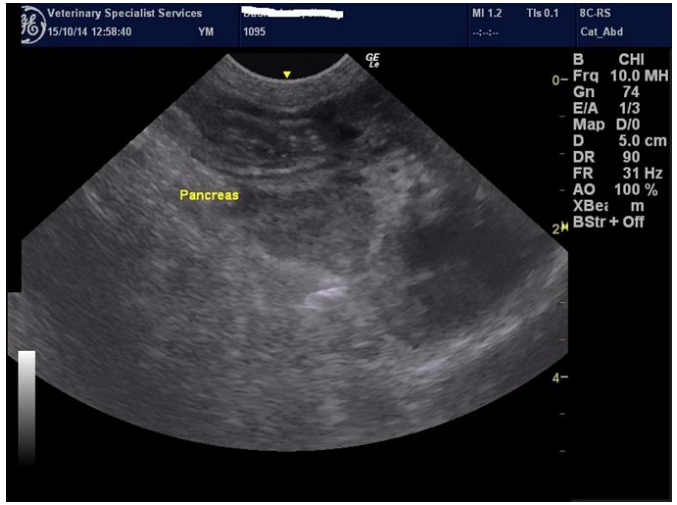
Toru SATO [1], Koichi OHNO [1,*], Takashi TAMAMOTO [1], Mariko OISHI [1], Hideyuki KANEMOTO [1], Kenjiro FUKUSHIMA [1], Yuko GOTO-KOSHINO [1], Masashi TAKAHASHI [1], Hajime TSUJIMOTO [1]

Diagnosis of Acute Pancreatitis

Diagnosis of Acute Pancreatitis- Multimodal

+ Signalment
+ Clinical signs
+ Supportive blood results
+ Pancreatic lipases
+ Supportive imaging
+ Pancreatic FNA
+ Pancreatic biopsy?





Specific Diagnostics for Acute Pancreatitis

Canine Pancreatic Lipases

- Immunological Assays (PLI)
  - Spec cPL® (quantitative)
  - SNAP cPL® (semi quantitative)
- Catalytic Methods
  - Standard lipases 1,2 Diglyceride
  - DGGR lipases
- Most sensitive and specific marker for pancreatitis

Spec cPL®

- Most sensitive and specific marker for diagnosis of pancreatitis
- Uses 2 sets of monoclonal antibodies against canine pancreatic lipase (ELISA)
- Doesn't detect extra pancreatic lipases
- Validated in dogs (and fPL incats)
- Not affected by icterus, haemolysis or lipaemia

0-200 ug/L pancreatitis unlikely
200-400 ug/L pancreatitis possible
> 400 ug/L pancreatitis probable

	Cut-off 200	400
Sensitivity	43-94%	21-90%
Specificity	66-95%	74-100%

J Vet Intern Med 2015

Clinical Utility of Diagnostic Laboratory Tests in Dogs with Acute Pancreatitis: A Retrospective Investigation in a Primary Care Hospital

M. Yuki, T. Hirano, N. Nagata, S. Kitano, K. Imataka, R. Tawada, R. Shimada, and M. Ogawa

Lateral Flow Immunoassay- SNAP cPL®

- Very good agreement with Spec cPL®
  - 94-97.4% agreement
- 97.5% agreement for normal results
- 90% agreement for abnormal results
- Please use conjugate with correct lot number!!

Lipase assays: aren’t they all the same?

Activity assays

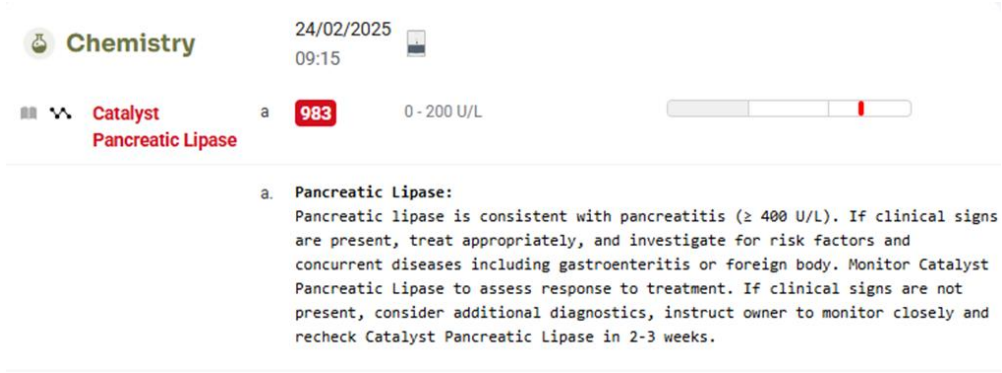
- Chemical reagent that mimics fat
- Measure amount of reagent breakdown over a specific time
- Various substrates available
- Specificity for pancreatic lipase varies among available assays
- Traditionally measured in U/L
- Examples include the Catalyst® Pancreatic Lipase Test and the assay used at IDEXX Reference Laboratories

