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VETERINARY MEETING & EXPO

Clinical Approach to Chronic GI Disease in the Feline Patient

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CONFLICT OF INTEREST DISCLOSURE

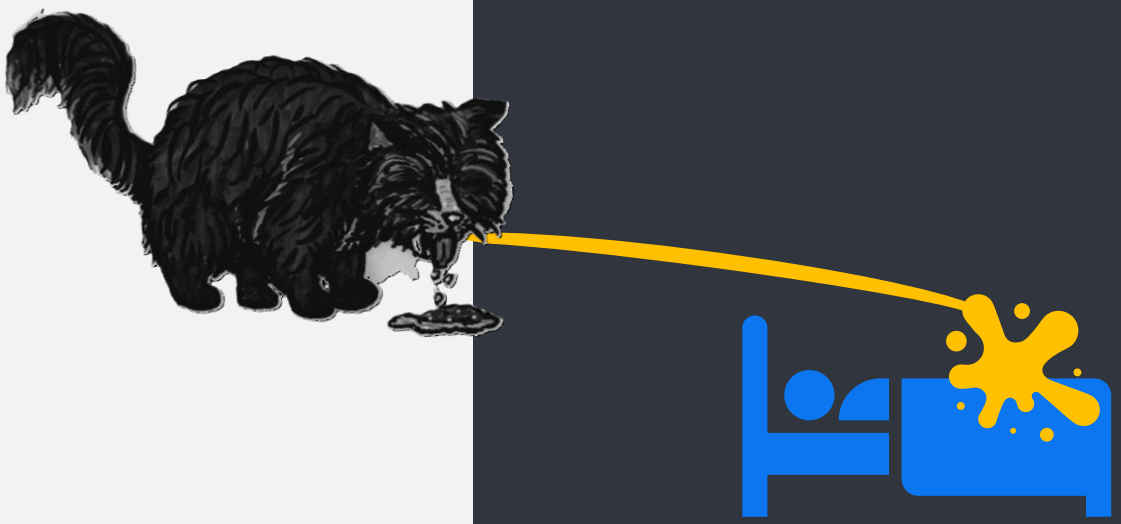
I am a full-time IDEXX employee

The information contained herein is intended to provide general guidance only. Diagnosis, treatment, and monitoring should be patient specific and is the responsibility of the veterinarian providing primary care.

Learning objectives

1. Define feline chronic enteropathy (CE)
2. Describe common clinical presentations
3. Formulate a systematic diagnostic approach to the feline patient with gastrointestinal signs
4. Examine how to integrate diagnostic results with clinical picture for feline patients with CE
5. Evaluate treatment strategies and long-term management plans in feline CE using case examples and literature review

Up to 20-30% of veterinary visits in companion animals are reported to be related to vomiting or diarrhea



Jergens AE, Heilmann, RM (2022) Canine Chronic Enteropathy – Current state of the art and emerging concepts. Front. Vet. Sci.

Impact of feline chronic enteropathy (CE) in veterinary medicine

1. Prevalence unknown; likely the most common cause of causes of primary GI disease in cats
2. One of the most neglected chronic diseases of cats
3. Clinical signs not specific, inconsistent across cases
4. Idiopathic (IBD) is the most common cause of feline CE

Source: Feline IBD; TX vet foundation 2016, Erin Dresner DVM, MS, DABVP: https://www.tvmf.org/articles/feline-inflammatory-bowel-disease/#:~:text=Several%20individual%20diseases%20associated%20with,diagnose%20and%20treat%20your%20cat.

Definition of feline chronic enteropathy

Journal of Veterinary Internal Medicine Open Access

J Vet Intern Med. 2023 May 2;37(3):794–816. doi: 10.1111/jvim.16690

ACVIM consensus statement guidelines on diagnosing and distinguishing low-grade neoplastic from inflammatory lymphocytic chronic enteropathies in cats

Sina Marsilio [1,†,✉], Valerie Freiche [2,†], Eric Johnson [3], Chiara Leo [4], Anton W Langerak [5], Iain Peters [6], Mark R Ackermann [7,8]

Author information · Article notes · Copyright and License information

PMCID: PMC10229359 PMID: 37130034

At least 3 weeks duration, signs of gastrointestinal disease (GI) where extra-GI, metabolic, and infectious causes have been ruled out

Prioritization of differential list for ***GI signs*** changes with age

Intestinal parasites

Toxin

Antibiotics, medications

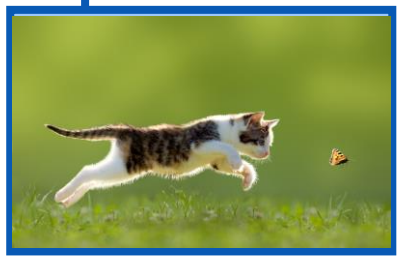
Metabolic disease

Neoplasia

Young

Older

Dietary indiscretion or foreign body

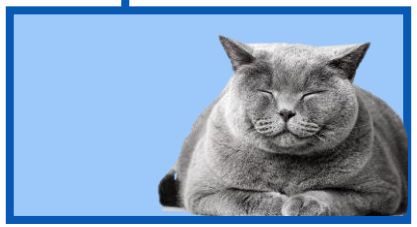


Viral infection

Infectious agents

Stress

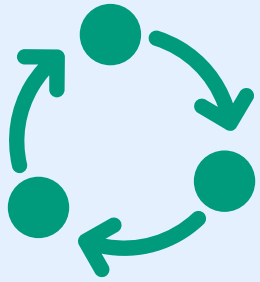
Inflammatory disease



Endocrine disease

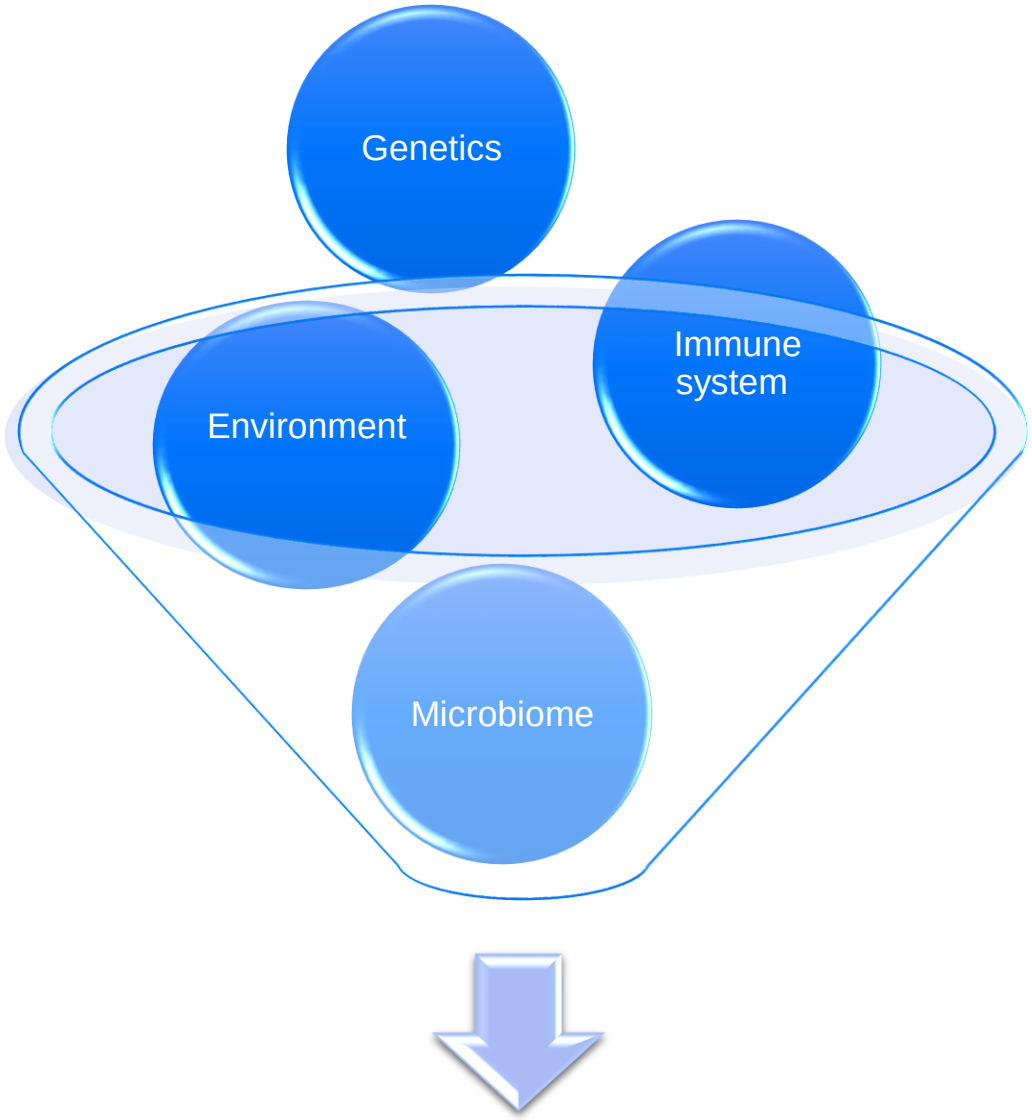
IDEXX

Etiopathogenesis

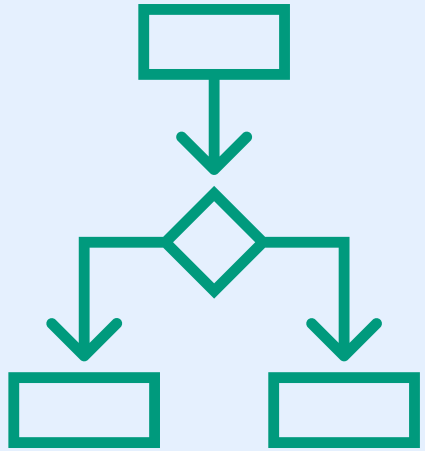


Exact cause of CIE is unknown; we do know it is multifactorial

- Environmental influences
- Exaggerated immune response
- Interplay between innate and adaptive immune responses
- Imbalanced microbiome



