

The History, Mystery, and Bemoaning of Feline Triaditis

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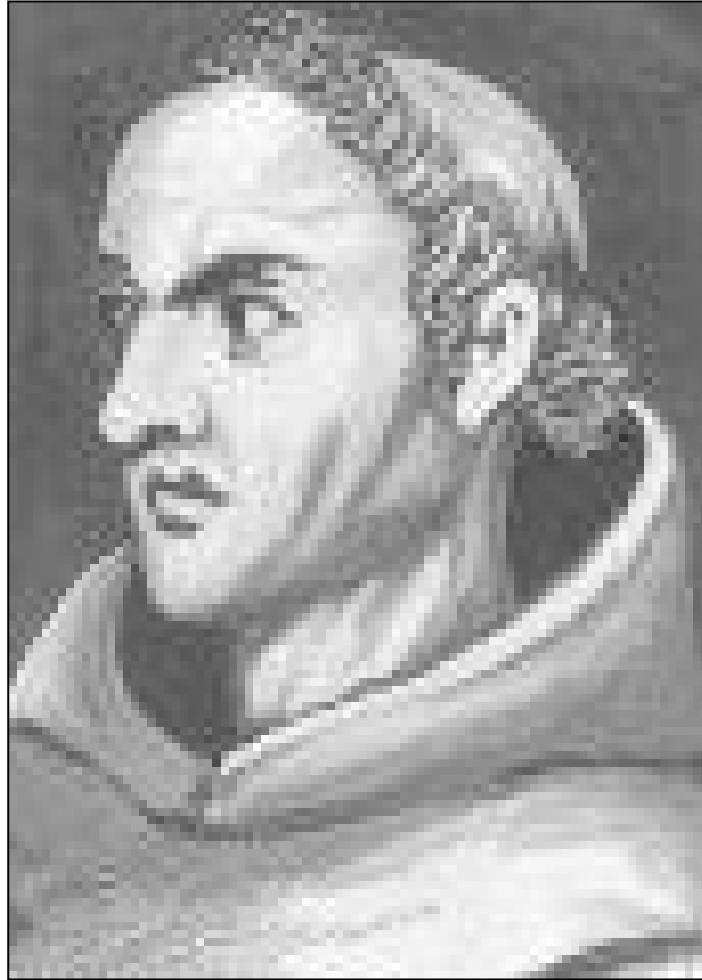
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LABORATORIES
VETERINARY SCIENCES, INC.



**Christian
Veterinary Mission**

Occam's Razor

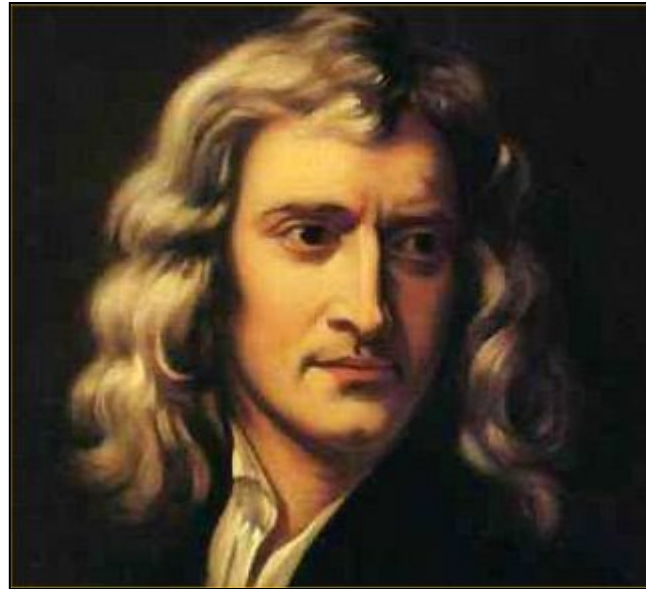


Franciscan friar Father William of Ockham

*entia non sunt multiplicanda praeter
necessitatem*

“Entities must not be multiplied
beyond necessity”

Sir Issac Newton



“We are to admit no more causes of natural things than such as are both true and sufficient to explain their appearances. Therefore, to the same natural effects we must, so far as possible, assign the same causes.”



Contemporary Medicine

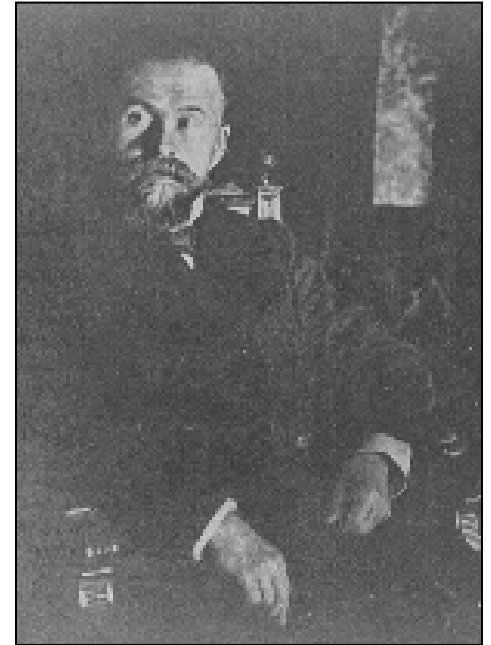
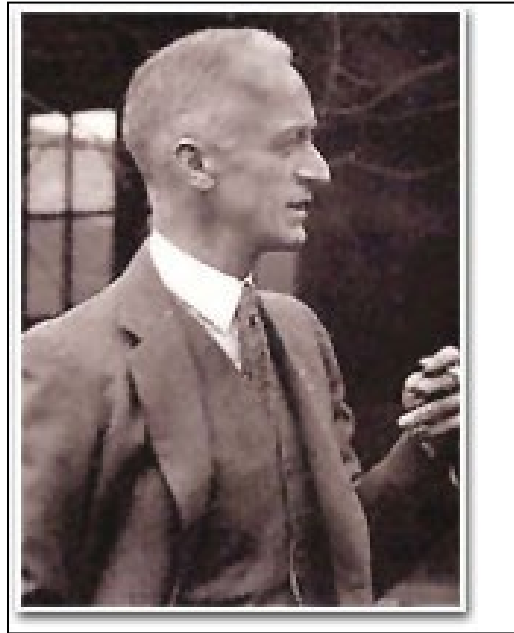
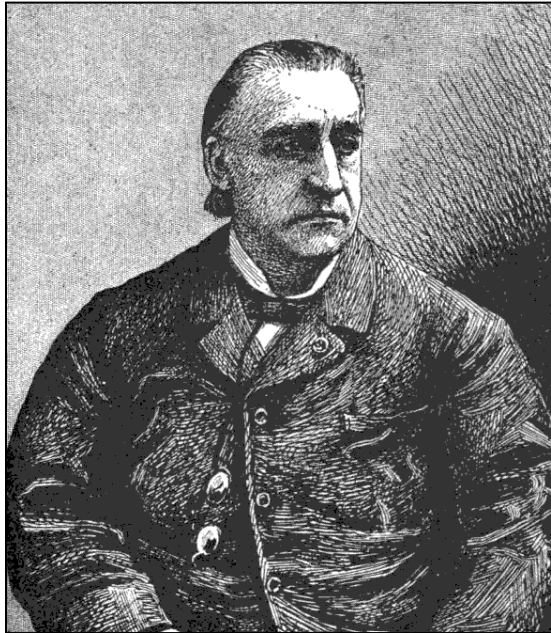
The Rule of Diagnostic Parsimony

- When diagnosing a given illness or disease a doctor should strive to look for the fewest possible causes that will account for all the symptoms.



“The simplest explanation
is most likely the correct
one.”

“Historically, physicians whose names are revered today are those who applied Occam's razor to identify new diseases. There's Charcot's triad for cholangitis, Cushing's triad for increased intracranial pressure, Wernicke's triad of thiamine deficiency, and so on.”



“Dr. Hickam”

The image shows the classic Google logo, consisting of the word "Google" in its signature multi-colored font. The letters are blue, red, yellow, blue, green, and red from left to right. A small "TM" trademark symbol is located to the upper right of the final letter 'e'. The logo is centered within a white rectangular frame.



OCTOBER SKY

**“John Hickam” (played by Chris Cooper);
coal mine superintendent, with
Homer Hickam (played by Jake Gyllenhaal)**



Dr. John Hickam

Duke University



Hickam's Dictum

“Patients can have as many diseases as they damn well please.”

Why does it matter?

Dr. C.F.M. Saint



Somerset Hospital South Africa

Saint's Triad

- Hiatal hernia
- Gallbladder Disease
- Diverticulosis



Dr. Sanjay Saint

“NO KNOWN PATHOPHYSIOLOGICAL RELATIONSHIP”

Hilliard A. A., Weinberger S. E., Tierney L. M. Jr., Midthun D. E., and Saint S. (2004): *Occam's Razor versus Saint's Triad.*, N Engl J Med 350:599-603

Comorbidity Poster Child



Feline Triaditis

“Alpo” 5 yo MN DSH



PC: Lethargy, Anorexia, Vomiting

History



st was original

BONUS: What most likely next work-up of

1 year p

Rx: Stable

but recent weight loss

Dx IBD

genetic diet

loss

Physical Examination



Febrile



Minimum Data Base

CBC

26K WBC

PMNs

left shift

PCV 40%

TP 6.2 G/dL



Hyperbilirubinemia

Chem

t. bili

4.5 μ g/dL

↑ ALT, ALP

UA

3+ bilirubin

~~PRE-HEPATIC~~

HEPATIC

POST-HEPATIC



Cornell Feline Health Center

Supporting Cat Health with Information and Health Studies.