Immunoassays

- Specific antibodies against canine or feline pancreatic lipase
- Measures the amount of antibody binding to pancreatic lipase
- High specificity for pancreatic lipase
- Measured in µg/L
- Examples include the Spec cPL®, Spec fPL®, SNAP® cPL™, and SNAP® fPL™ tests

Catalyst PL = DGGR Lipase

- More specific for pancreas than general lipase
  - Substrate hydrolysed by pancreatic lipase
- Heparin or serum
- Correlates well with Spec cPL®
- Moderate to severe haemolysis may impact results
- Icterus or lipaemia don’t affect results
- Low in most cases of EPI



Catalyst Pancreatic Lipase

- Validated range in dogs
  - 30-2000 U/L
- One test validated for both dogs and cats.
- Accurate and specific quantitative results that align with the IDEXX Reference Laboratories Spec cPL® and Spec fPL® tests.

Perform the Catalyst® Pancreatic Lipase Test if clinical signs† of pancreatitis are present or if lipase on chem 17 profile is substantially elevated‡

Pancreatic lipase	Pancreatic lipase	Pancreatic lipase
Canine ≥ 400 U/l Feline ≥ 8.8 U/l	Canine 201–399 U/l Feline 4.5–8.7 U/l	Canine ≤ 200 U/l Feline ≤ 4.4 U/l
Pancreatic inflammation/injury is present	+ **Consider other causes for clinical signs** + In cases of chronic pancreatitis elevation of pancreatic lipase can be intermittent	

If not performed previously:
abdominal imaging and CBC, chemistry profile and urinalysis

Consider presence of extrapancreatic disease as cause of clinical signs
(foreign body, enteropathy, acute kidney injury [AKI], hepatopathy, hypoperfusion, thrombus)

Consider rechecking with the Catalyst Pancreatic Lipase Test:
+ In 2–3 weeks
+ If clinical signs worsen

No other overt disease – pancreatitis very likely
ascause of clinical signs

Evidence of other disease present/ secondary pancreatic inflammation/ injury likely present – recheck with Catalyst Pancreatic Lipase Test after primary disease resolves