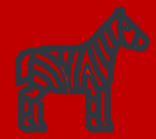
Classification



Feline chronic enteropathy (feline CE)

Chronic inflammatory enteropathy (CIE)

Small cell lymphoma (SCL)
or
Low grade intestinal T-cell lymphoma (LGITL)



Zebras

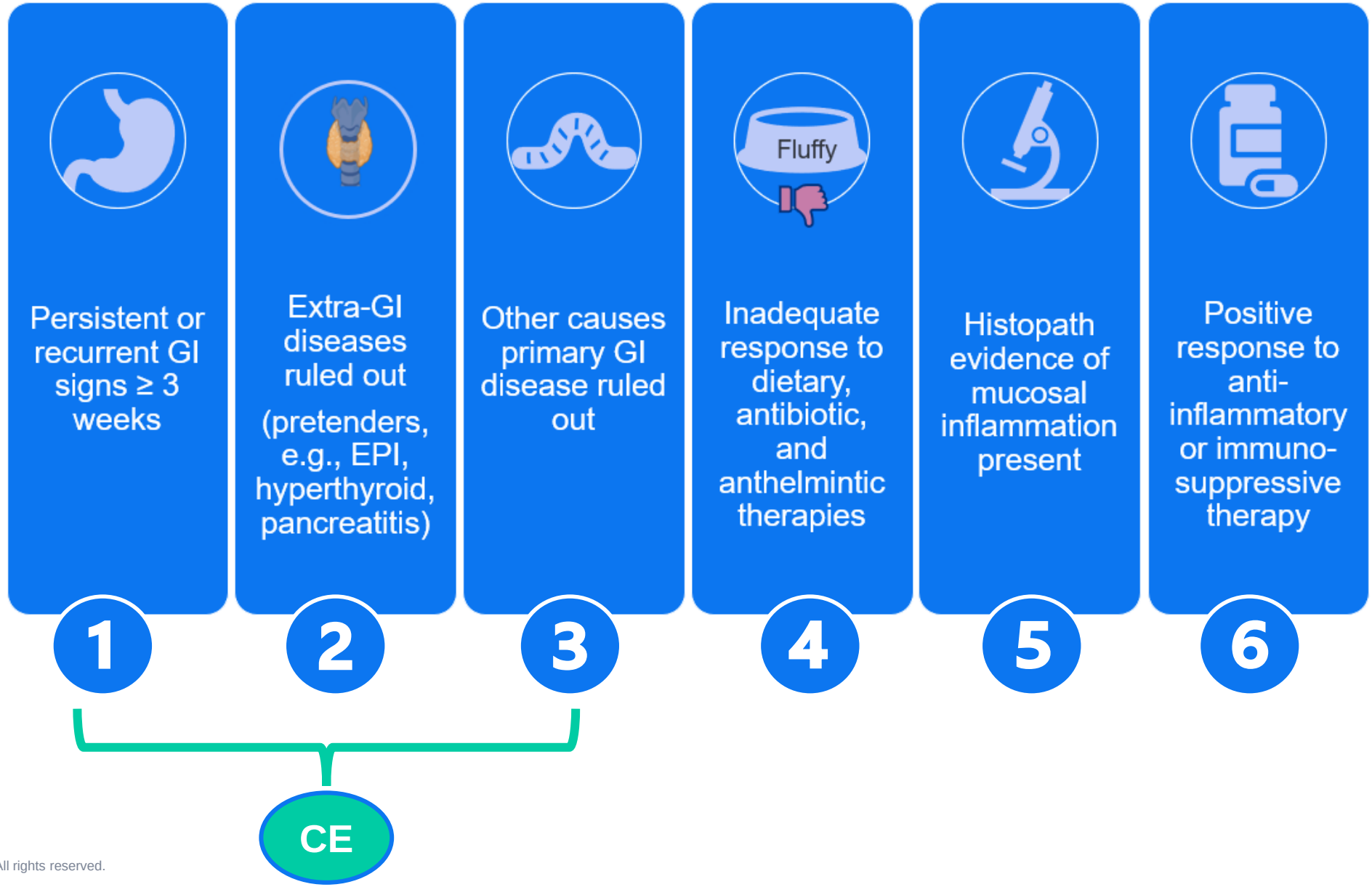
Immunosuppressive-responsive (IRE/IBD)

Food responsive (FRE)

Antibiotic responsive (AR)
?

1.Marsilio, JSAP, 2021
2.Bandara et al.,JSAP, 2023;
3.Marsilio et al..,JVIM, 2023
4.Guilford et al., JVIM 2001

Feline chronic inflammatory enteropathy (CIE/IBD) – a subset of CE



Diagnosis

Diagnosis starts with asking the right questions!!!

Image credit: Pixabay

All the gory details…

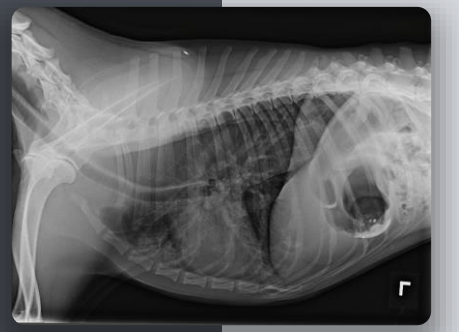
Acute or chronic symptoms

Vomiting or regurgitation

Diarrhea or constipation

Small or large bowel diarrhea

Characterization and objectification are key



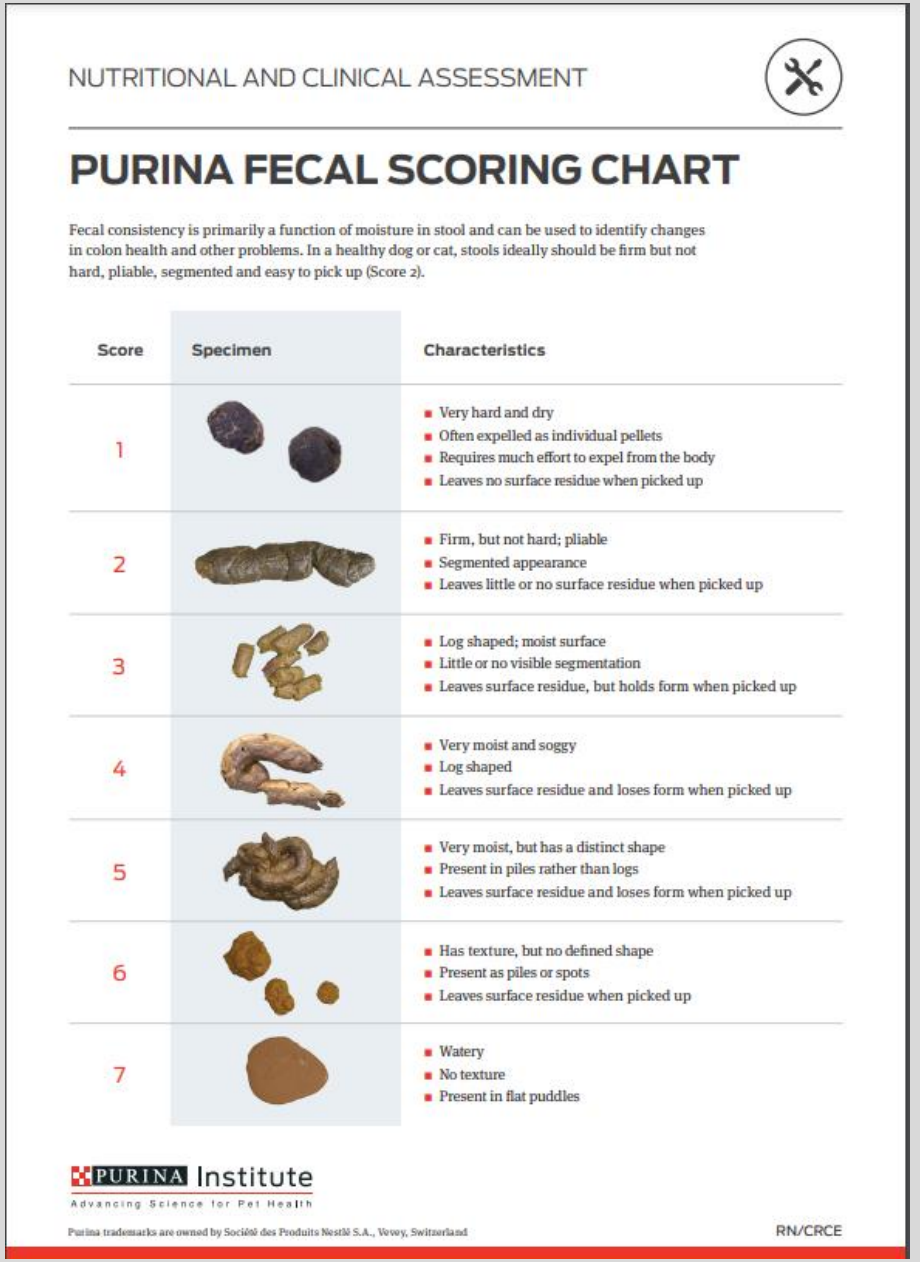
Vomiting vs. Regurgitation

- Active vs. passive
- Relation to eating
- Shape of material expelled
- Presence/absence of digested vs. undigested food
- Change in appetite
- Presence/absence of weight loss

Large or Small-Bowel Diarrhea

- Frequency
- Urgency
- Straining
- Quantity
- Presence of mucus/fresh vs. digested blood/undigested food
- Posture
- Presence/absence of weight loss
- Change in appetite

Purina fecal score



NUTRITIONAL AND CLINICAL ASSESSMENT

PURINA FECAL SCORING CHART

Fecal consistency is primarily a function of moisture in stool and can be used to identify changes in colon health and other problems. In a healthy dog or cat, stools ideally should be firm but not hard, pliable, segmented and easy to pick up (Score 2).

