VMX

VETERINARY MEETING & EXPO

The SHOW OF SHOWS

WONDERS! WOWS! WISDOM!

JANUARY 13-17 ORLANDO, FL & ONLINE

Presented By:

NAVC

YOUR VETERINARY COMMUNITY

VETERINARY MEETING & EXPO

Gut Feeling

Clinical Approach to Feline Chronic Enteropathy

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Sunday, January 14, 2024

Conflict of Interest Disclosure:

Celeste Clements and **Nancy Sanders** have financial interest, arrangement or affiliation with:

Name of Organization	**Relationship**
IDEXX Laboratories, Inc	Employees, own stock

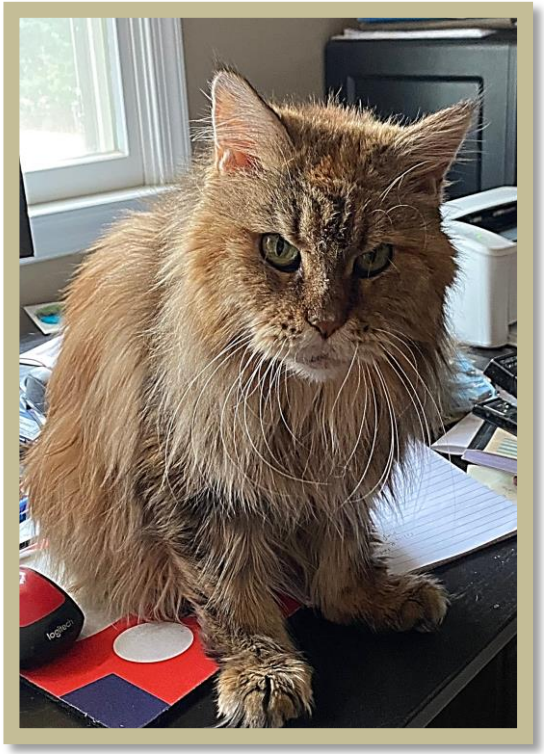
Disclaimer: The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With 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.

Learning Objectives

After participating in this session, attendees should be able to:

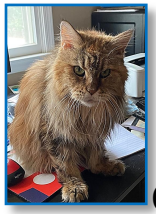
- Define and discuss feline chronic enteropathy (CE)
- Summarize the diverse etiologies of chronic feline gastrointestinal signs
- Develop and justify an evidence-based plan to diagnose CE
- Plan management of feline patients for a spectrum of care
- Locate expert resources and research novel approaches to improve feline gut health

“A Tale of Two Kitties”



Discovery

OC



Discovery, 18 yo, FS, Maine coon

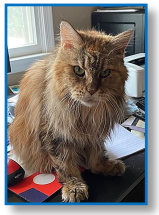
CC: Vomiting, lethargy, anorexia for ~2d

Hx:

- Moved from FL 4 days ago
- Vomiting watery fluid 2-3x, stopped eating and drinking ~36 hours ago
- No D/C/S/PU/PD
- No toxins or other cats
- Diet consistent- commercial canned and dry, free fed, treats
- Weight loss over years
- Occasional sporadic cough

PE:

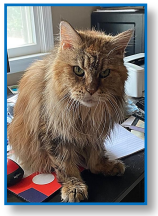
- Wt. 10.47#
- T 101°F, HR 140 bpm, RR 32/m
- BARH, MM moist, CRT <2s
- BCS 5/9; MCS moderate muscle loss
- Oral: Moderate dental tartar
- Normal retinal and cervical exam
- CV: Normal auscultation, no murmur or gallop
- RESP: Normal bronchovesicular sounds bilaterally, eupneic
- ABD: Soft, nonpainful, no masses, organomegaly or fluid wave
- LN: WNL



Discovery, 18 yo, FS, Maine coon

Problems:

- Vomiting, anorexia, lethargy
- Weight loss, 2 pounds over 2 years
- Sporadic cough
- Reduced MCS



Discovery, 18 yo, FS, Maine coon

Differentials?

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

Intestinal parasites

Toxin

Antibiotics, medications

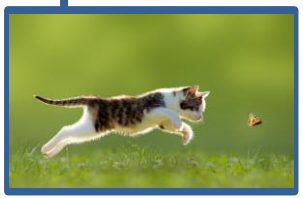
Metabolic disease

Neoplasia

Young

Older

Dietary indiscretion or foreign body



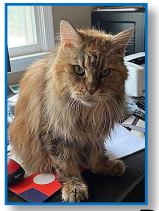
Viral infection

Infectious agents

Stress

Inflammatory disease

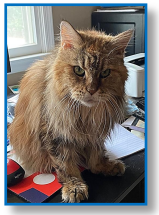
Endocrine disease



Discovery, 18 yo, FS, Maine coon

Differentials:

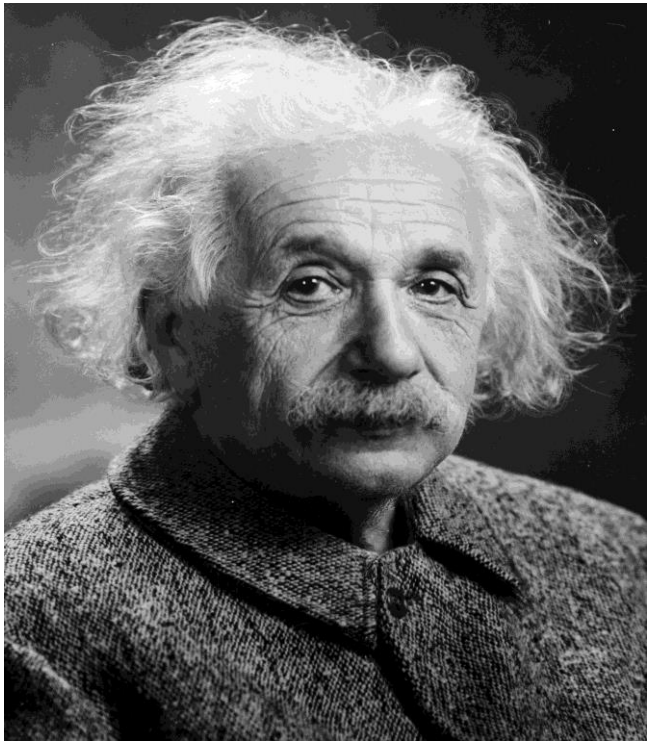
- Vomiting, anorexia
  - GI
    - Hairball
    - Food-related
    - Foreign body/toxin
    - Gastroenteritis (*IBD*)
    - Pancreatitis
    - Cancer *(SCL)*
    - Constipation
    - Parasites
  - Extra-GI
    - Hyperthyroidism
    - Kidney or liver disease
    - Diabetes mellitus
    - Cardiomyopathy
- Lethargy ∞
- Weight loss
  - GI
    - Pancreatitis
    - Gastroenteritis (*IBD*)
    - Exocrine pancreatic insufficiency
    - Cancer
    - Constipation
    - Parasites
  - Extra-GI
    - Hyperthyroidism
    - Kidney or liver disease
    - Diabetes mellitus
    - Cardiomyopathy



Discovery, 18 yo, FS, Maine coon

Differentials, continued:

- Sporadic cough
  - Feline asthma/ bronchitis
  - Cardiomyopathy
  - Heartworm disease
- Reduced muscle condition
  - Sarcopenia (age related)
  - Cancer cachexia
  - Hyperthyroidism
  - Cardiac cachexia
  - Kidney or liver disease



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

--Albert Einstein

Feline Chronic GI Disease

Inflammatory Bowel Disease (IBD)

Cancer

Food Allergy

Zebras

Feline Chronic GI Disease

Inflammatory Bowel Disease (IBD)

Cancer

Food Adversity

Zebras

Feline Chronic Enteropathy

Chronic inflammatory enteropathy (CIE)

Small cell lymphoma (SCL)

Zebras

Immunosuppressant responsive (IRE/IBD)

Food responsive (FRE)

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

Feline chronic enteropathy (CE) …

… chronic (at least 3 weeks' duration) signs of gastrointestinal disease where extra-gastrointestinal, metabolic, and infectious causes have been ruled out.

Marsilio et al., JVIM,2023

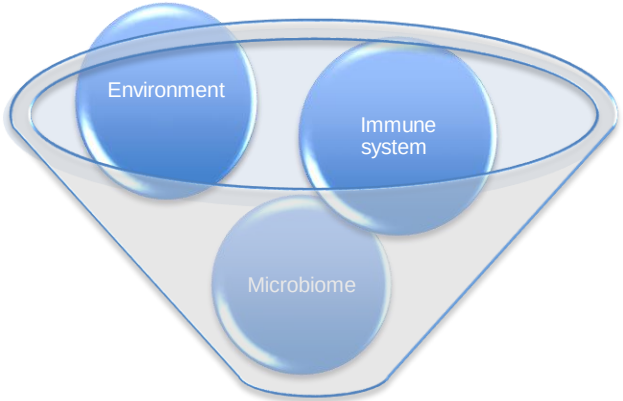
Feline Chronic Enteropathy

Lymphoplasmacytic enteritis (LPE)

Low-grade intestinal T-cell lymphoma (LGITL)

Marsilio S, Freiche V, Johnson E, et al.
ACVIM consensus statement guidelines on diagnosing and distinguishing low-grade neoplastic from inflammatory lymphocytic chronic enteropathies in cats. *J Vet Intern Med*. 2023; 37(3): 794-816. doi:10.1111/jvim.16690