Imaging for Acute Pancreatitis

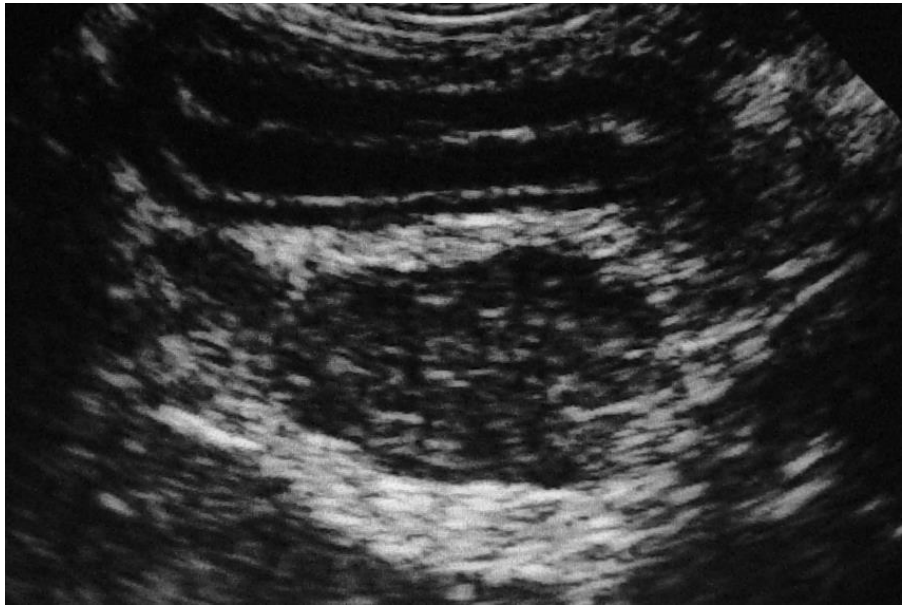
Ultrasound

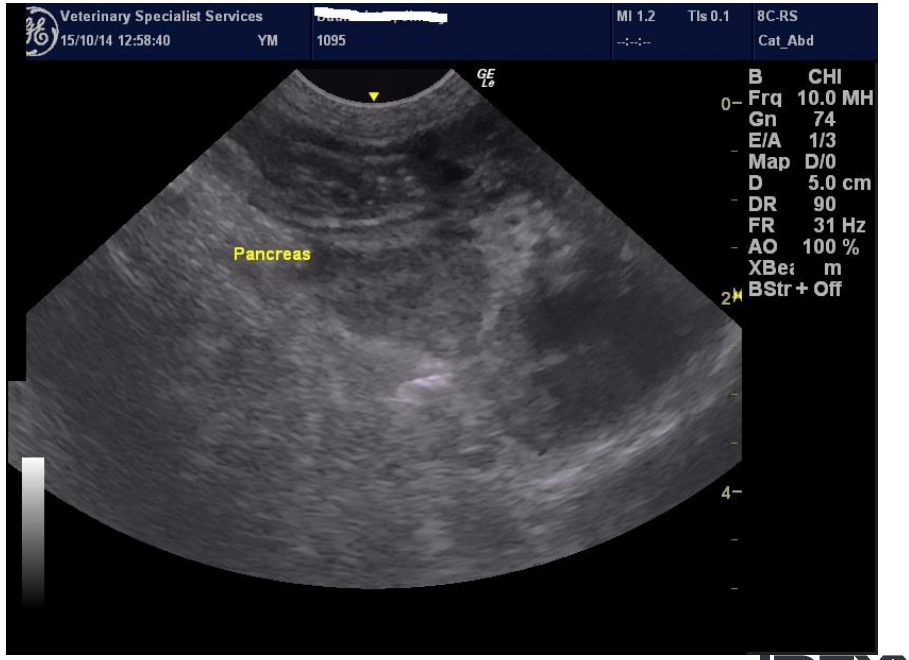
+ Large, hypoechoic pancreas
+ Hyperechoic peripancreatic fat
+ Dilation of ducts

+ Better for diagnosing acute necrotising pancreatitis

+ US resolution can lag behind clinical improvement

+ US evidence of pancreatitis in absence of other evidence should be interpreted with caution





Pancreatic FNA

+ Can be useful to diagnose AP
  + Diagnostic in 74% cases
  + Neutrophils and pancreatic acinar cells
+ Safe
+ Correlates with histology in 91%
+ Localised lesions may be missed

Cytologic findings and diagnostic yield in 92 dogs undergoing fine-needle aspiration of the pancreas