Score	Specimen	Characteristics
1		■ Very hard and dry ■ Often expelled as individual pellets ■ Requires much effort to expel from the body ■ Leaves no surface residue when picked up
2		■ Firm, but not hard; pliable ■ Segmented appearance ■ Leaves little or no surface residue when picked up
3		■ Log shaped; moist surface ■ Little or no visible segmentation ■ Leaves surface residue, but holds form when picked up
4		■ Very moist and soggy ■ Log shaped ■ Leaves surface residue and loses form when picked up
5		■ Very moist, but has a distinct shape ■ Present in piles rather than logs ■ Leaves surface residue and loses form when picked up
6		■ Has texture, but no defined shape ■ Present as piles or spots ■ Leaves surface residue when picked up
7		■ Watery ■ No texture ■ Present in flat puddles

PURINA Institute
Advancing Science for Pet Health

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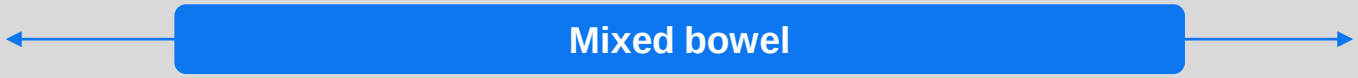
RN/CRCE

Source:https://www.purinainstitute.com/centresquare/nutritional-and-clinical-assessment/purina-fecal-scoring-chart; shared with permission 2023.

Small or large bowel diarrhea?

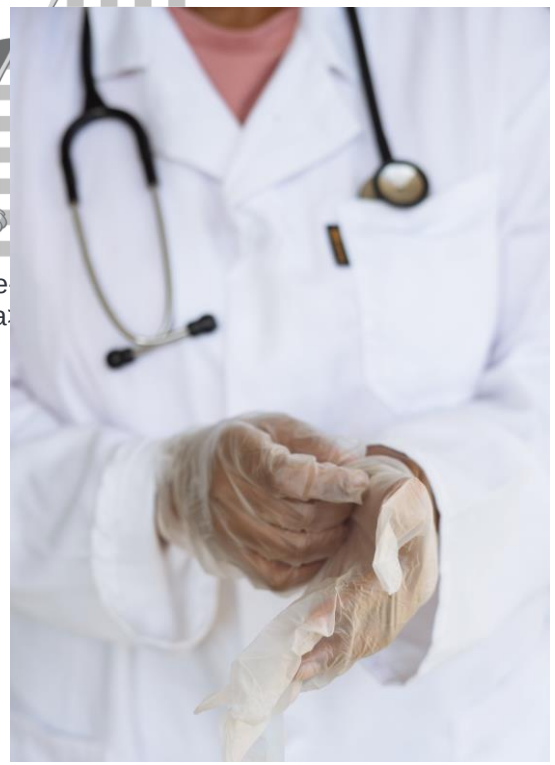
	Small Bowel	Large Bowel
+ Weight Loss	★ Often	Rarely
+ Appetite	★ N, ↓, or occasionally ↑	Generally normal
+ Volume	N, or mild/moderate ↑	Generally ↓
+ Frequency	N, or mild/moderate ↑	↑
+ Urgency	Sometimes	Often
+ Tenesmus	No	★ Often
+ Blood	Sometimes (melena)	★ Often (hematochezia)
+ Mucus	No	★ Often
+ Albumin	★ Normal or ↓	Normal



Diarrhea or constipation!!??

Constipation or diarrhea?

<a href="https://www.vecteezy.com/free
vector/cat">Cat Vectors by Vecteezy



- Productive vs. non-productive
- Mucus
- Tenesmus
- Other GI signs
- Labs
- PHYSICAL EXAMINATION !
  - Observe
  - Rectal
  - Abdominal palpation
- +/- Radiographs

Cat presents for diarrhea

Why are categorization, classification, and minute details so important?

Develop

An ordered, reasonable list of differential diagnoses (ddx)

Prioritize

Diagnostic recommendations

Guide

Empirical & symptomatic therapy

Direct

Best approach for invasive procedures

Ultimate goal

Most efficient and cost-effective way to definitive diagnosis

Prioritization if diagnostics for cats with chronic GI signs

Tier 1

- Minimum data base: CBC, Chemistry, UA
- Fecal parasite (vs. empirical deworming)
- Retroviral testing
- Thyroid hormone (T4) (> 6yrs)
- fPL
- TLI
- Cobalamin/folate

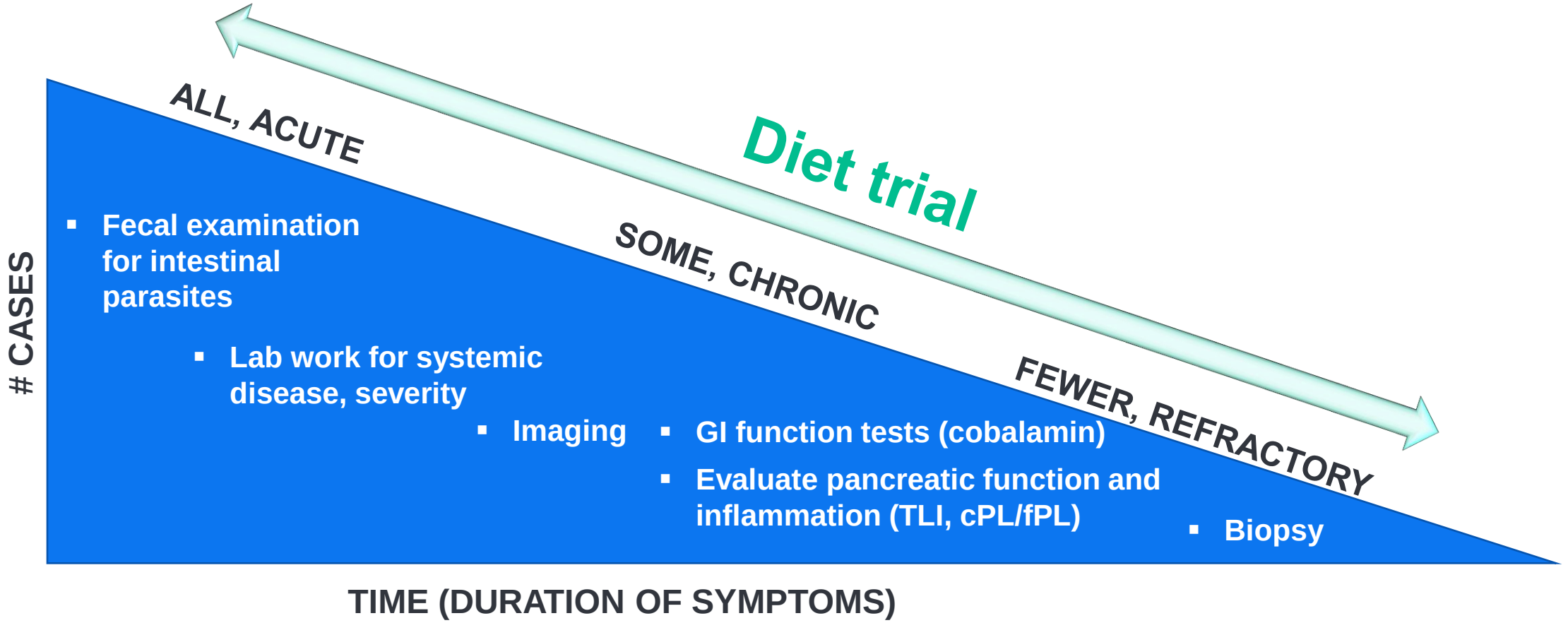
Tier 2

- fPL/TLI/cobalamin/folate
- Diarrhea RealPCR Panel™
- Regional infectious disease
- Diagnostic imaging
- Dysbiosis Index?
- Food elimination trial