[CVM](#) > [Departments, Centers and Institutes](#) > [Cornell Feline Health Center](#) > [Health Information](#) > [Feline Health Topics](#) >

#1 Post-Hepatic Differential

Feline Pancreatitis: Serious

The outcome can be lethal when a cat's pancreas starts to digest its own tissue. Here are the signs to look for.

[Suggested Articles](#)



**Lethargy, Anorexia, Vomiting
Weight Loss, diarrhea
Febrile (or hypothermic)
Dehydrated, Icteric**



ACVIM consensus statement on **pancreatitis** in **cats**.

Forman MA, Steiner JM, Armstrong PJ, Camus MS, Gaschen L, Hill SL, Mansfield CS, Steiger K.

J Vet Intern Med. 2021 Mar;35(2):703-723. doi: 10.1111/jvim.16053. Epub 2021 Feb 15.

“...but the consensus panel agrees...”

Etiology: 95% IDIOPATHIC

not BCS, dietary, hyperTG, drug hx, or manipulation (sx, biopsy)

rarely parasites (toxoplasma, etc.) or viruses (parvovirus, calicivirus, etc.), neoplasia

-hypotension associated with anesthesia

-trauma, organophosphates, hyperCa⁺⁺(?), snake envenomation (?)

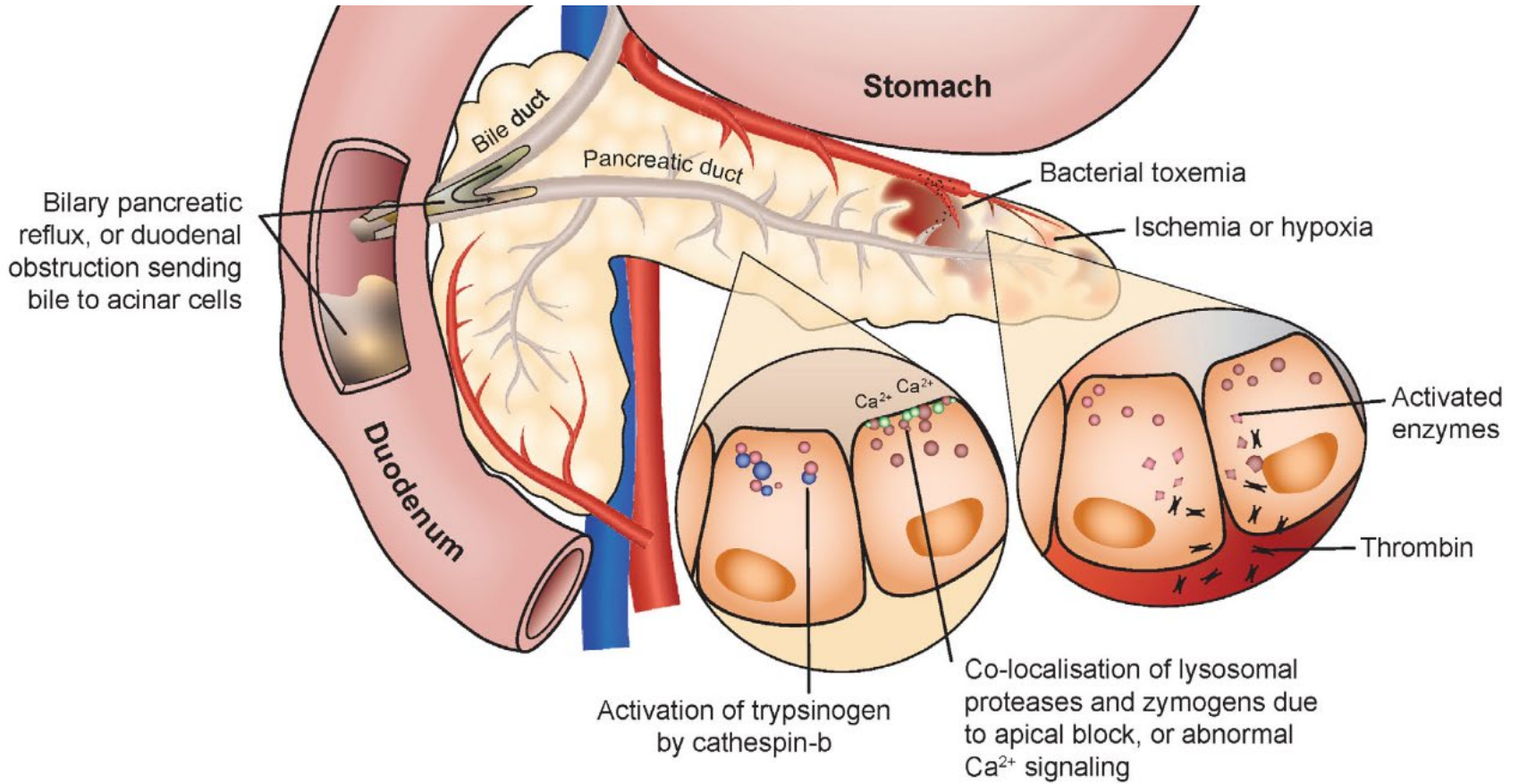
-Autoimmune (AIP) (?)

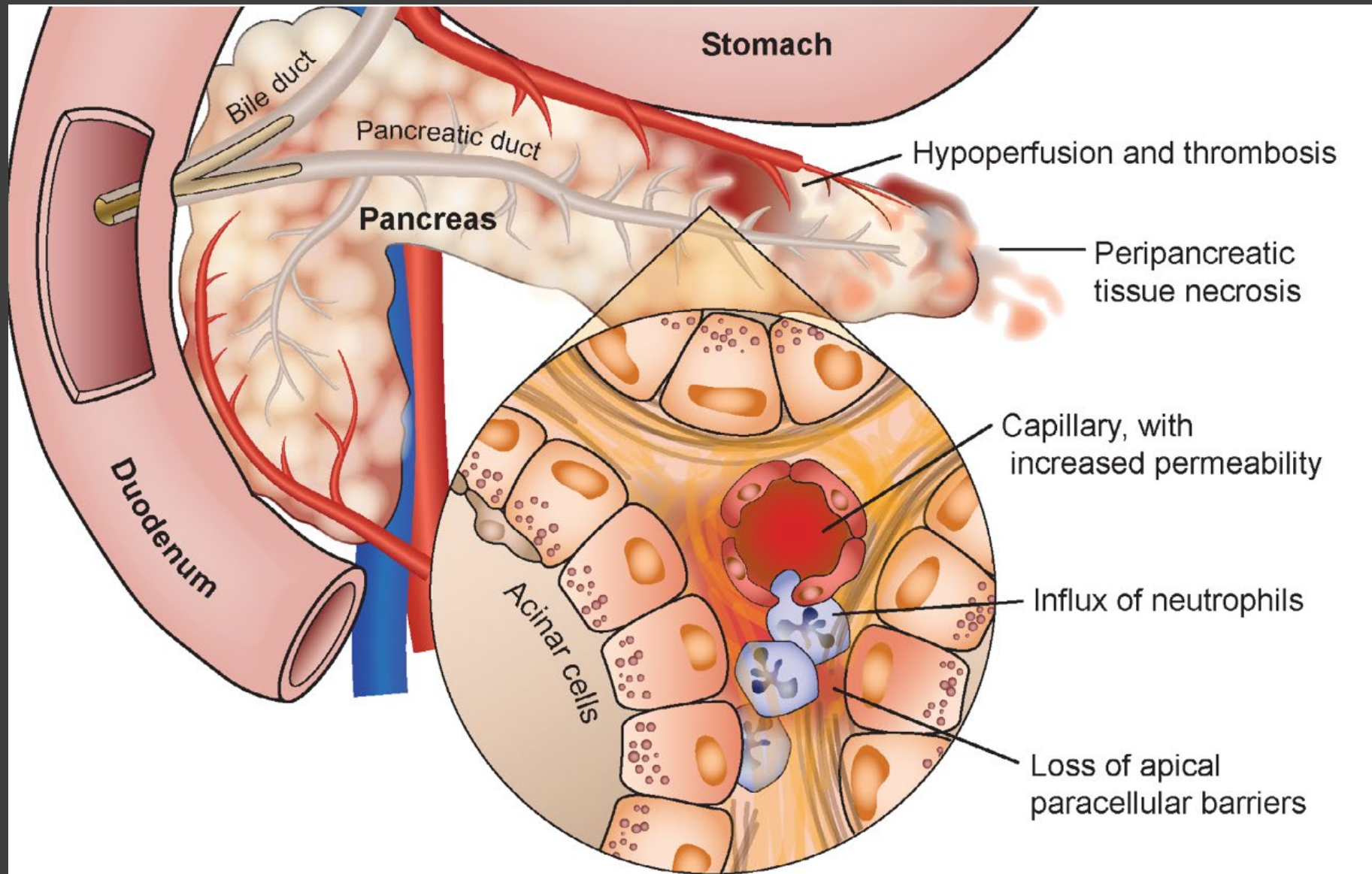
Type 1: IgG-4-associated systemic disease