Journal of Veterinary Diagnostic Investigation
2015, Vol. 27(2) 236–240

DOI: 10.1177/1040638715574862
jvdi.sagepub.com

Amy P. Cordner, Leslie C. Sharkey,[1] P. Jane Armstrong, Kaitlyn D. McAteer

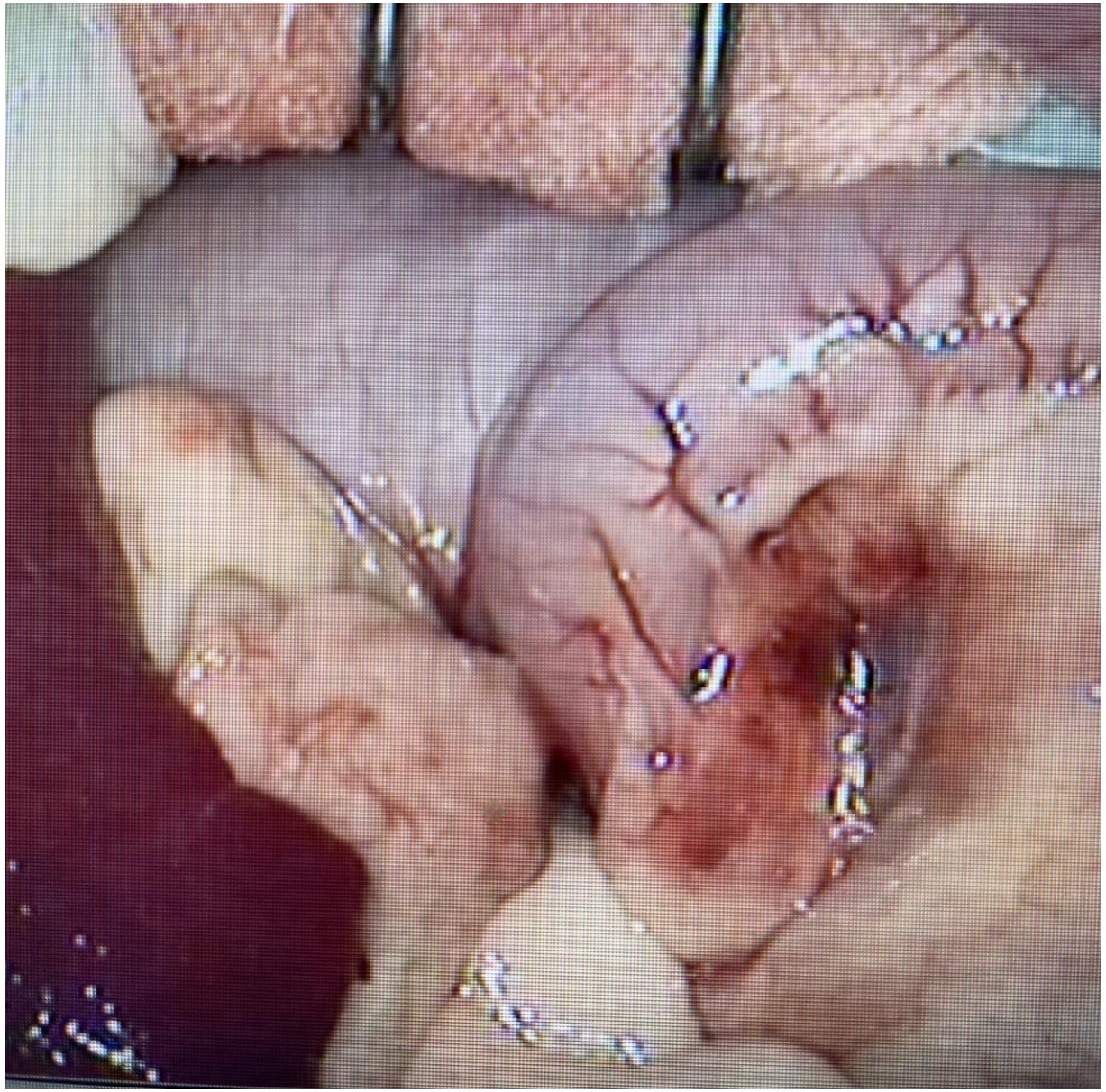
Pancreatic Fluid

- Not frequently identified
- Generally considered safe to aspirate
  - Sterile vs septic
- Very few cases found to be septic

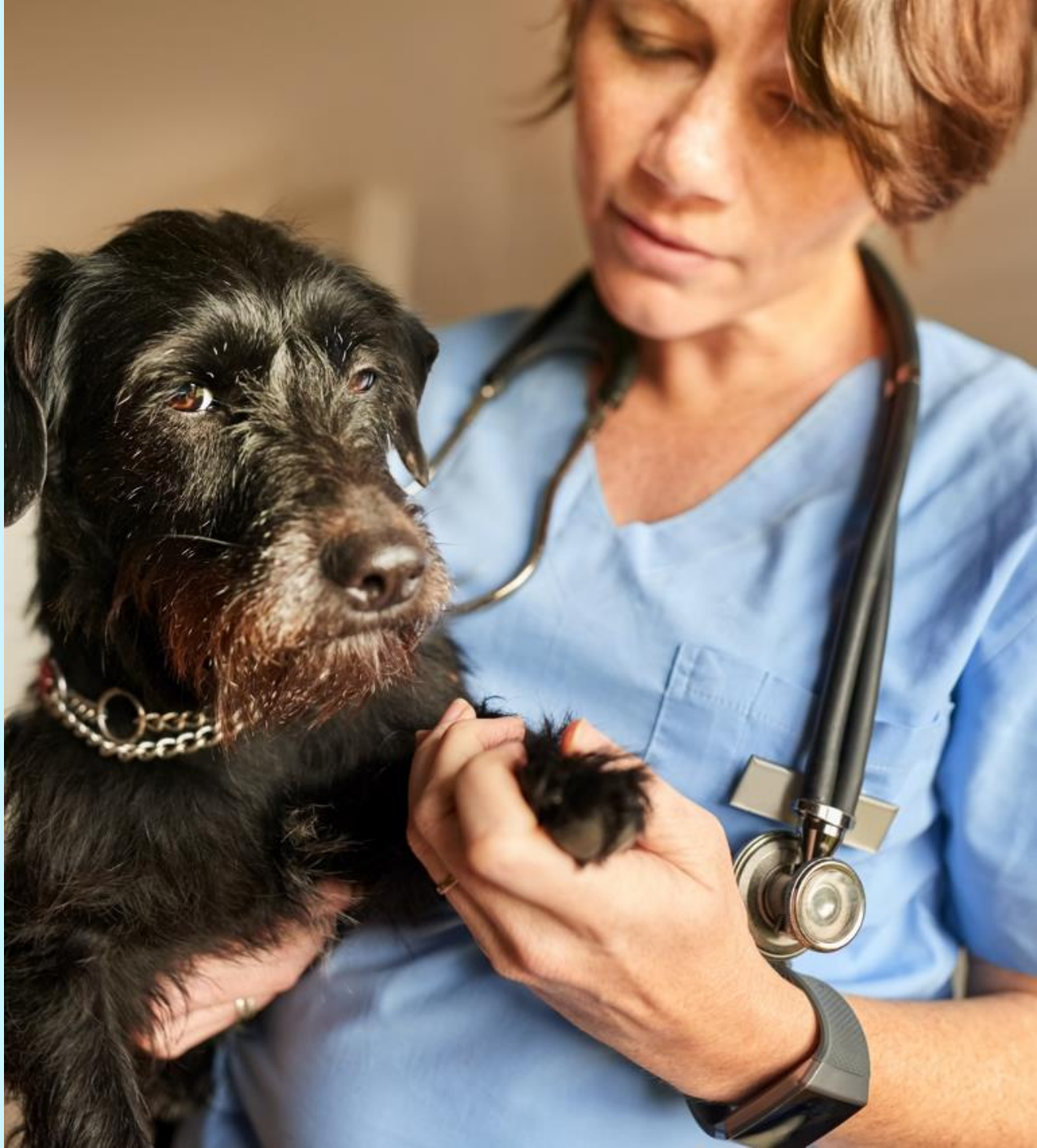
Talbot CT, Cheung R, Holmes EJ, Cook SD. Medical and surgical management of pancreatic fluid accumulations in dogs: A retrospective study of 15 cases. *J Vet Intern Med*. 2022; 36(3): 919-926. doi:10.1111/jvim.16411