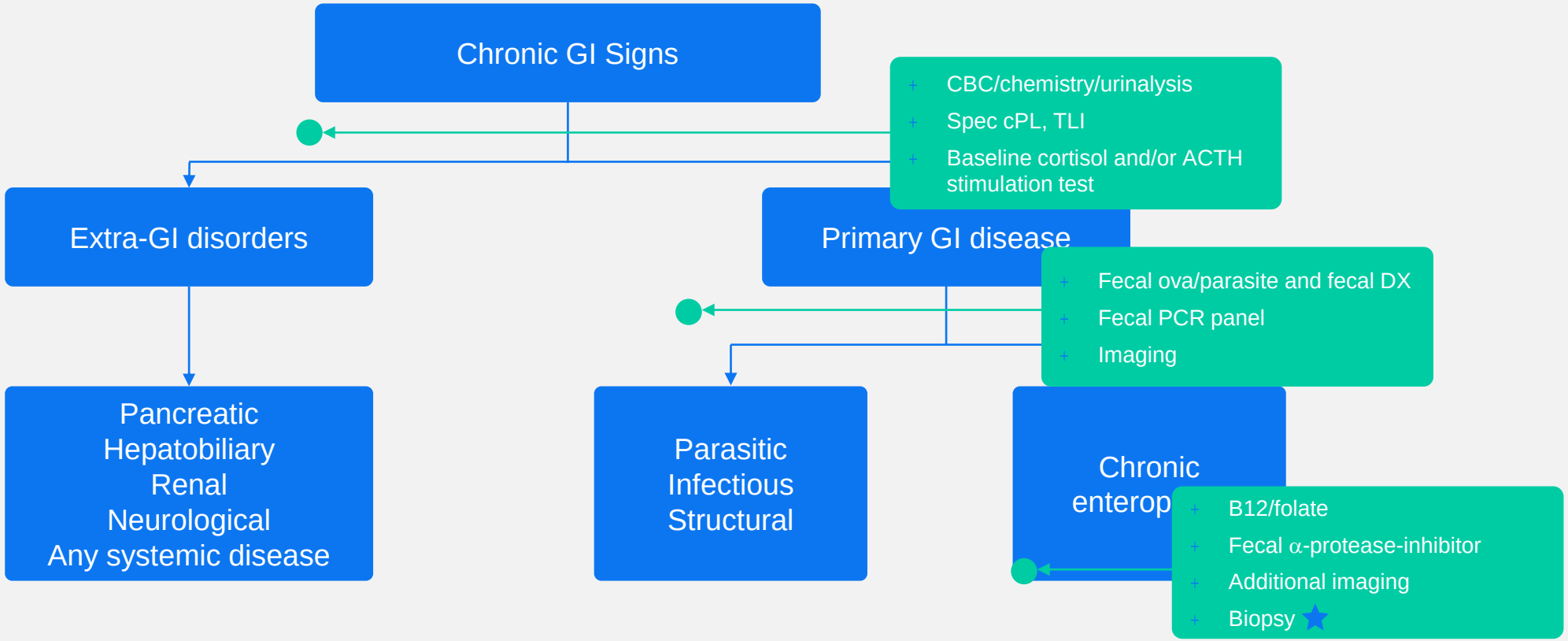
Tier 3

- GI biopsy
  - Histopath
  - Special stains
  - IHC
  - PARR
  - PCR

Stepwise approach to GI disease



Rule-out extra-GI disorders and non-inflammatory enteropathies



Clinical picture: feline CE

Common presentation

- Signalment
  - DSH, Siamese
  - Avg age 8 yrs (1.3-16 yrs)
  - LGITL 12.5 yrs (4-20 years)
- Clinical signs
  - Weight loss
  - Vomiting
  - Anorexia
  - Diarrhea
  - 1 or 2 clinical signs common

Common physical examination findings

- Underconditioned
- Intestinal thickening or “ropey”
- Nodules or masses
- Mesenteric lymphadenomegaly
- Sometimes very normal

Common or classic screening lab abnormalities

- Inflammatory leukogram
- +/- Eosinophilia
- Mild to moderate anemia, non-regenerative
- Markers of chronic GI bleeding
  - Microcytosis
  - Low reticulocyte-Hgb
  - Disproportionately elevated BUN
- Albumin
- Globulins

Laboratory biomarkers overlap and thus ***do not*** differentiate CIE/IBD from LGITL

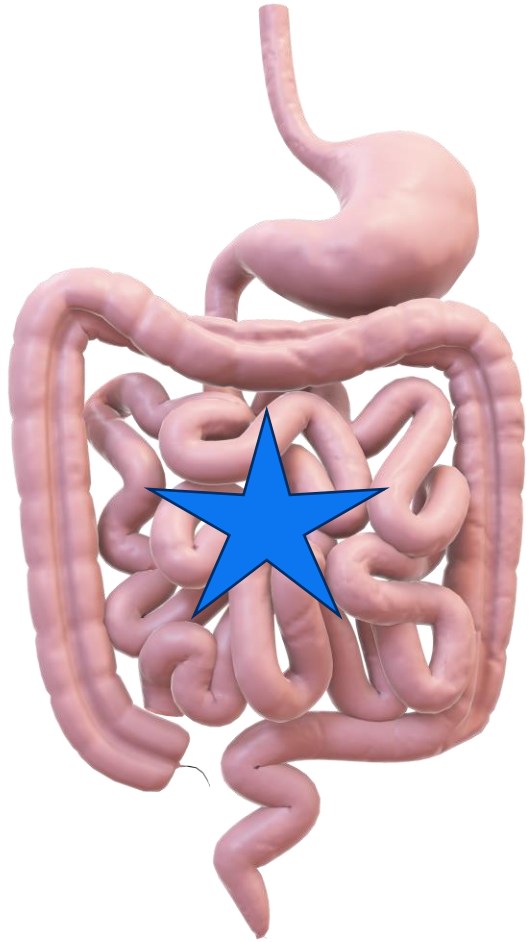
• Albumin ↓ or N	GI protein loss, inflammation
• Globulins ↑, N, or ↓	GI protein loss, inflammation
• Cobalamin ↓ or N	Absorption
• Folate* ↓, N, or ↑	Absorption and dysbiosis
• PLI ↑ or N	Pancreatic inflammation
• TLI ↑, N, or ↓	Pancreatic inflammation, function

*False increase possible with hemolysis

Marsilio et al., JVIM, 2023

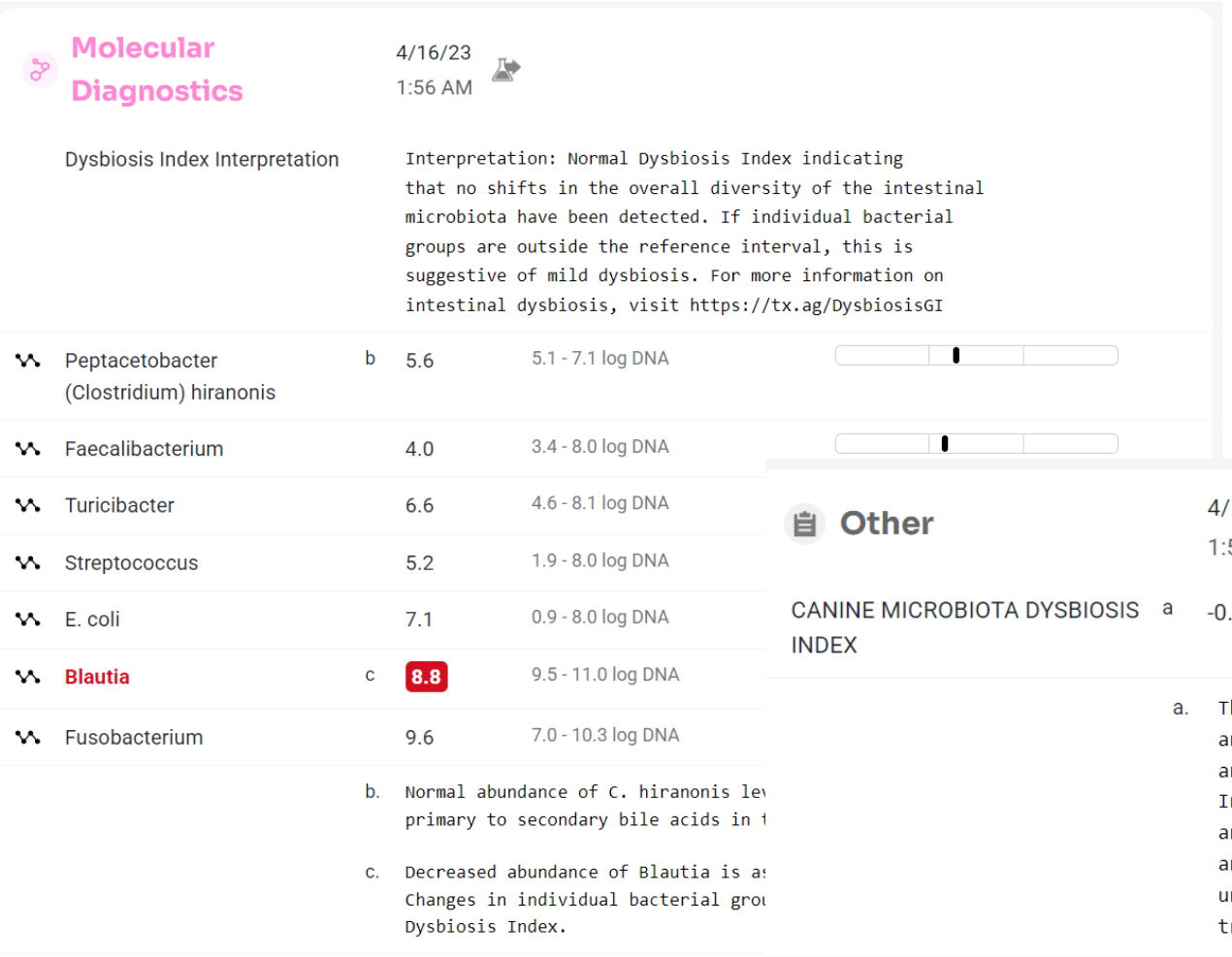
Anatomic distribution of CE

- Any GI segment affected
- Site predilection of disease:
  - Jejunum
    - Ileum
    - Duodenum
      - Stomach
      - Colon



Marsilio et al., JVIM 2023

Dysbiosis index



Molecular Diagnostics 4/16/23 1:56 AM

Dysbiosis Index Interpretation		Interpretation: Normal Dysbiosis Index indicating that no shifts in the overall diversity of the intestinal microbiota have been detected. If individual bacterial groups are outside the reference interval, this is suggestive of mild dysbiosis. For more information on intestinal dysbiosis, visit https://tx.ag/DysbiosisGI		
Peptacetobacter (Clostridium) hiranonis	b	5.6	5.1 - 7.1 log DNA	
Faecalibacterium		4.0	3.4 - 8.0 log DNA	
Turicibacter		6.6	4.6 - 8.1 log DNA	
Streptococcus		5.2	1.9 - 8.0 log DNA	
E. coli		7.1	0.9 - 8.0 log DNA	
Blautia	c	**8.8**	9.5 - 11.0 log DNA	
Fusobacterium		9.6	7.0 - 10.3 log DNA	

b. Normal abundance of C. hiranonis lev primary to secondary bile acids in t

c. Decreased abundance of Blautia is as Changes in individual bacterial grou Dysbiosis Index.