Type 2: associated w/CE

-Association

DM, CE, Hepatic Lipidosis, cholangitis, nephritis, IMHA

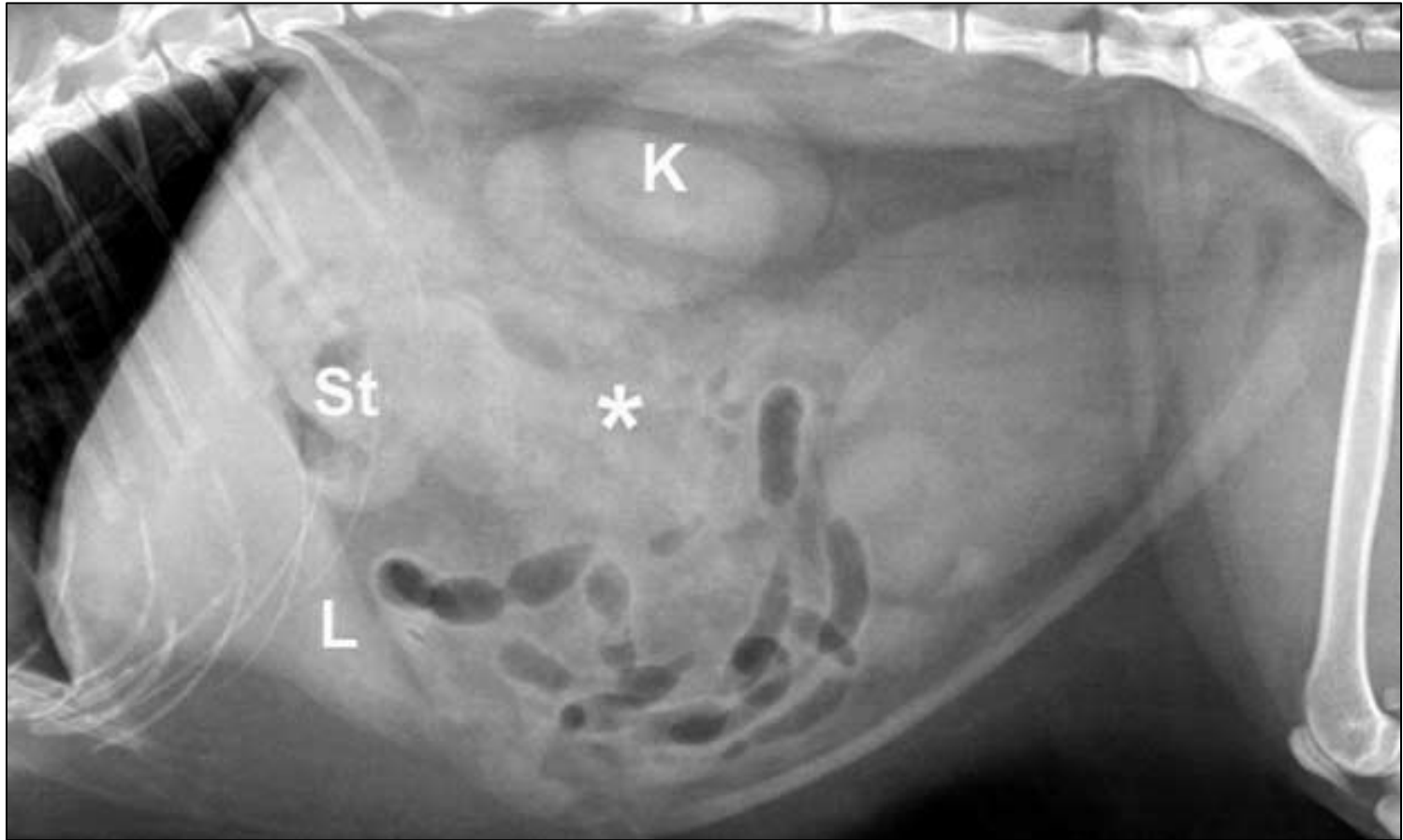




2 Local and systemic inflammation ensues in acute pancreatitis, which is independent of trypsin activation, but dependent on stimulation of the NF κ B pathway

Radiographs

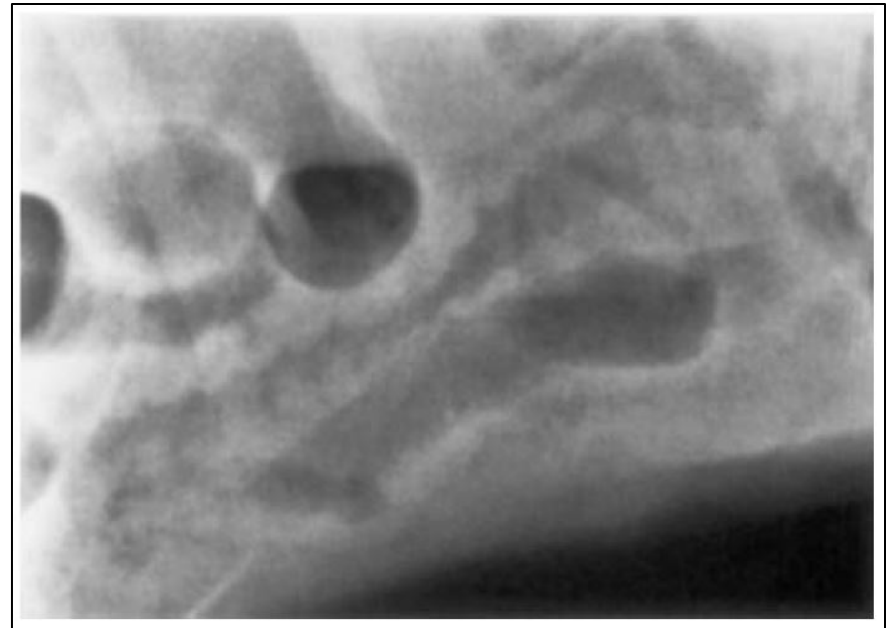
“Abdominal radiography is neither sensitive nor specific for the diagnosis of pancreatitis in cats”

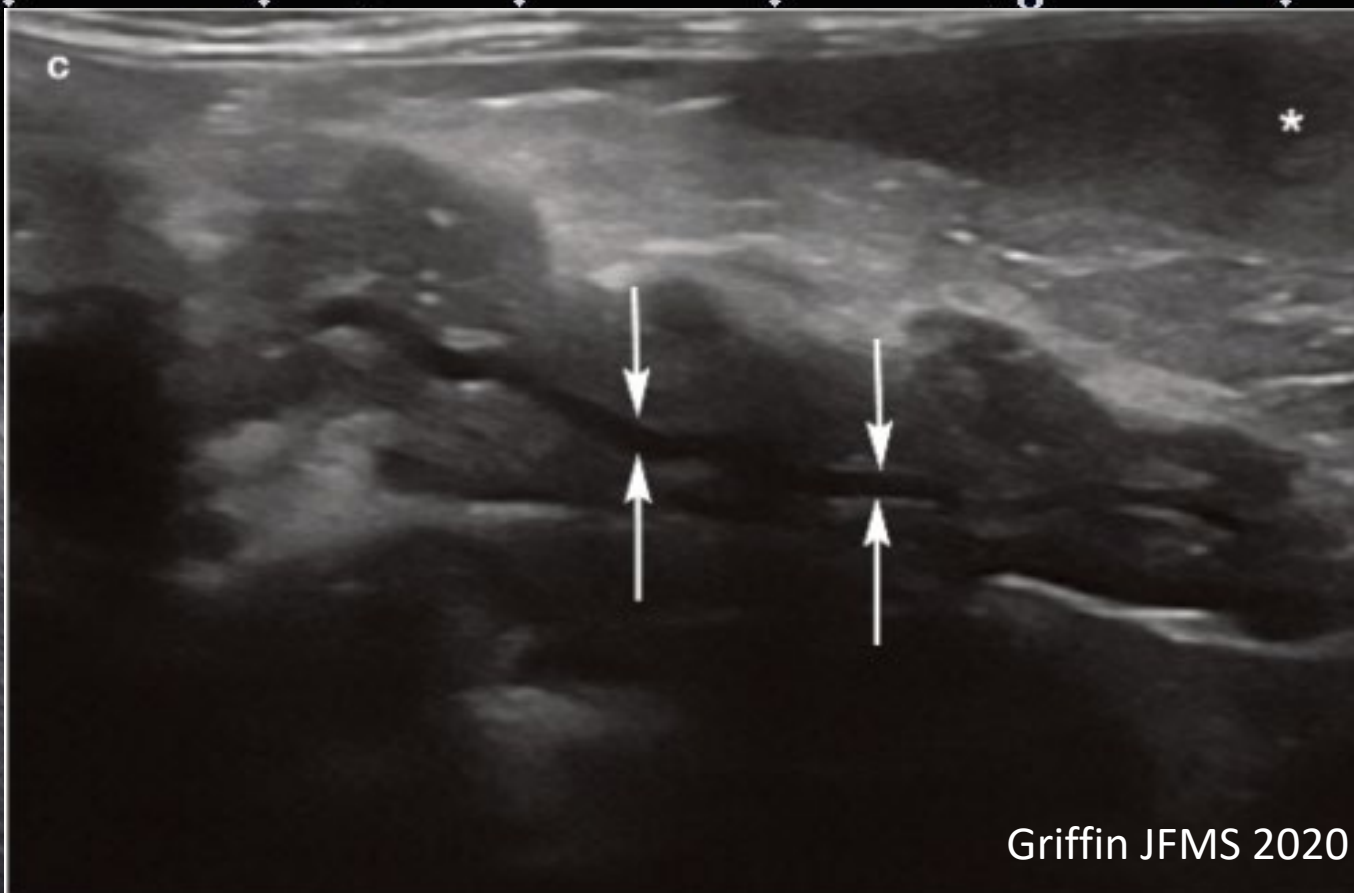


Corrugated Small Intestines

Moon et al Vet Radiol Ultrasound 2003

- Retrospective – corrugated bowel
- 18 dogs, 6 cats
- Pancreatitis 12/24
- Peritonitis 4/24
- Enteritis 2/24
- Pancreatic neoplasia
 - 2/24





Ultrasonography remains the most routine diagnostic imaging modality for cats suspected of having pancreatitis and should be considered part of the minimum database in these cats.