Pancreatic Biopsy

- Gold standard for diagnosis
- May not be a good anaesthetic candidate
- May be patchy distribution
  - Multiple biopsies
- Doesn’t change treatment

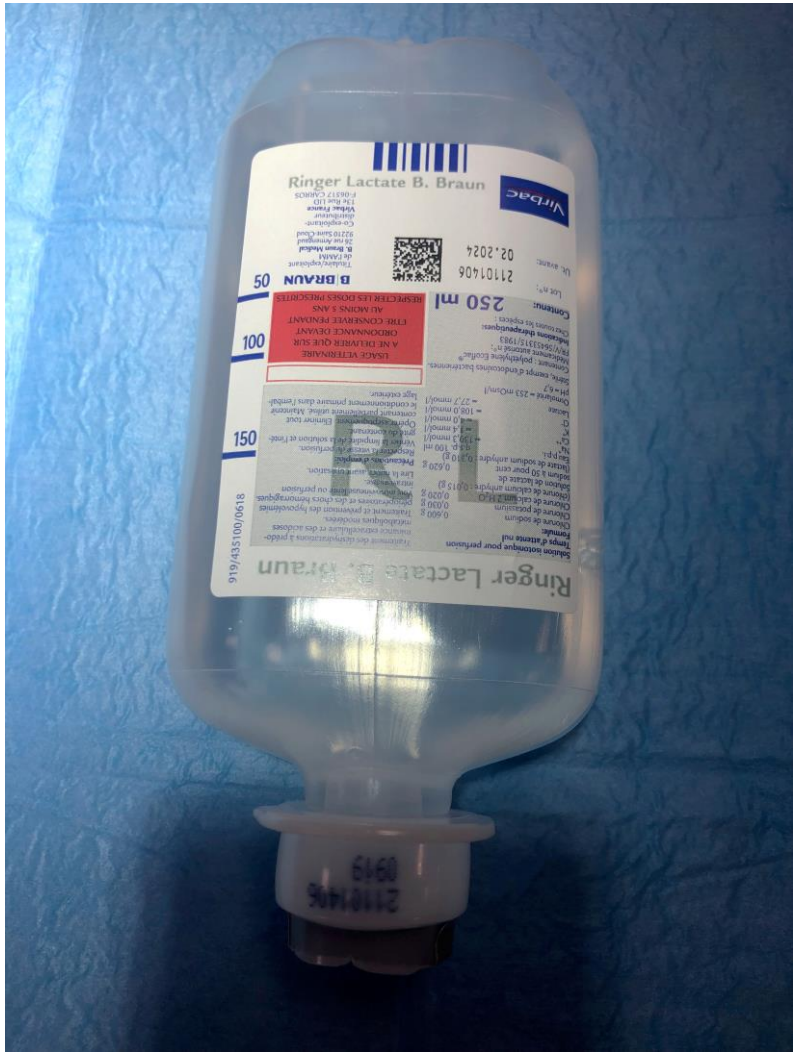


Management of Acute Canine Pancreatitis



Fluid Therapy

- Balanced isotonic solution
  - Lactated Ringers (Hartmann's)
- Individualised approach
- Potassium supplementation
- Fluid overload detrimental!
  - Interstitial oedema
  - Third spacing
  - Worsening hypoalbuminaemia