Other 4/16/23 1:56 AM

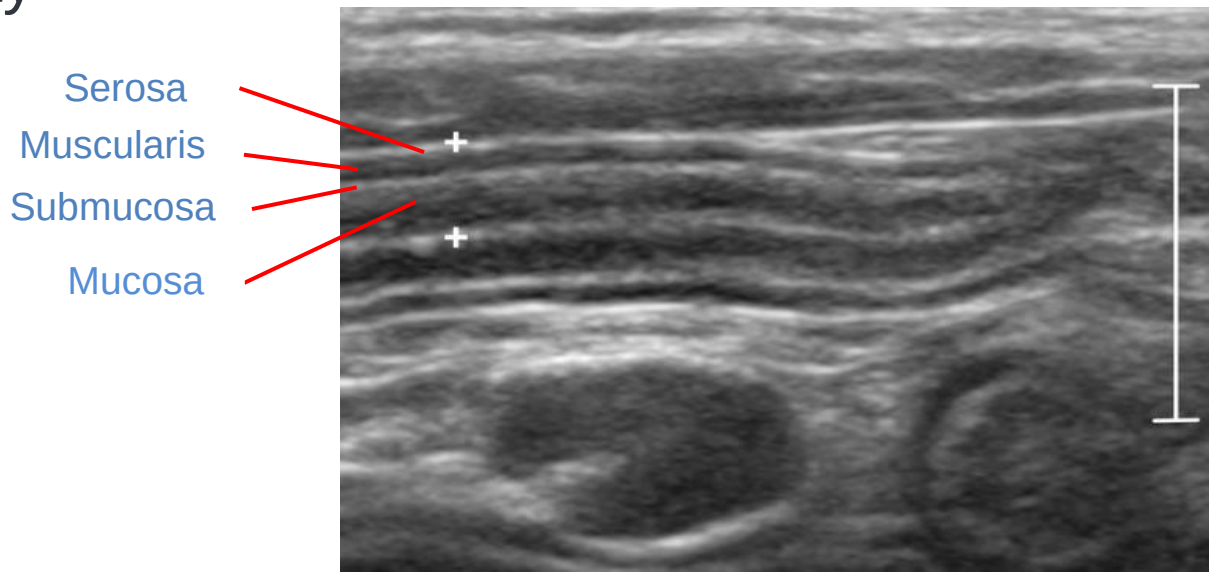
CANINE MICROBIOTA DYSBIOSIS INDEX	a	-0.5

a. The DI reference interval is < 0. The Dysbiosis Index (DI) quantifies seven key bacterial groups and provides an assessment of the overall diversity and shifts in the fecal microbiota. An increased dysbiosis index and/or changes in the individual bacterial groups result from alterations in the intestinal environment. Intestinal dysbiosis impacts not only the health of the intestinal tract, but also the overall health of the animal. Common causes include chronic enteropathy, exocrine pancreatic insufficiency (EPI), and recent antibiotic or proton-pump inhibitor administration. Resolution of dysbiosis requires addressing the underlying cause and may also include dietary modification, prebiotics, probiotics and/or fecal transplantation. The Dysbiosis Index is performed at the Gastrointestinal Laboratory at Texas A&M University.

- Considering fecal microbiota transplant
- Evaluating response to FMT
- Evaluating donor

Diagnostic imaging

- Radiographs have limited diagnostic utility [1]
  - Obstructive pattern
  - Radiopaque foreign material
  - Mineralization
- Abdominal ultrasound (AUS)
  - Cross sectional evaluation, esp. thickness
  - Anatomic location
  - Mural architecture
  - Mesenteric lymph node [2]
  - Other organs, esp. pancreas, liver
  - Effusion [2]
  - Assist sampling



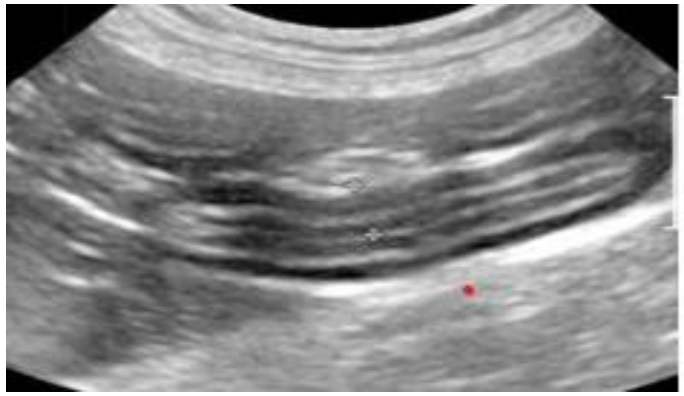
Normal jejunum, 2.7 mm

Figure adapted from: Paulin et al., BMC Vet Res, 2018
https://creativecommons.org/licenses/by/4.0/

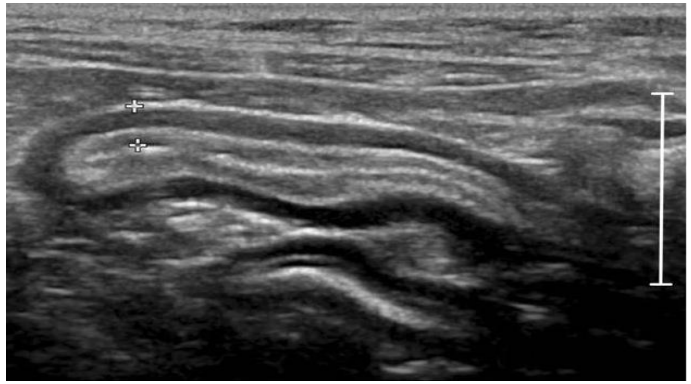
1.Marsilio et al., JVIM, 2023
2. Freiche et al., JVIMJ,2021 a
3. Di Donato et al., JFSM, 2014

Diagnostic imaging with sonography useful but not discriminatory (II/III)

- Cross sectional evaluation
- Anatomic location
- Mural architecture
- Mesenteric lymph node [2]
- Other organs, esp. pancreas, liver
- Effusion [2]
- Hypomotility
- Assist sampling



Diffuse thickening with eos. enteritis, 3.9 mm.



Marked muscularis thickening with LGAL (LGITL). Overall thickness normal 2.5 mm.