Left Pancreas

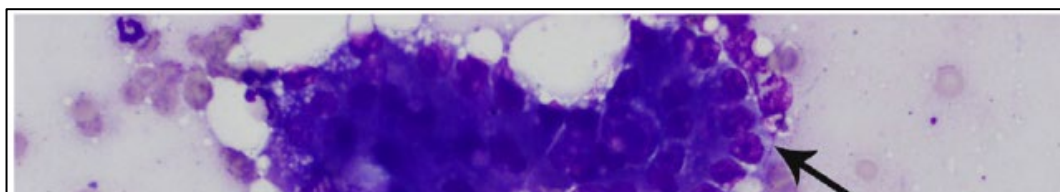
> J Feline Med Surg. 2015 Oct;17(10):858-63. doi: 10.1177/1098612X14557910. Epub 2014 Nov 4.

Safety of ultrasound-guided fine-needle aspiration of the feline pancreas: a case-control study

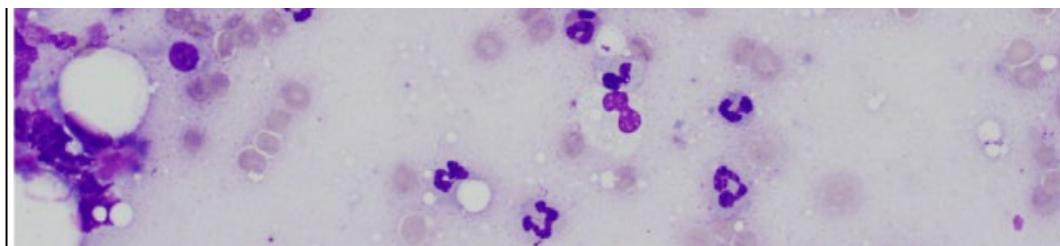


Sarah K Crain¹, Leslie C Sharkey², Amy P Cordner³, Christina Knudson⁴,
P Jane Armstrong²

Affiliations + expand



The cytologic recovery rate for the pancreatic samples was 67%. Correlation with histopathology, available in seven cases, was 86%. Pancreatic FNA in cats is a safe procedure



Feline Pancreatic Lipase Immunoreactivity

Forman et al JVIM 2004

- **Prospective: Healthy vs. Pancreatitis cats**
- **Spec fPLI (P<.0001) & U/S (P=.0073)**
- **fTLI & CT no difference**
- **Spec fPLI sensitive (100%) & specific (100%)**
- **U/S sensitive (80%) & specific (88%)**
- **“The authors suggested that a positive Spec fPL result indicated pancreatitis as a probable diagnosis, but that the test cannot be used to rule out pancreatitis”**



Gastrointestinal Laboratory

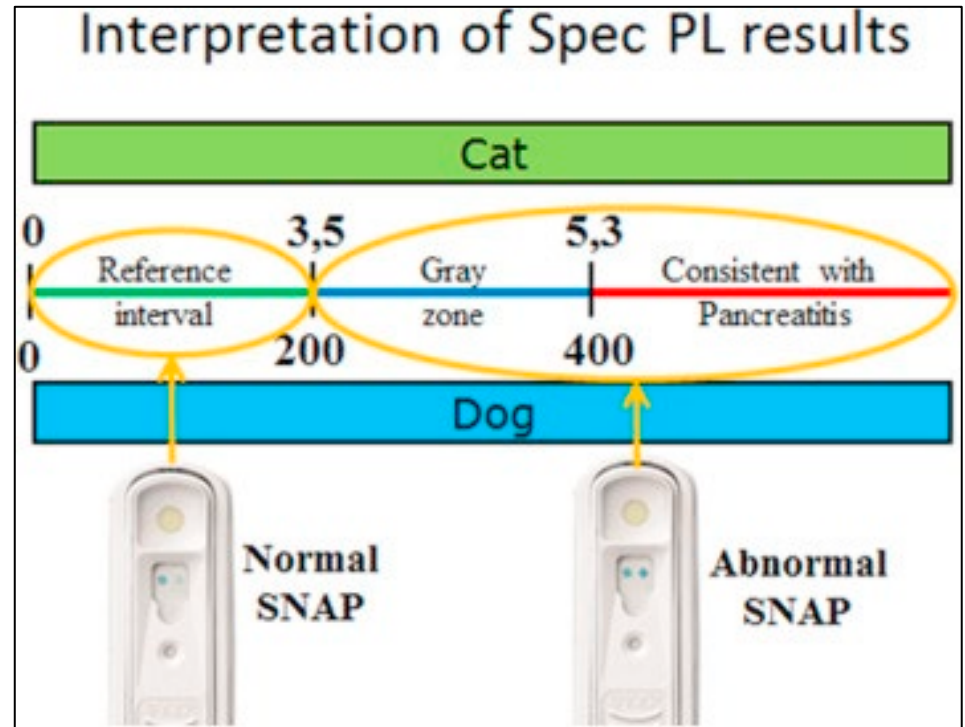
Dr. Jörg M. Steiner

Department of Small Animal Clinical Sciences

Texas A&M University, 4474 TAMU

College Station, TX 77843-4474

SNAP fPL

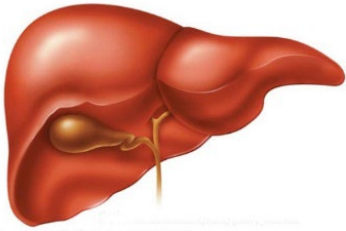


“Cats with a “normal” result are unlikely to have pancreatitis, whereas those with an “abnormal” result might have pancreatitis or a Spec fPL in the equivocal range”

#1 Hepatic Differential

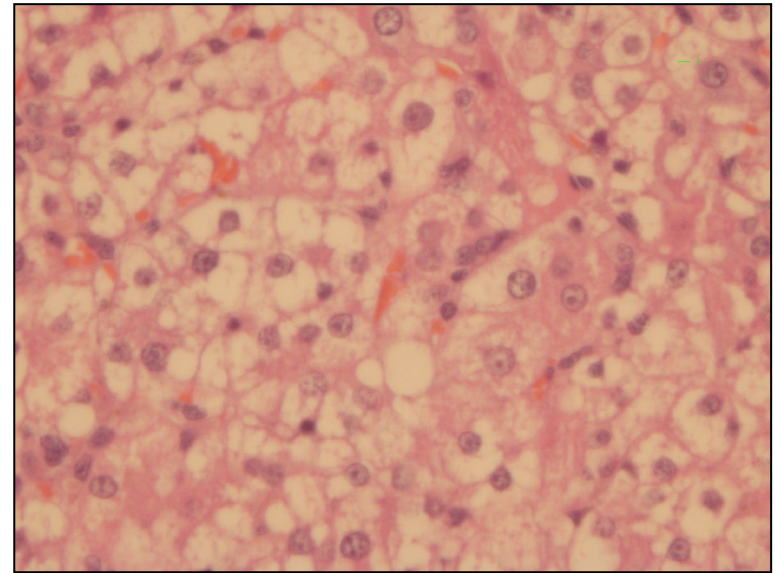
- Mature neutrophilia w/mild left shift
- Elevated Liver enzyme activity
- Total bilirubin $4.5 \mu\text{g/dL}$ (0.0 – 0.1)

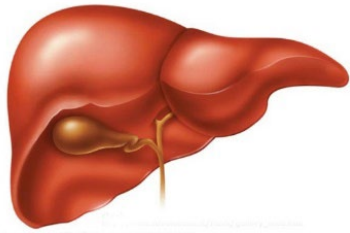




Feline Cholangitis

Neutrophilic
Lymphoplasmacytic
[Liver Flukes]





Feline Cholangitis

- Clinical Signs: lethargy, anorexia, vomiting, ptyalism
- PE: jaundice, febrile, dehydrated, cranial abdominal pain
- Diagnostics = ALT, ALP, t. bilirubin, CBC
- Abdominal Ultrasound: thick GB wall, echogenic particulate matter
 - tortuous & dilated cystic and common bile ducts