How Much Fluid?- Daily Fluid Requirements

+ 30 x BW kg + 70 = ml/day

+ 132 x BW $kg^{0.75}$
  + For cats use 80 x BW $kg^{0.75}$

+ 40-60ml/kg/day

Pardo M, Spencer E, Odunayo A, Ramirez ML, Rudloff E, Shafford H, Weil A, Wolff E. 2024 AAHA Fluid Therapy Guidelines for Dogs and Cats. J Am Anim Hosp Assoc. 2024 Jul 1;60(4):131-163.

Calculating Fluid Requirements

+ Fluid deficit = % dehydration x Bodyweight (kg) x 1000

+ Add maintenance fluids = 40-60mls/kg/day

+ Add ongoing losses (vomiting, diarrhoea, polyuria)

+ Total requirements = deficit + maintenance + ongoing losses

Example

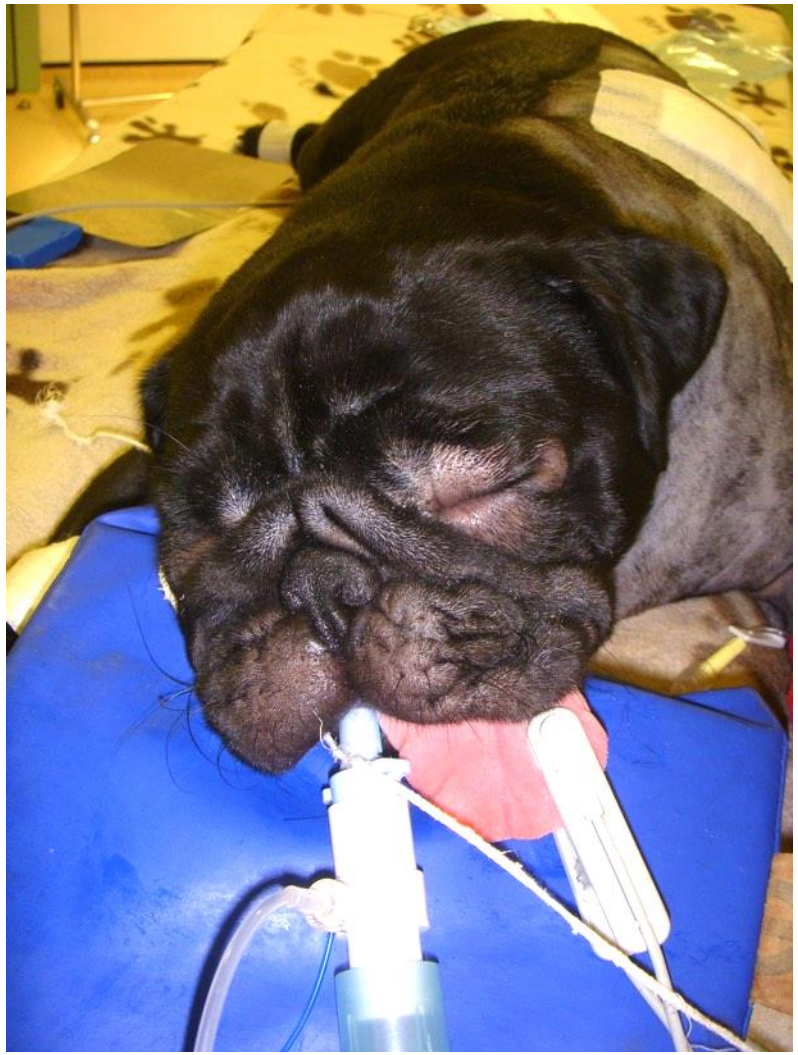
- 30kg dog which is 10% dehydrated
  - tachycardia, dry mm, prolonged CRT

- Fluid deficit = 3000mls (0.10 x 30 x 1000)
- Maintenance = 1500mls (50 x 30)
- Total fluid requirement for 24 hours

= 4500mls/day!!!!! + ongoing losses = 187ml/h

How Long?- Avoid Fluid Overload with ROSE

- **R**esuscitation
  - Rapid administration over a few mins
  - Fluid boluses of balanced crystalloids
- **O**ptimisation
  - Maintain effective circulation
  - Lasts a few hours
- **S**tabilisation
  - Maintenance fluid therapy
  - Lasts a few days
  - Weigh patient twice daily
- **E**vacuation
  - Patient eliminates excess fluids via the kidneys
  - May lead to oedema if vascular damage present