Figures adapted from: Paulin et al., BMC Vet Res, 2018
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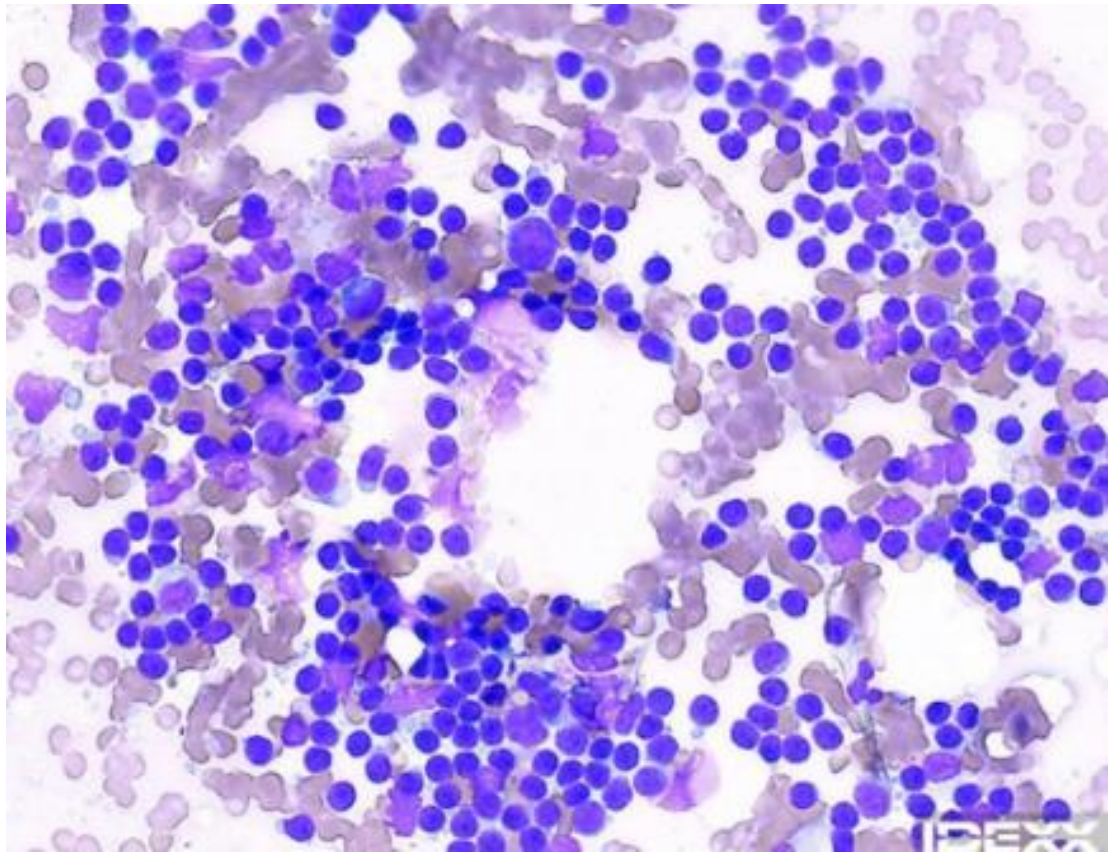
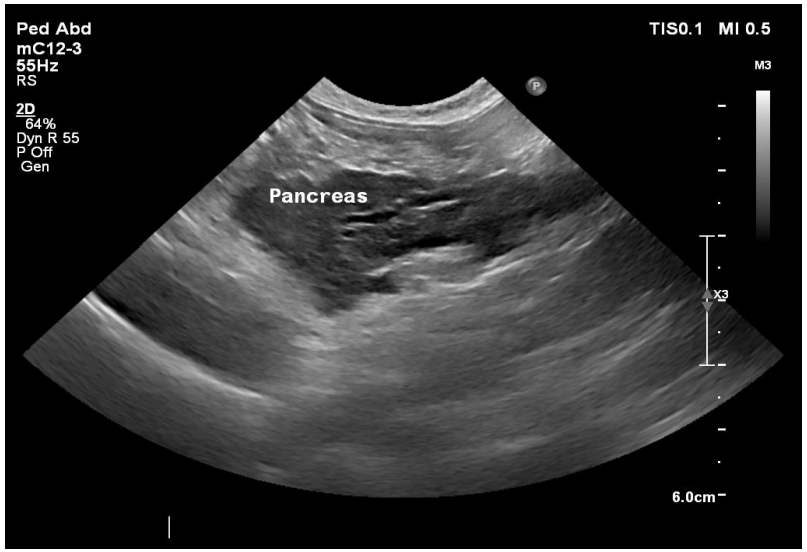
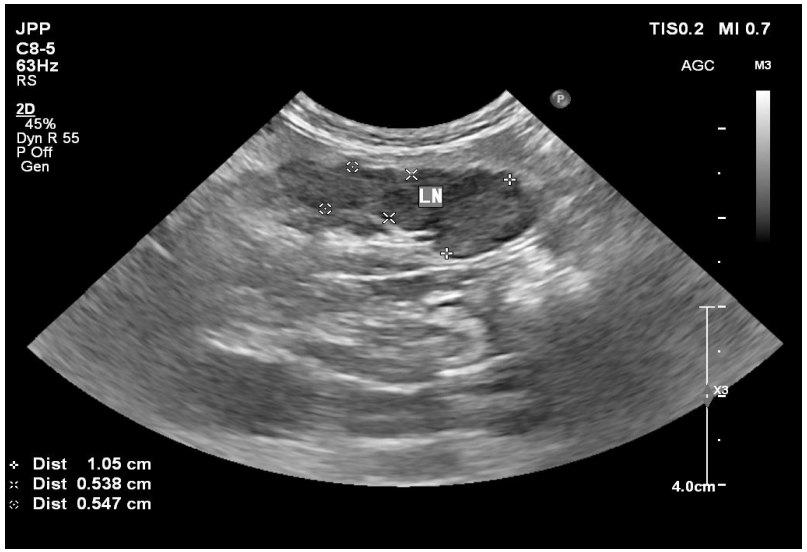
1.Marsilio et al., JVIM, 2023
2.Freiche et al.,JVIM, 2021a
3. Zwingenberger et al., JVIM, 20[illegible]

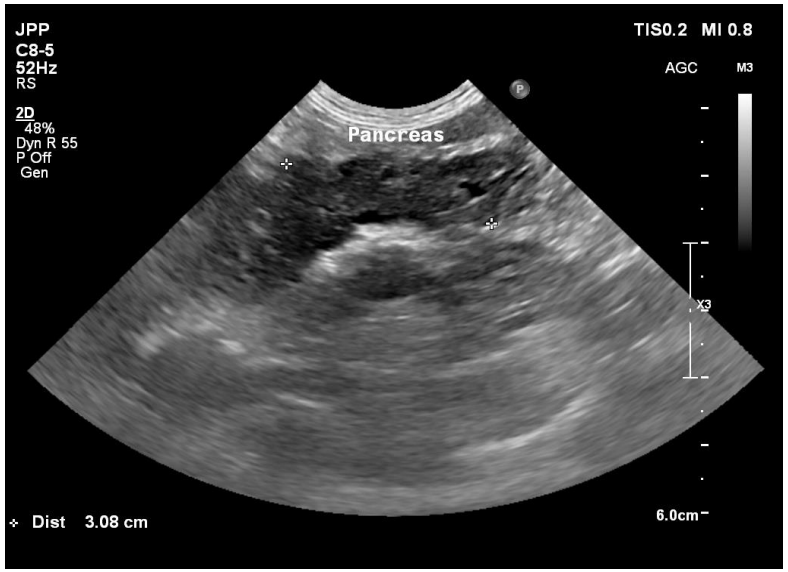
Cytology – helpful for GI disease?

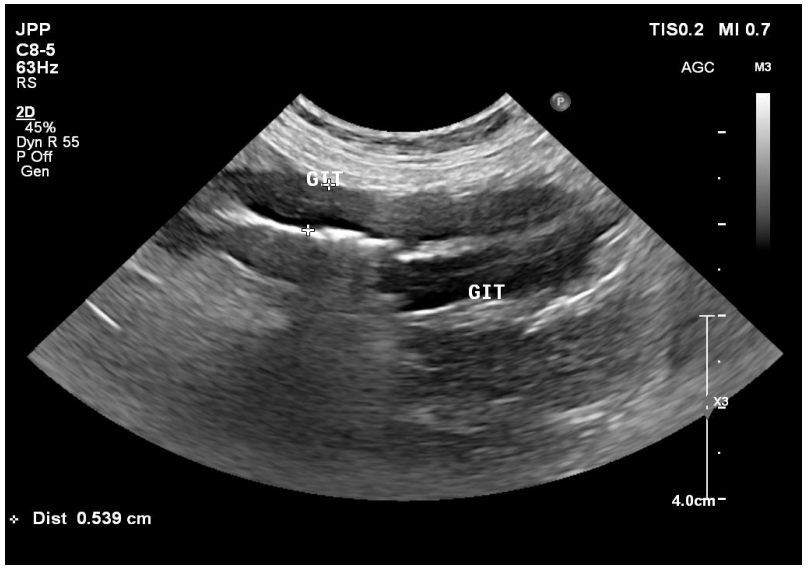
- Abdominal masses
- Lymphadenopathy
- Organomegaly
- Effusion
- Cystic structures
- Bloody diarrhea