Percutaneous ultrasound-guided cholecystocentesis

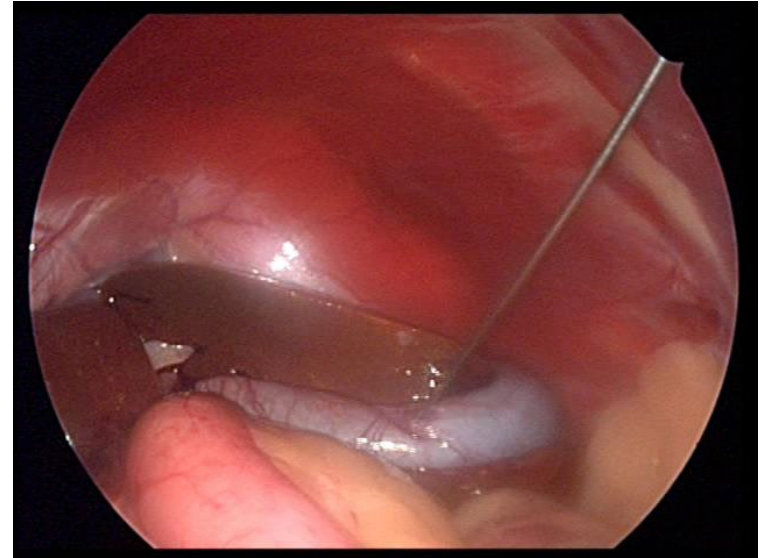


Rt ventral abdominal approach
22-gauge 1.5-in (3.81 cm) spinal needle
complete drainage of bile
(Savary-Bataille et al 2003)

Feline Cholangitis

Neutrophilic

- Cholecystocentesis
- Cytology & Culture
- Bacterial infection

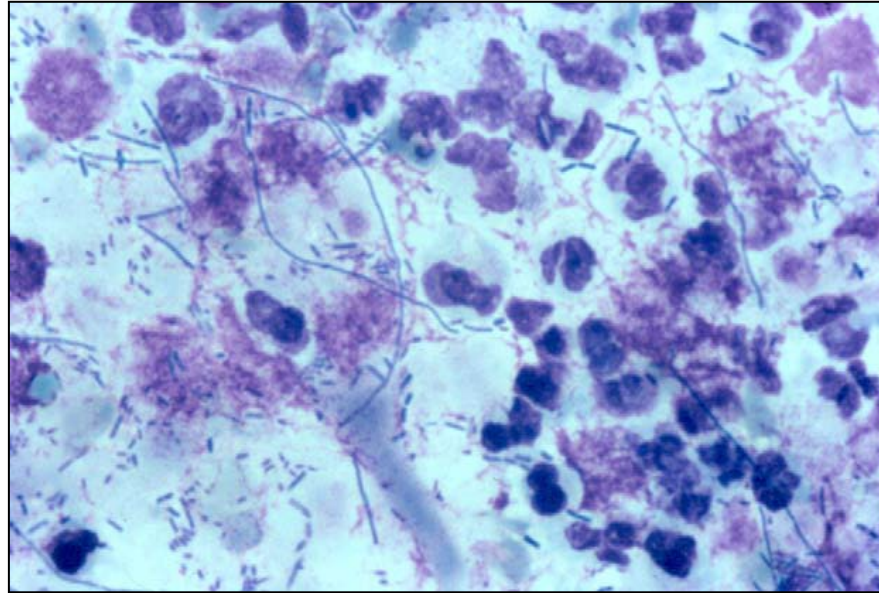


22 g

US-guided: thru R-medial liver lobe

Cytology: Diff-Quik & Gram-stain of bile

Degenerate neutrophils, intra & extra-cellular
Gm- Gm+ rods, Gm+ cocci

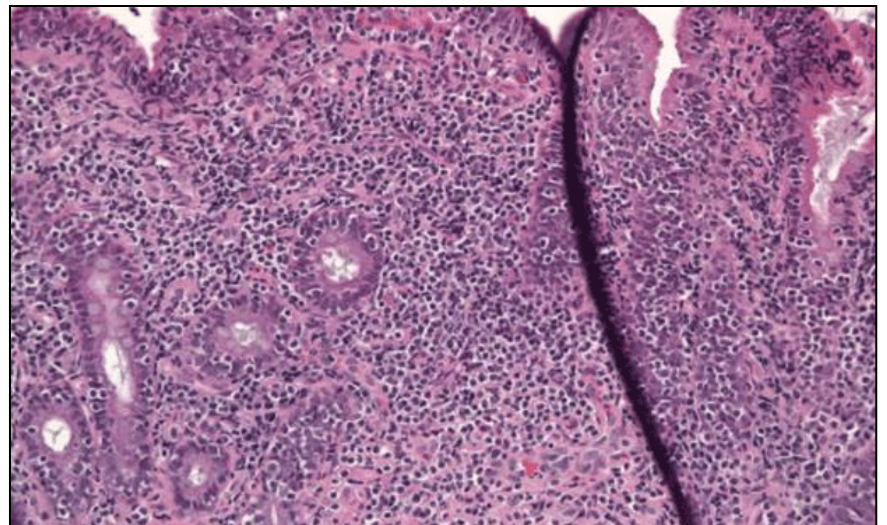


Brain et al. JFMS 2006

E coli, Salmonella, Klebsiella, Enterobacter, Bacteroides,
Strep, Enterococcus, Actinomyces, Pasteurella, Clostridium

Histopathology

- Liver – mod. suppurative cholangiohepatitis
- Pancreas – severe subacute LP pancreatitis w/ lobular atrophy
- Historical Endoscopy: moderate LP IBD



Feline “Triaditis”

- Relationship between inflammatory hepatic disease and inflammatory bowel disease, pancreatitis, and nephritis in cats.

Weiss DJ et al. JAVMA 1996

Feline Triaditis

- Cholangitis
 - (replaces Cholangiohepatitis - WSAVA)
- Pancreatitis (83%)
- Inflammatory Bowel Disease (50%)
- All Three – 39%



WSAVA World Congress 2011

T. Ishida, Tokyo Japan



- “a newly formed term”
- Lost In Translation
- Inflammation with 3 specific signs
 - Vomiting on white carpet
 - Vomiting on a couch
 - Vomiting on the owner’s bed
- Inflammatory dz involving 3 specific organs

Feline “Triaditis” All the Rage

- VIN search “All Resources” Feline Triaditis = 2867 hits
- Ettinger textbook 6th ed
- Sm Anim Gastroenterology (Steiner ed.)
- Problem-based Feline Medicine (J Rand)
- F Gaschen/Deb Zoran: “relatively common”
- J Steiner/K Richter: “Feline pancreatitis often concurrently occurs with cholangitis and IBD...” (Clin Vet Advisor 2nd)
- M Gaspar (VIN) “Remember that pancreatitis in cats is generally associated with concurrent GI disease (\pm cholangiohepatitis)”
- M Scherk 2010 “Triaditis, (enteritis, cholangitis and pancreatitis) appears to be more common than any of these component conditions on its own.”



Pancreatitis and **triaditis** in **cats**: causes and treatment.

Simpson KW.

J Small Anim Pract. 2015 Jan;56(1):40-9. doi: 10.1111/jsap.12313.

PMID: 25586805

PubMed



Prevalence and Clinicopathological Features of **Triaditis** in a Prospective Case Series of Symptomatic and Asymptomatic **Cats**.

Fragkou FC, Adamama-Moraitou KK, Poutahidis T, Prassinos NN, Kritsepi-Konstantinou M, Xenoulis PG, Steiner JM, Lidbury JA, Suchodolski JS, Rallis TS.



Triaditis: Truth and Consequences.

Lidbury JA, Mooyottu S, Jergens AE.

Vet Clin North Am Small Anim Pract. 2020 Sep;50(5):1135-1156. doi:

10.1016/j.cvsm.2020.06.008. Epub 2020 Jul 15.

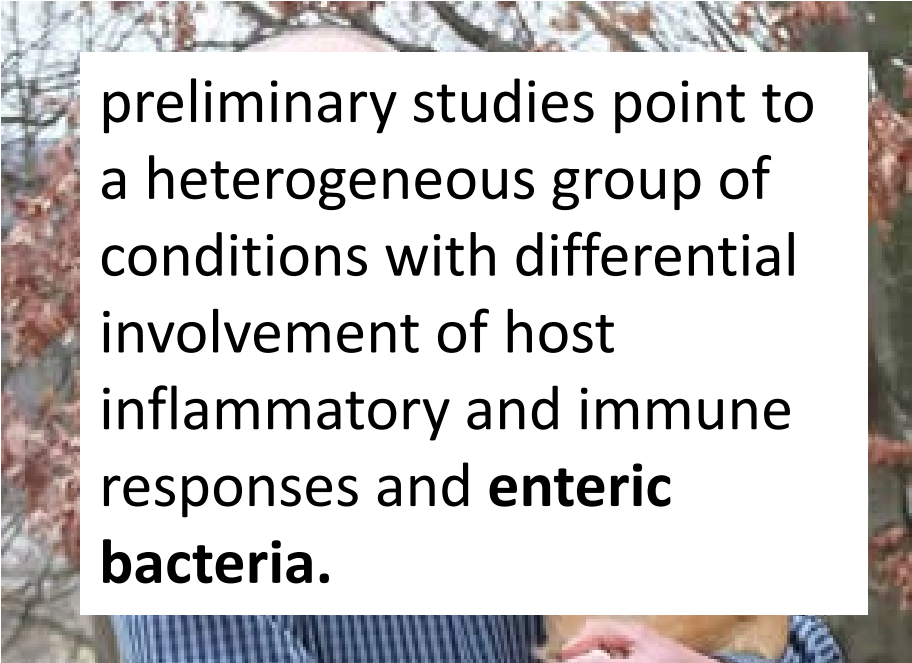


Feline comorbidities: What do we really know about **feline triaditis**?