Pain Management

- Opioids
  - + Methadone
  - + Fentanyl
  - + Buprenorphine
- + NDMA antagonists
  - + Ketamine
- + CRIs
  - + Lidocaine CRI
  - + MLK/FLK
- + Paracetamol
- + NSAIDs???- no

Nutritional Support

- NPO NOT recommended
- Early enteral nutrition recommended

- Highly digestible
- Low fat (<20g fat/1000kcal)

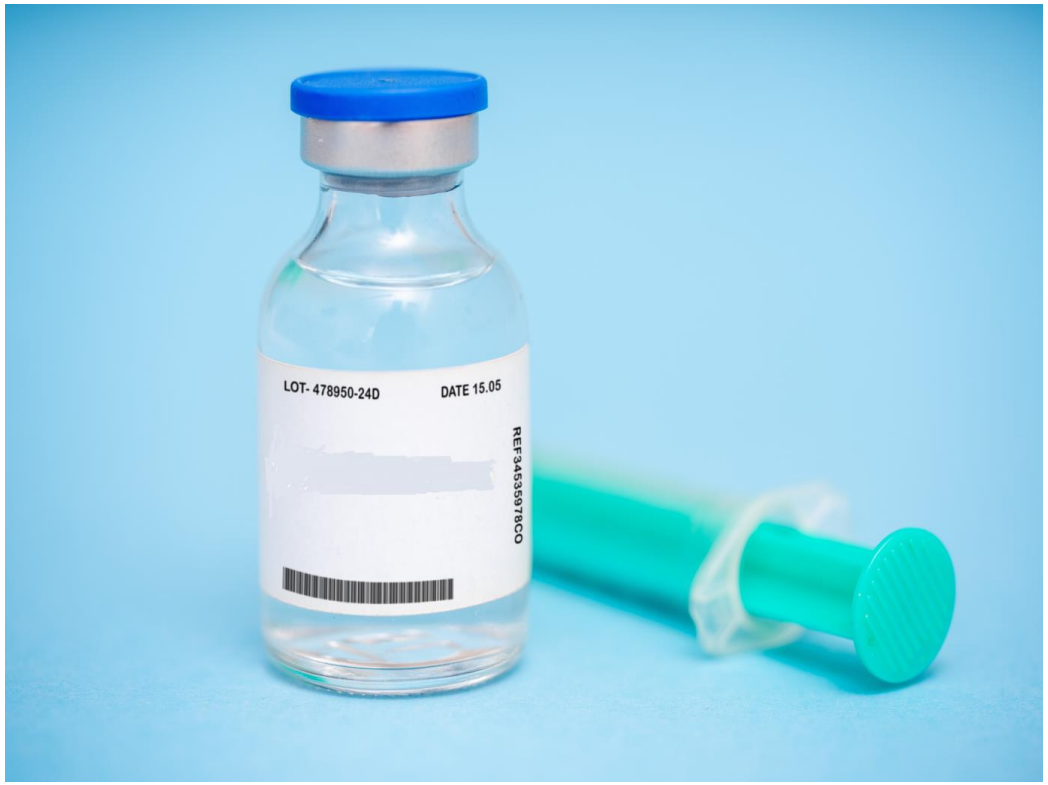
- Feeding tubes

- Appetite stimulants
  - Mirtazapine (0.5-1.5mg/kg q24h)
  - Capromorelin (3mg/kg q24h)

Zollers B, Wofford JA, Heinen E, Huebner M, Rhodes L. A Prospective, Randomized, Masked, Placebo-Controlled Clinical Study of Capromorelin in Dogs with Reduced Appetite. J Vet Intern Med. 2016 Nov;30(6):1851-1857.

Anti-emetics

- Maropitant
  - Selective NK-1 receptor antagonist
  - Blocks substance P
  - Acts on central & peripheral pathways
- Ondansetron
  - 5-HT3 antagonist
  - Anti-emetic & anti- nausea
- Metoclopramide?
  - Dopamine D2 antagonist
  - Weak antiemetic
  - Prokinetic in upper GIT
  - Not really recommended in AP



Lorenzutti AM, Martín-Flores M, Litterio NJ, Himelfarb MA, Invaldi SH, Zarazaga MP. A comparison between maropitant and metoclopramide for the prevention of morphine-induced nausea and vomiting in dogs. Can Vet J. 2017 Jan;58(1):35-38. PMID: 28042152; PMCID: PMC5157735.

Other drugs?