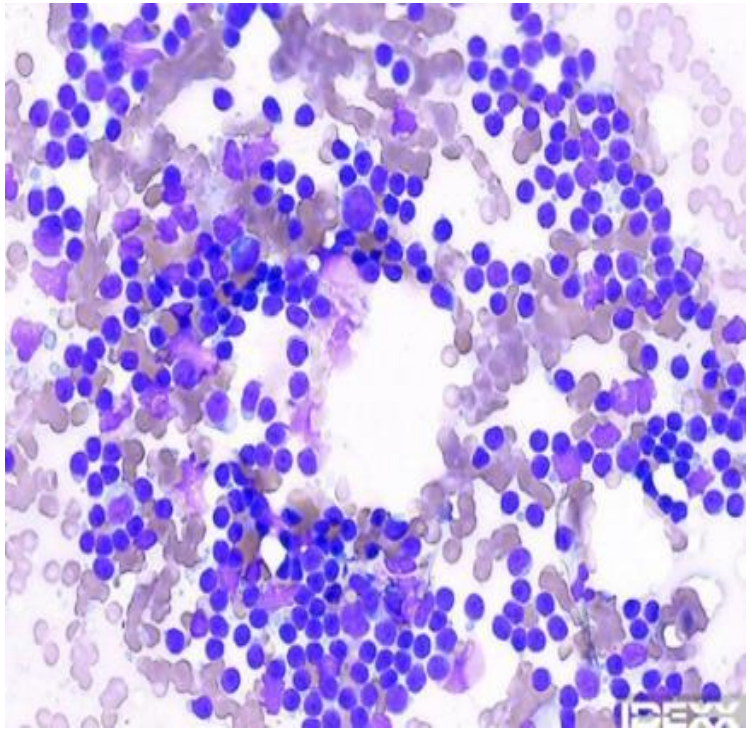








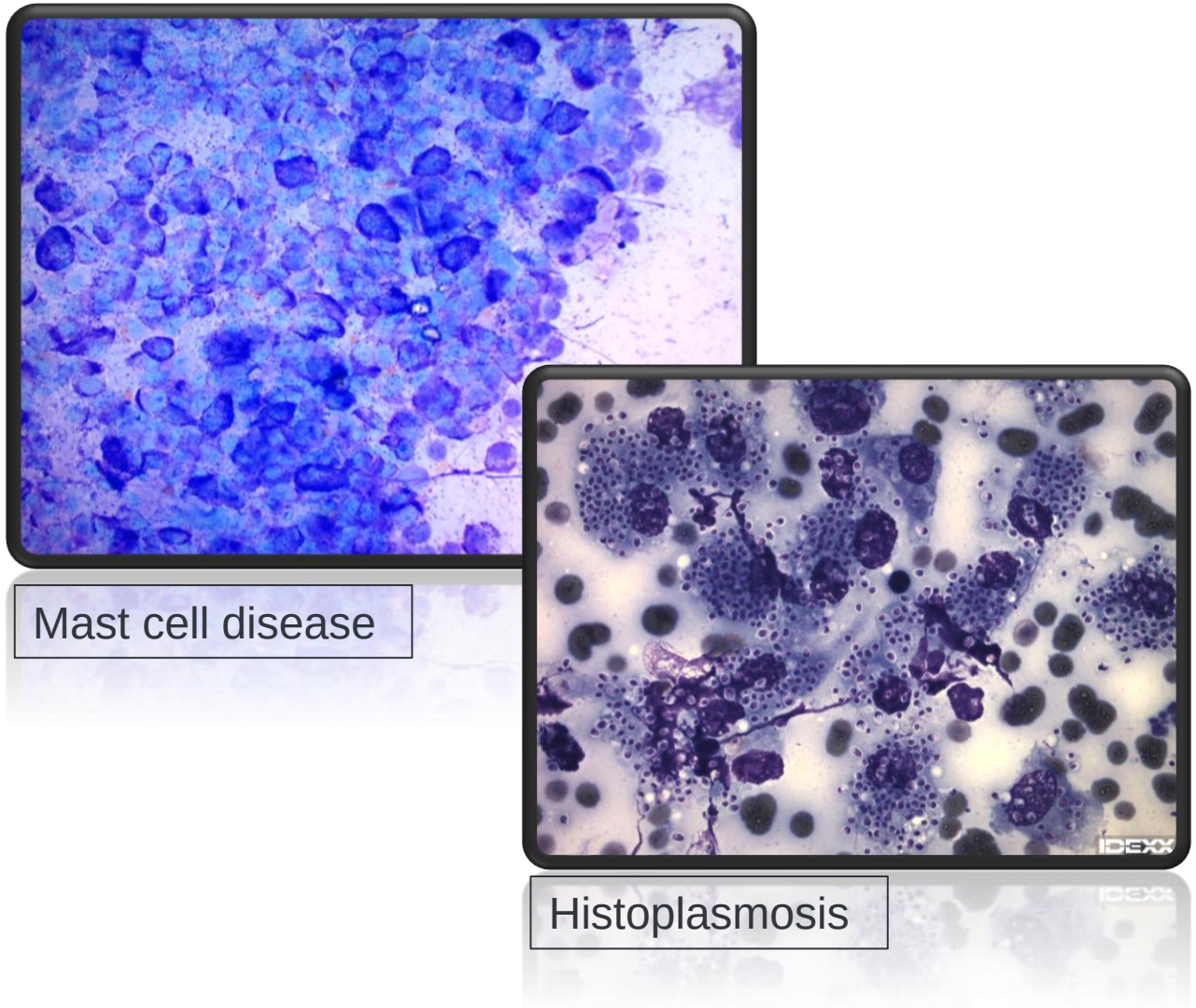
AUS images courtesy of Atlantic Veterinary Internal Medicine & Oncology, Annapolis, MD



Cytology of FNA of mesenteric lymph node

BUT…cytology **cannot** differentiate LPE from LGITL (III)

- Can be diagnostic for
  - High grade LSA
  - Mast cell neoplasia
  - Plasma cell tumor
  - Fungal infection



Marsilio et al., JVIM, 2023

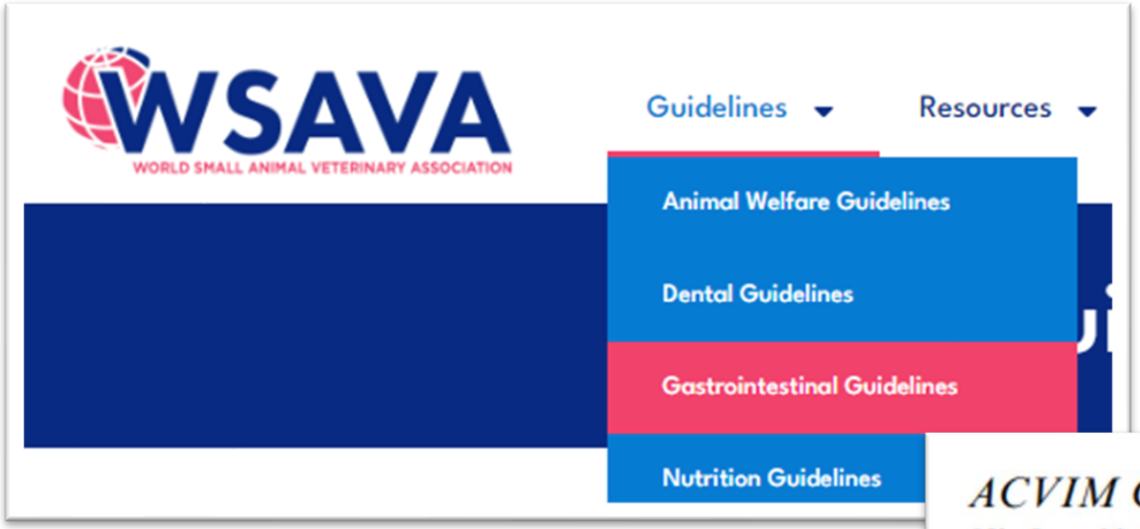
Histopathology as gold standard

- Laparotomy, laparoscopy, endoscopy
- Sample variables affecting diagnostic quality
  - Source
  - Number
  - Processing
- Pathology assessment

Picture courtesy of N. Sanders

Marsilio et al., JVIM, 2023

Resources for guidelines and standardization of diagnosis are helpful!



Resources

- Upper GI Endoscopy Report Form
- Lower GI Endoscopy Report Form

ACVIM Consensus Statement

J Vet Intern Med 2010;24:10–26

Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) provide the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection of relevant topics, identification of panel members with the expertise to draft the statements, and other aspects of assuring the integrity of the process. The statements are derived from evidence-based medicine whenever possible and the panel offers interpretive comments when such evidence is inadequate or contradictory. A draft is prepared by the panel, followed by solicitation of input by the ACVIM membership, which may be incorporated into the statement. It is then submitted to the Journal of Veterinary Internal Medicine, where it is edited prior publication. The authors are solely responsible for the content of the statements.

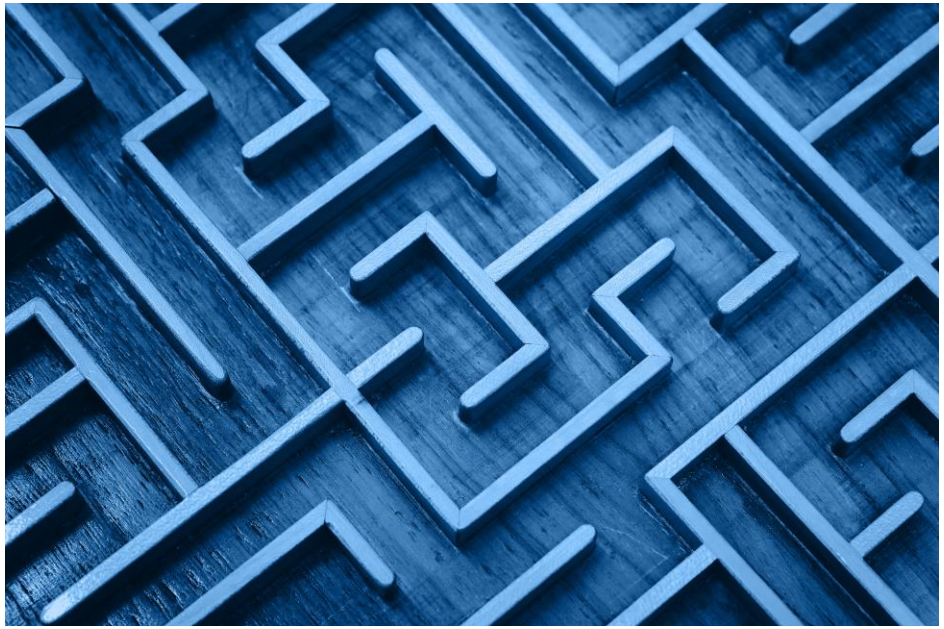
Endoscopic, Biopsy, and Histopathologic Guidelines for the Evaluation of Gastrointestinal Inflammation in Companion Animals

The WSAVA International Gastrointestinal Standardization Group: R.J. Washabau, M.J. Day, M.D. Willard, E.J. Hall, A.E. Jergens, J. Mansell, T. Minami, and T.W. Bilzer

Key words: Cat; Colon; Dog; Duodenum; Endoscopy; Histopathology; Intestine; Stomach.