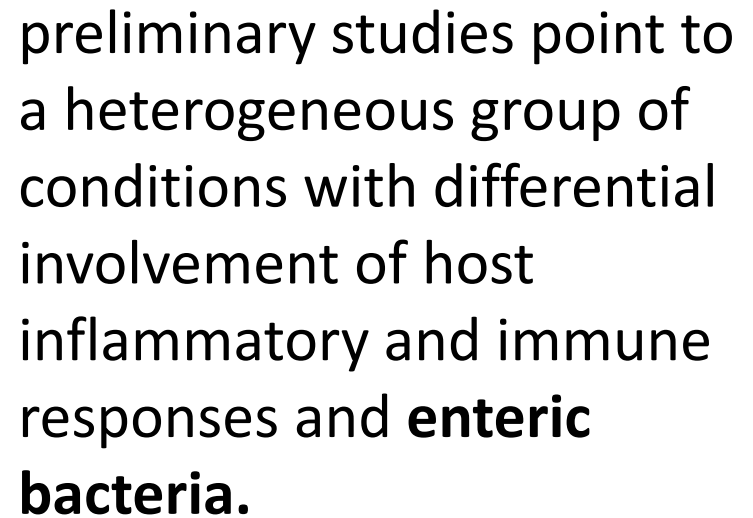
Černá P, Kilpatrick S, Gunn-Moore DA.

J Feline Med Surg. 2020 Nov;22(11):1047-1067. doi: 10.1177/1098612X20965831.

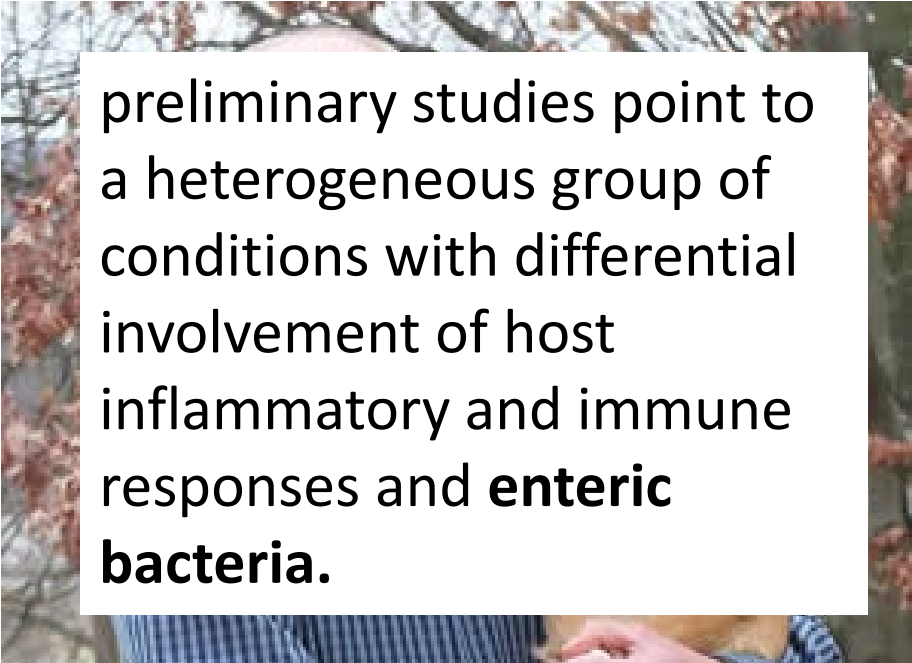
PMID: 33100169



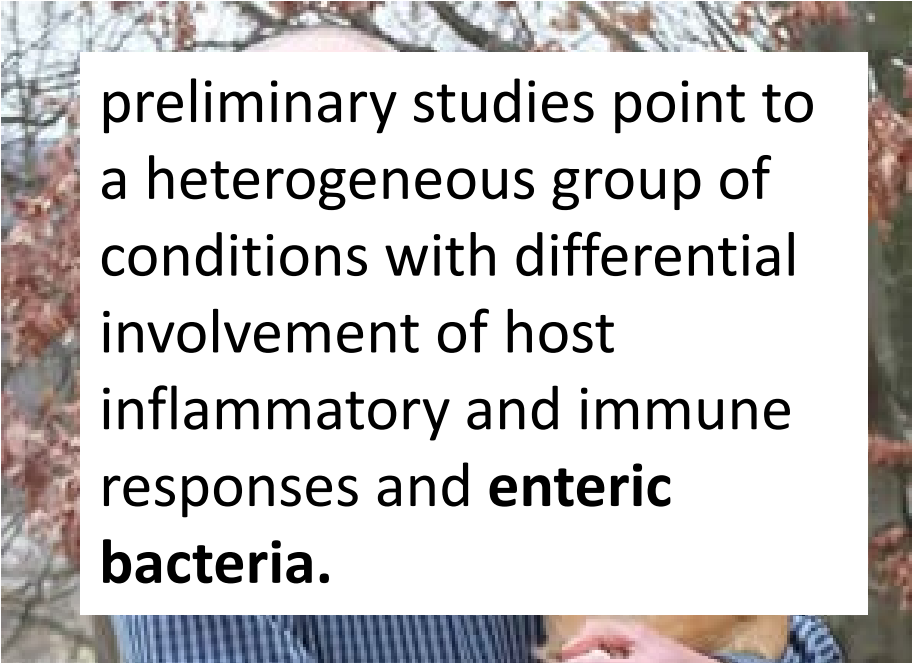
...it is known to include **infectious, autoimmune and physical components**. What is not known is whether different organs are affected by different diseases, or the same process; indeed, triaditis may be **part of a multiorgan inflammatory disease**.



preliminary studies point to a heterogeneous group of conditions with differential involvement of host inflammatory and immune responses and **enteric bacteria**.



It remains unclear whether enteric bacteria are a **primary cause or a secondary consequence** of pancreatitis and whether this may vary between individual cats.



Another challenge is determining an appropriate dietary approach for these patients. **The choice of diet** should be made based on which disease process seems to be the most severe.

WSAVA World Congress 2013

Stanley L. Marks, UC-Davis

BVSc, PhD, DACVIM (SAIM, Onc) DACVN



- Triaditis, a lay-term, hi prevalence
 - “may reflect common underlying disease mechanism”
- Cholangitis > pancreatitis/IBD
 - Temporal nature, specific cause...?
- Fact of Fiction?
 - A dearth of published prospective studies
 - “all cats with cholangitis should be evaluated for concurrent IBD and pancreatitis”

Dearth /dərTH/ 1. a scarcity or lack of something
"there is a dearth of evidence"