- Anti-thrombotics (severe cases)
  - Necrotising pancreatitis & signs of hypercoagulability
- Omeprazole
  - No clear indication
  - Increased risk of aspiration pneumonia if aspiration occurs
  - Only if melaena/haematemesis
- Corticosteroids
  - Not currently recommended
  - Pro-coagulant
- Antibiotics
  - Not recommended!
  - Only if pyrexia, left shift, melaena

New Horizons? -Fuzapladib

+ Leukocyte function antigen inhibitor (LFA-1)
+ Prevents extravasation of neutrophils into pancreas
+ Injectable drug given IV daily for 3 days
+ Not yet available in Europe

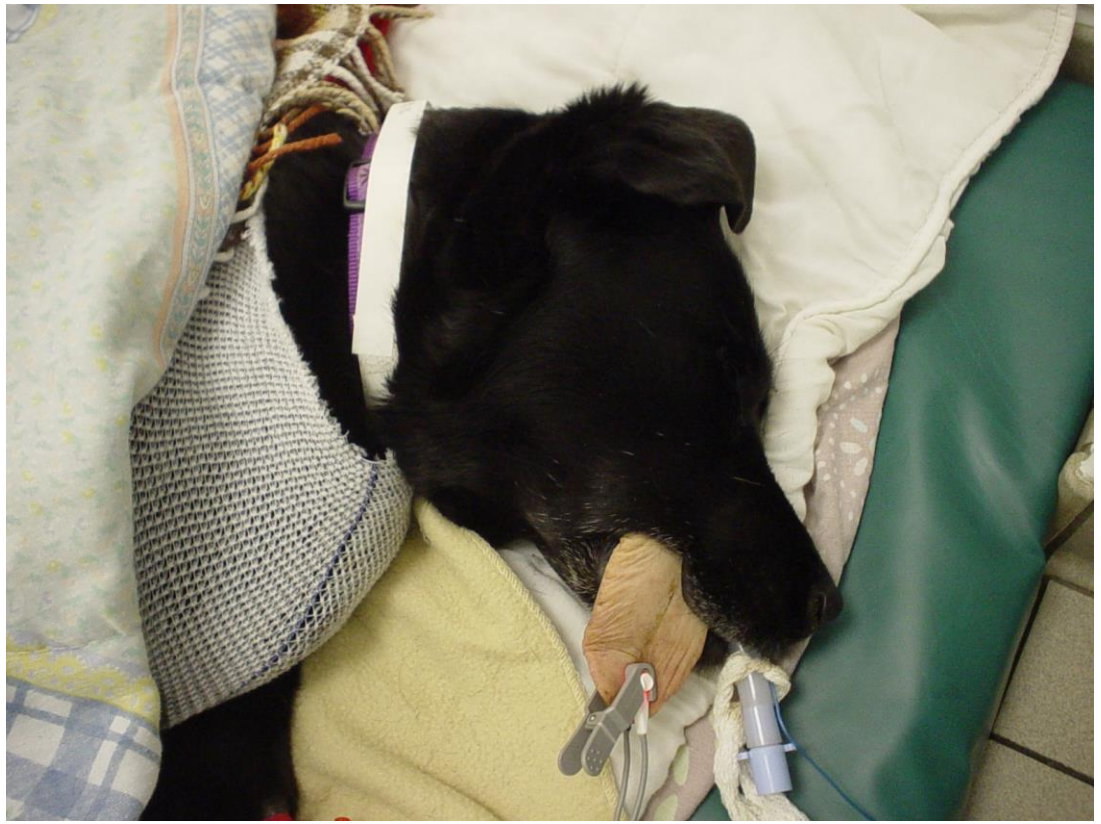
Multicenter Study > J Vet Intern Med. 2023 Nov-Dec;37(6):2084-2092. doi: 10.1111/jvim.16897. Epub 2023 Oct 9.

Fuzapladib in a randomized controlled multicenter masked study in dogs with presumptive acute onset pancreatitis

Joerg M Steiner [1], Chantal Lainesse [2], Yuya Noshiro [3], Yumiko Domen [4], Heather Sedlacek [5], Stephen E Bienhoff [5], Kelly P Doucette [6], David L Bledsoe [6], Hiroshi Shikama [7]

Prognosis

- Depends on severity of disease
- High morbidity and mortality in severe cases
  - Mortality from 20-42%
- Higher mortality with comorbidities or complications
  - Pancreatic fluid accumulation
  - Diabetes mellitus
  - Kidney disease
  - Coagulopathy
  - SIRS



Cook AK, Breitschwerdt EB, Levine JF, Bunch SE, Linn LO. Risk factors associated with acute pancreatitis in dogs: 101 cases (1985-1990). J Am Vet Med Assoc. 1993 Sep 1;203(5):673-9.

Any Questions?