Ancillary testing for ambiguous cases

- Immunohistochemistry (IHC)
- PCR Amplification Receptor Rearrangement (PARR)
- Histology guided mass spectrometry[1]
  - Sensitivity 86.7%, Specificity 91.7%
- Fecal microbiome[2]
- Fecal calprotectin[3]



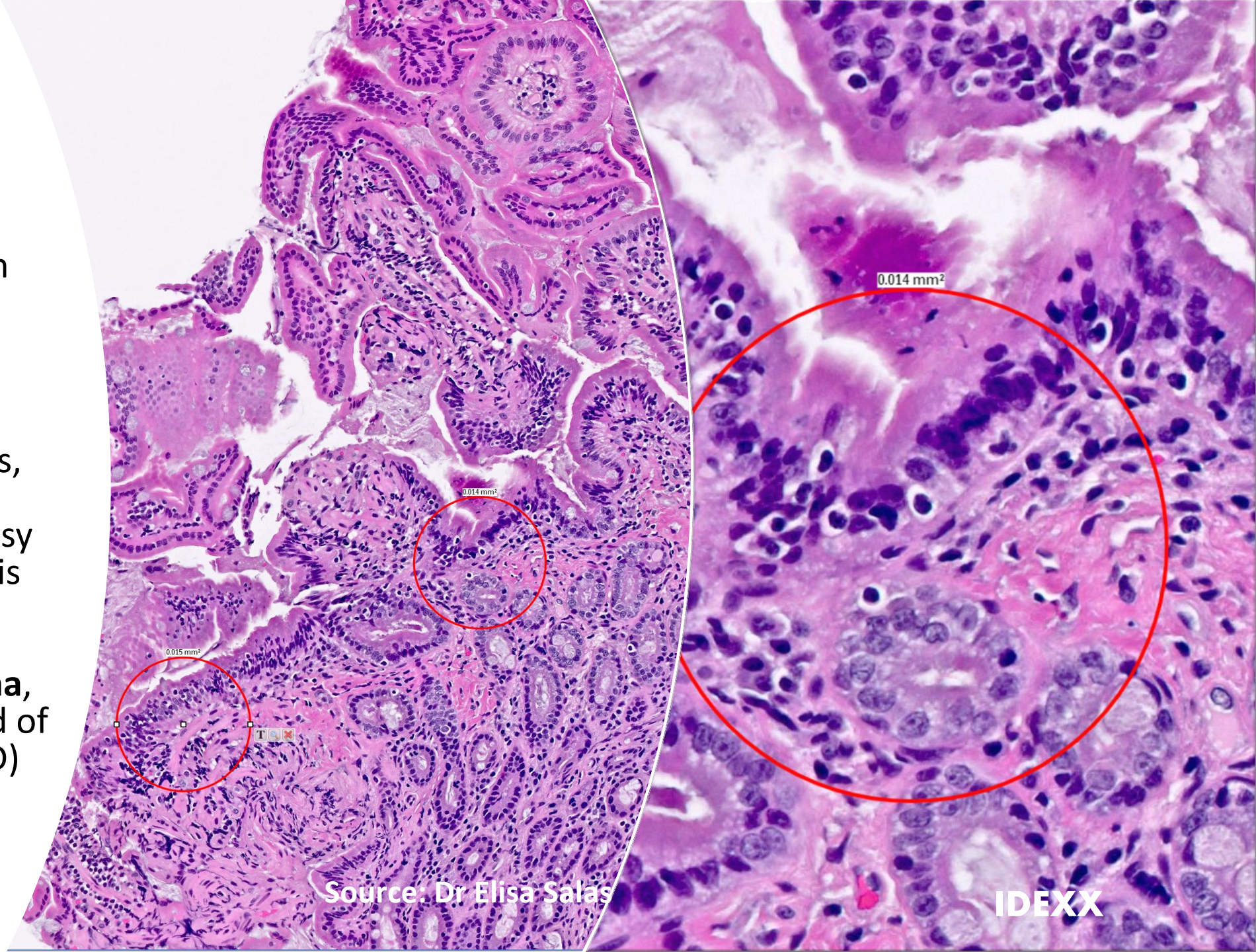
1.Marsilio et al., JVIM, 2020
2.Marsilio et al., SciRep, 2019
3. Riggers et al., Vet Sci, 2023

Clive, 14 yo, FS, DSH

CC: vomiting & diarrhea

PARR testing – Clonal with strong polyclonal background

Molecular clonality results, in conjunction with the provided history and biopsy report, support a diagnosis of very early **emerging epitheliotropic small cell small intestinal lymphoma**, arising from a background of chronic inflammation (IBD)



Source: Dr Elisa Salas

IDEXX

Treatment

CIE treatment basics

- Empirical treatment for parasites
  - Protozoa in particular
- Metronidazole trial?
- Diet
  - Novel hydrolyzed protein for CIE (LPE); also low fat for lymphangiectasia
  - Failure on one diet ≠ failure to all diets
- Immunosuppressive treatment CIE
  - Corticosteroids
    - Prednisolone – 2 mg/kg PO (or transdermal) q 24hrs (can go up to 4mg/kg/day with caution!)
    - Dexamethasone 0.2 mg/kg IV, SQ, or PO q 24hrs
    - Budesonide 1-3 mg (per cat) PO q 24hrs; 0.125 mg/kg q 6-24hrs
  - Chlorambucil: various protocols; once a day, 2mg/cat q 2-3 days, daily X 4 days q 3weeks
  - Cyclosporine 5 mg/kg PO q 24hrs if refractory to prednisolone
  - Budesonide alternative (for cats with adverse effects of prednisolone or dexamethasone)
  - Mycophenolate
- Thromboprophylaxis?

ONLY corticosteroid + 1 other immuno-suppressive drug!!!

Jergens AE. Feline Idiopathic Inflammatory Bowel Disease: What we know and what remains to be unraveled: What we know and what remains to be unraveled. *Journal of Feline Medicine and Surgery*. 2012;14(7):445-458. doi:10.1177/1098612X12451548

Additional CIE treatments/supportive care

- Soluble fiber
- Cobalamin
- Folate
- Probiotics
- Prebiotics
- Supportive care
  - Ondansetron/dolasetron
  - Maropitant
  - Capromorelin
  - Cyproheptadine/mirtazapine
  - Metoclopramide
  - Cisapride
  - Fluids
  - Nutritional support (feeding tubes)

Jergens AE. Feline Idiopathic Inflammatory Bowel Disease: What we know and what remains to be unraveled: What we know and what remains to be unraveled. *Journal of Feline Medicine and Surgery*. 2012;14(7):445-458. doi:10.1177/1098612X12451548

Cobalamin is low in many cats with chronic enteropathies

- Cats (and dogs) need dietary source
- Primarily absorbed in ileum
  - ≈1% passively absorbed along entire GI tract
  - Serum levels decreased with ileal mucosal disease
- Cobalamin <200 ng/ml, albumin <2 gm/dL associated with poor prognosis
- Supplement when <400 ng/ml
  - Oral
    - 250-2,000 *u*g (total, see dosing on TAMU website chart) PO q24hrs X 12 weeks
    - Re-check 1 month after discontinuation
  - Injectable
    - 250-1,500 *u*g (total, see dosing on TAMU website chart) subQ, q1 week X 6 weeks, then once 1 month later
    - Re-check 1 month after last injection

Simpson KW, Fyfe J, Cornetta A, Sachs A, Strauss-Ayali D, Lamb SV, Reimers TJ. Subnormal concentrations of serum cobalamin (vitamin B12) in cats with gastrointestinal disease. J Vet Intern Med. 2001 Jan-Feb;15(1):26-32. doi: 10.1892/0891-6640(2001)015<0026:scoscv>2.3.co;2. PMID: 11215907.

https://vetmed.tamu.edu/gilab/research/cobalamin-information/

FCEIA (FCE activity index)

- Numerical measure of inflammatory activity in cats with CE, including IBD and FRE
  - Initial assessment of disease severity
  - Measure of clinical response
- Retrospective IBD data (n=59); prospective IBD or FRE (n=23)
- Variables
  - GI signs of activity/ attitude, appetite , vomiting, diarrhea, wt loss
  - Endoscopic lesions
  - Laboratory changes of TP, ALT/ALP, phosphorus (albumin, WBC, PCV)
  - Pretreatment, pre-scoping scores did not differ between IBD, FRE
  - All 17 IBD patients (100%) complete remission after 3 weeks ≥75% reduction FCEIA

Jergens et al., JVIM 2010

SCL/LGITL treatment goal of 2-3 years

- Median survival 1148 days (15-2479)[1]
- Median survival 2 years[2]
- Median survival 719 days (range 4-1272)[3]

1.Pope et al., Vet med Sci., 2015
2.Paulin et al., BMC , 2018
3.Freiche et al.,JVIM 2021b

Feline chronic enteropathy is often complicated by…

Complications of disease

- PLE
- Hypercoagulability/thromboembolism
- Pancreatitis
- Exocrine pancreatic insufficiency
- Cholangiohepatitis
- Wasting

Complications of treatment

- Insulin resistance
- Diabetes mellitus
- Iatrogenic hyperadrenocorticism
- PU/PD
- Fluid retention
  - Congestive heart failure
- Hypercoagulability

Common comorbidities

- Pancreatitis
- Cholangiohepatitis
- CKD
- Hyperthyroidism

Systematic approach to chronic diarrhea

Exclude GI parasites and extra-GI causes of diarrhea
CBC, Chemistry, UA, fecal O&P/Ag

Other non-invasive diagnostics
cPL, cortisol, fecal PCR, biomarkers (CRP, sRAGE, 3-BrY, NMH...)

Unstable Patient
Weight loss, hyporexia, hypoalbuminemia

Imaging
GI-Panel + Dysbiosis-Index

Biopsy

Immunosuppression or other specific therapy

FMT? Antibiotic Therapy?
Bile Acid Binder?

Stable Patient
Monitor clinical signs for a short period

Diet Trial

No improvement

ement
e diet

Spectrum of care (SoC)

- Filter available, evidence-supported care options with client-specific lens
  - Goals & expectations
  - Limitations
- Patient factors
- Veterinarian factors
- Open communication
- Human-animal bond is a focus

1.Brown et al.,JAVMA, 2021
2.Englar, JFMS, 2023 a,b

Takeaways:

- Feline CE is common, and weight loss may be the only sign
- Dietary management should be a priority
- Intestinal biopsy and histopathology are the gold standards for diagnosis; even ancillary test results may be ambiguous
- Prognoses are similar for chronic inflammatory enteropathy and small cell lymphoma
- Spectrum of care may support human-animal bond and your patient

Questions?

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