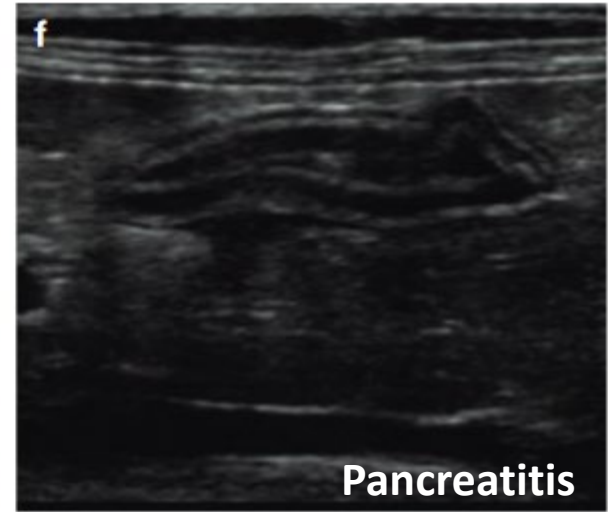
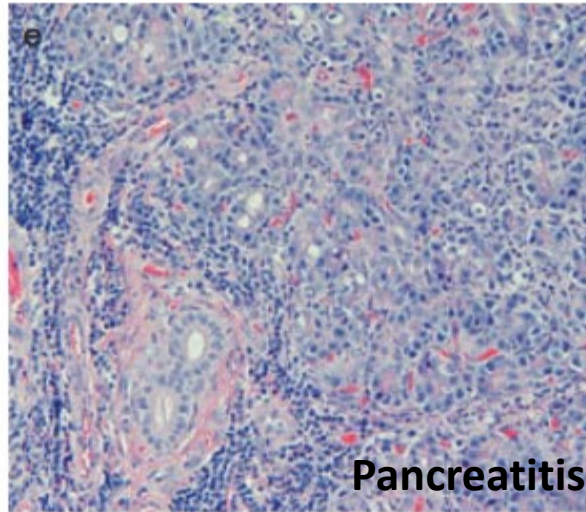
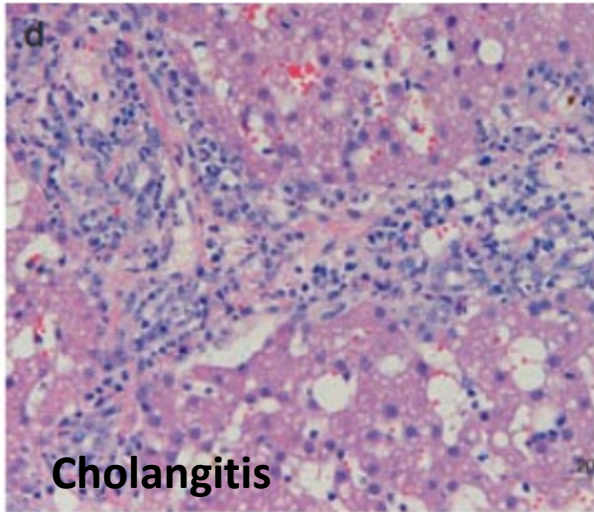
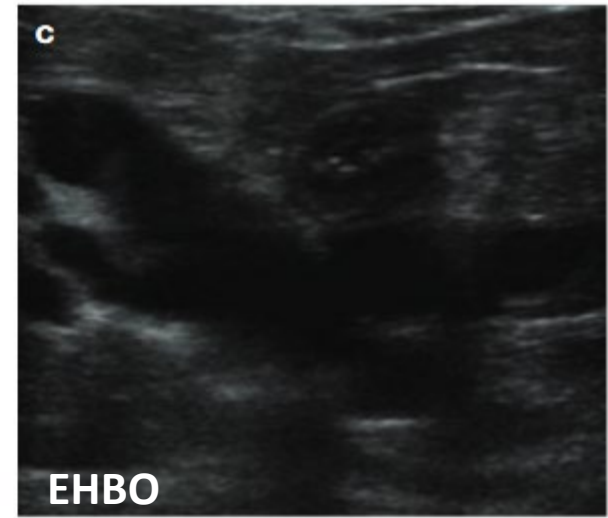
Bad hair day.

German AJ, German AC.

J Feline Med Surg. 2013 Jan;15(1):6-7.

PMID: 23254236



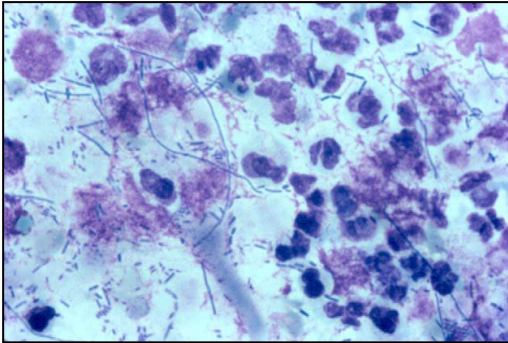


It was unclear whether the obstructing trichobezoar had *caused the triaditis*, or had occurred secondarily to *dysmotility arising from triaditis*.

Treating Feline Neutrophilic Cholangitis

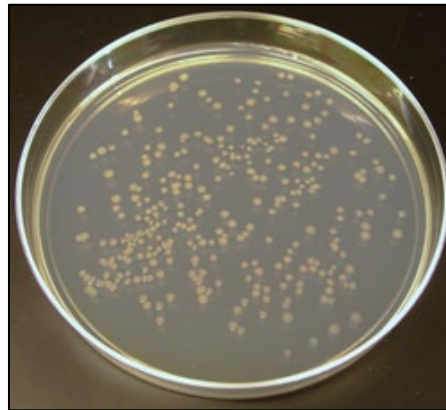


Non-Specific & Supportive
Fluids, Electrolytes, Nutrition, Pain
Vit K₁ {0.5-1.5 mg SQ, q12hr (2-3 doses)}



Ideally

Gallbladder Aspirate

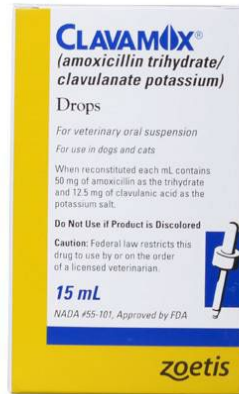


Culture



Antibiotic

Empirically Cover the Enterics



**Ampicillin
or
Clavimox**

+/-

**Metronidzole
or
Pradofloxacin**

2 months

Culture Negative or Empirically
IF chronic or IF antibiotic failure add
Prednisolone



1 mg/kg BID for 2 weeks;
1 mg/kg SID for 2 weeks;
0.5 mg/kg SID for 2 weeks;
0.5 mg/kg q48hr

Treating Feline Acute Pancreatitis



Non-Specific & Supportive
Fluids, electrolytes, acid/base, Nutrition, Pain
Antiemetics, Motility

Treating Feline Acute Pancreatitis

IV crystalloids

intravascular normovolemia

avoid volume overload

Maropitant (vomiting) and/or Ondansetron (nausea)

Metoclopramide (CRI), Cisapride (PO)

Buprenorphine, methadone, fentanyl, gabapentin

Mirtazapine (transdermal), capromorelin (PO)

Early Enteral Nutrition

Fresh Frozen Plasma = coagulopathy only

Vasopressors

Antibiotics – No, unless...

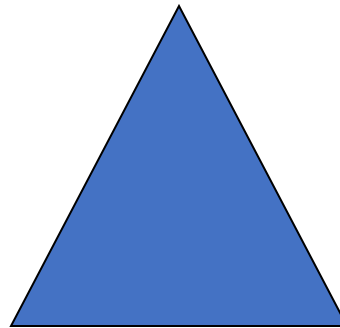
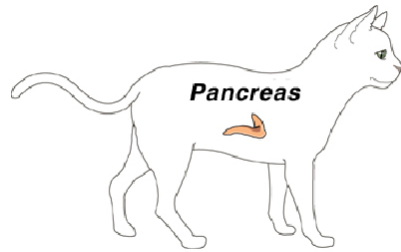
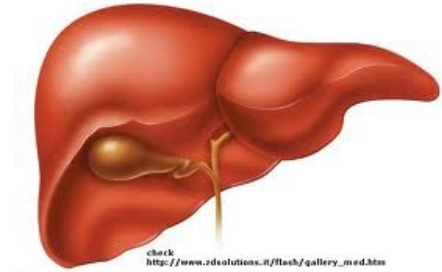
Corticosteroids...



Feline Triaditis

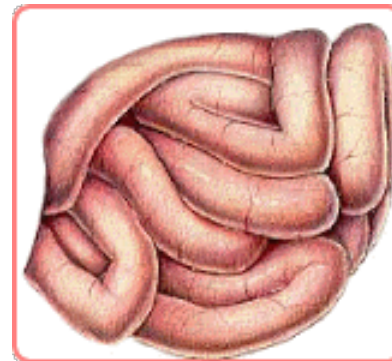
Immortality or The Vet Version of Saint's Triad?

CHOLANGITIS



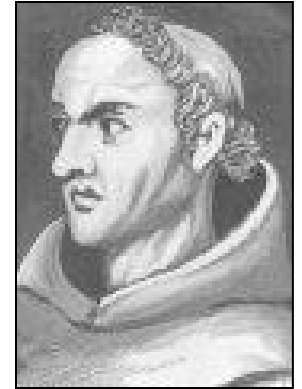
PANCREATITIS

IBD





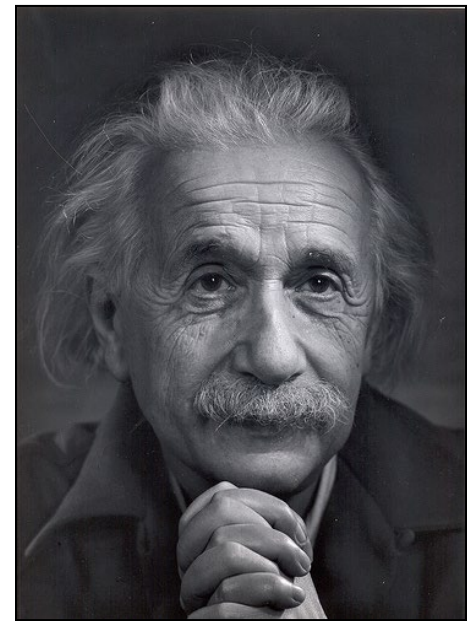
The Master



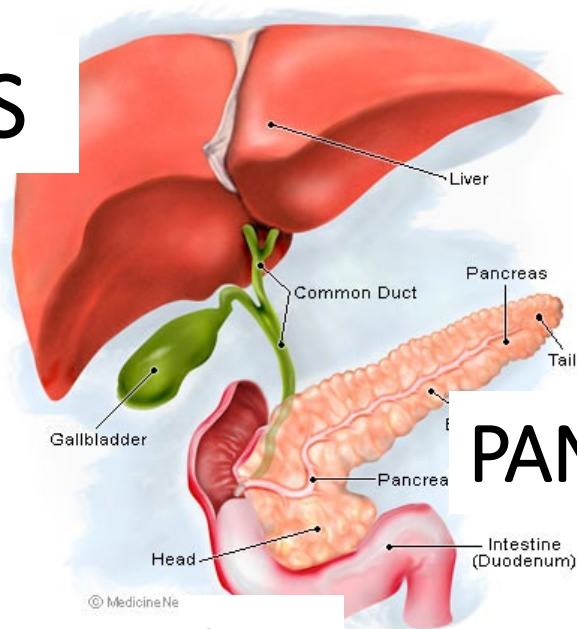
“One of the reasons that House appears to be such an exceptional diagnostician is that he is able to correctly apply Occam's razor and Hickam's dictum to the nth degree to diagnose even the most obscure of diseases.”

Albert Einstein's Thoughts

“Everything should be made as simple as possible, but not simpler.”



CHOLANGITIS



PANCREATITIS

IBD

Nutrition Quiz Question

“Management of feline pancreatitis is difficult and poorly defined. Considering the cat’s *proclivity* for development of hepatic lipidosis when deprived of adequate energy and nitrogen intake, keeping a feline patient off food while awaiting spontaneous resolution of pancreatic inflammation is an *unsound medical strategy*.”



Dr. Sharon Center

FDA NEWS RELEASE

FDA Conditionally Approves First Drug to Manage Acute Onset of Pancreatitis in Dogs



PANOQUELL®-CA1

Introducing the First FDA Conditionally Approved Innovative Solution for Acute Canine Pancreatitis

User Safety Warnings: Not for use in humans. Keep this medication out of reach of children. Limited data is available on the potential teratogenic effects of fuzapladib.

In case of accidental self-injection, skin contact, eye exposure, or accidental ingestion refer to the package insert.

To obtain a Safety Data Sheet, report suspected adverse drug experiences, or for technical assistance, contact Ceva Animal Health at 1-800-999-0297.

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or at www.fda.gov/reportanimalae.

 **PANOQUELL®-CA1**
(fuzapladib sodium for injection)

14 mg fuzapladib sodium per vial
4 mg/mL when reconstituted

For intravenous use in dogs only. Reconstitute before using.

PANOQUELL®-CA1 is a leukocyte function-associated antigen 1 (LFA-1) activation inhibitor.

Indication: For the management of clinical signs associated with acute onset of pancreatitis in dogs.

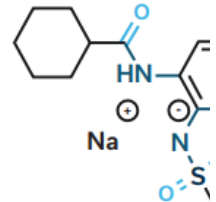
Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-567. It is a violation of Federal law to use this product other than as directed in the labeling.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.



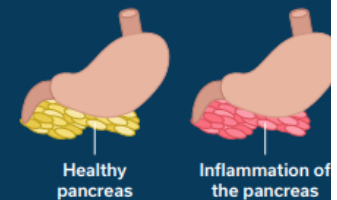
How it works - Take the "ITIS" out of pancreatitis.

PANOQUELL®-CA1 (fuzapladib sodium for injection) is a Leukocyte Function Associated Antigen-1 (LFA-1) activation inhibitor. LFA-1 plays a key role in extravasation, which is the process by which leukocytes leave the bloodstream to enter the tissues.



Role of LFA-1 in acute pancreatitis^{6,7}

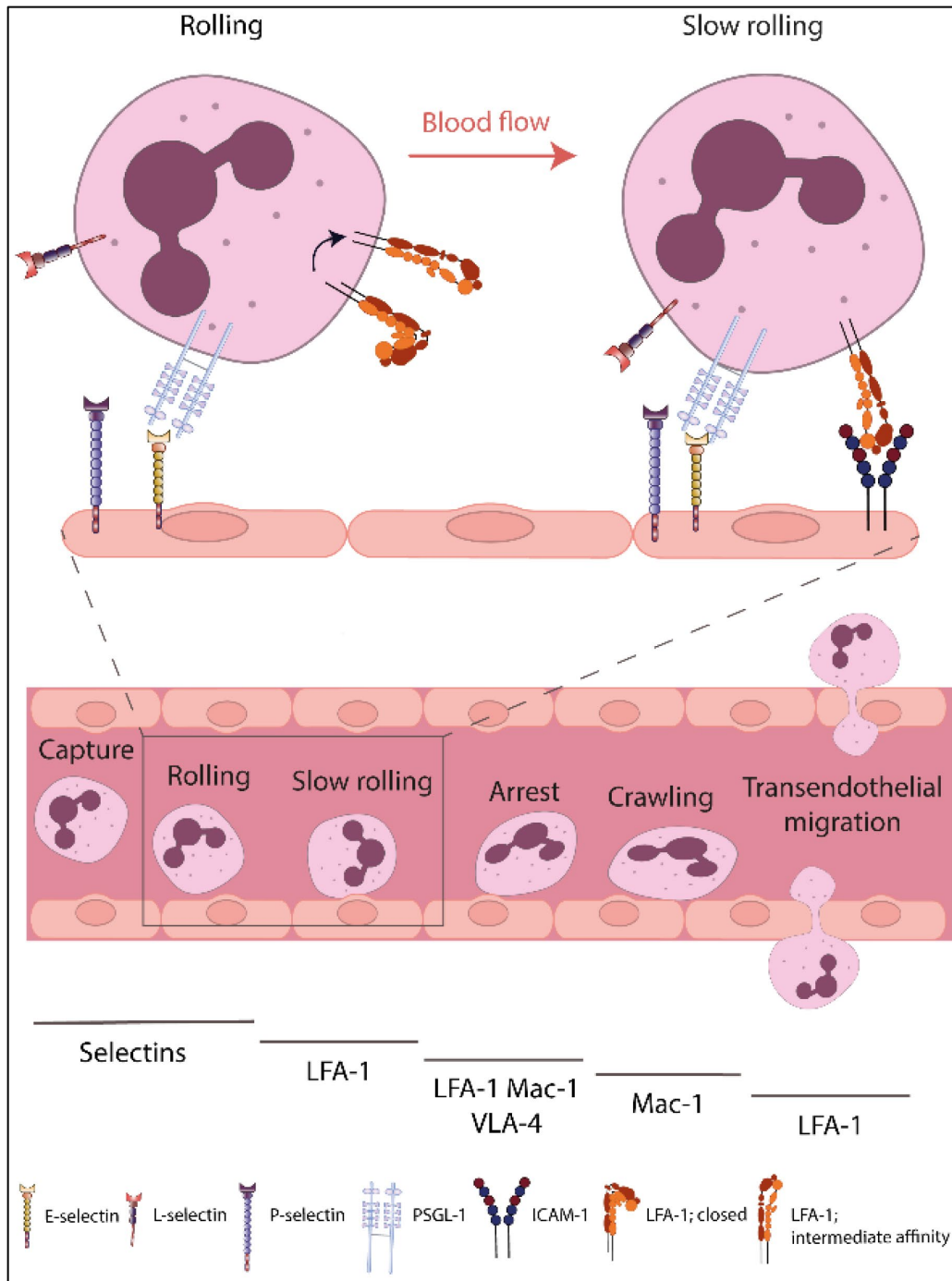
Infiltration of neutrophils is a hallmark of ACP. LFA-1 is essential to this process. LFA-1 is expressed on the neutrophil surface and its ligand, ICAM-1, is expressed on the vascular endothelium. Together they mediate neutrophilic-driven inflammation and migration into pancreatic and extrapancreatic tissues.



The activation of the LFA-1 by chemokines and the upregulation of its ligand, ICAM-1, lead to "arrest" of circulating neutrophils at the site of inflammation. Arrested neutrophils now stick to the blood vessel wall, "adhesion", and invade, "migration", into the tissues.

Once in the tissue, neutrophils release additional inflammatory mediators. These mediators attract more neutrophils and other inflammatory cells.

Especially in severe cases, there is extrapancreatic inflammation, potentially leading to multi-organ failure, systemic inflammatory response syndrome (SIRS) and death.



MCAI-5 is the “Modified Canine Activity Index” and uses these 5 signs to objectively measure severity of disease²:



DEHYDRATION



VOMITING



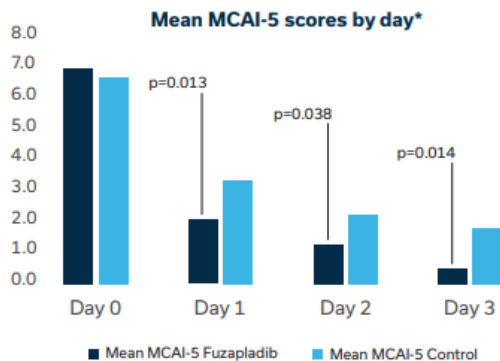
CRANIAL
ABDOMINAL PAIN



DECREASED
APPETITE



DECREASED
ACTIVITY



Statistically significant reduction in clinical signs to day 3 compared to control group

PANOQUELL[®]-CA1 is proven to quickly reduce clinical signs and measurable values such as canine pancreas-specific lipase (Spec cpL) and C-reactive protein (CRP) associated with ACP.⁴

*Dogs treated with fuzapladiB had a statistically significant reduction in MCAI-5 scores compared to control ($p=0.0135$), significant daily differences are compared to day 0.

⁴<https://animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFoi/1313>



Christian Veterinary Mission

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