Etiopathogenesis



Chronic inflammatory enteropathy

Polyclonal

?? → Clonal expansion →

Neoplasia

Monoclonal
Oligoclonal

1 Marsilio, JSAP, 2021
2. Marsilio et al., JVIM, 2023
3. Freiche et al., LabIn, 2021

Clinical presentations overlap

- Signalment [1]
  - DSH +/- Siamese
  - Age overlaps
    - LPE 1.3-16 yrs , Median 8 yrs
    - LGITL 4-20 yrs, Median 12.5 yrs
- Clinical signs
  - Weight loss > vomiting > anorexia> diarrhea[1]
  - One or two clinical signs is common[2]

1. Marsilio, JSAP, 2021,
2. Bandara et al., JSAP, 2023.

Physical exam

- Most will be underconditioned
- Intestinal thickening or ropiness
- Nodules or masses
- Mesenteric lymphadenopathy
- Normal PE

1. Bandara et al., JSAP, 2023.

Laboratory findings and biomarkers

- Albumin — GI protein loss, inflammation
- Globulins — GI protein loss, inflammation
- Cobalamin — Absorption
- Folate* — Absorption and dysbiosis
- PLI — Pancreatic inflammation
- TLI — Pancreatic inflammation, function

*False increase with hemolysis

Marsilio et al., JVIM, 2023

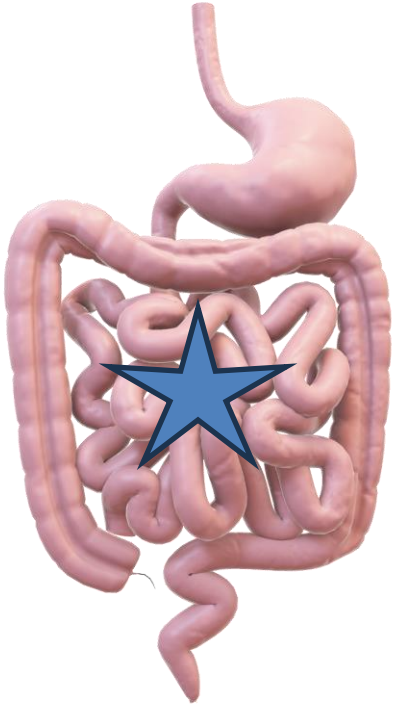
Laboratory findings and biomarkers don’t differentiate between LPE and LGITL (II)

- Albumin — N to decreased
- Globulins — N to increased or decreased
- **Cobalamin** — **N to decreased**
- Folate — N to increased or decreased
- PLI — N to increased
- TLI — N to decreased

Marsilio et al., JVIM,2023

Anatomic distribution of CE

- Any GI segment affected
- Decreasing involvement
  - Jejunum
    - Ileum
    - Duodenum
      - Stomach
      - Colon



Marsilio et al., JVIM 2023

Routine workup for chronic GI signs?

Tier 1

- Minimum data base: CBC, Chemistry, UA
- Fecal testing (deworming?)
- Retrovirus
- Thyroid hormone (T4) (> 6yrs)
- Pancreatitis- fPLI
- EPI- fTLI
- Cobalamin/folate

Tier 2

- Food elimination trial
- Diarrhea RealPCR Panel™
- Regional infectious disease
- Diagnostic imaging
- Dysbiosis Index?

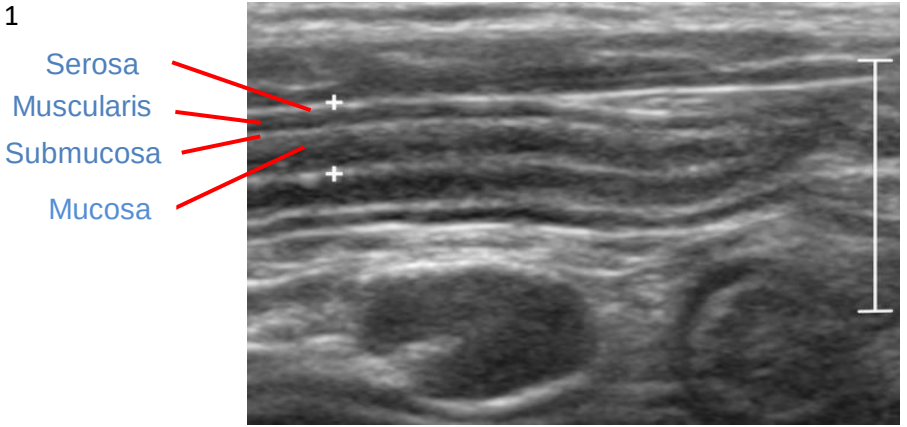
Tier 3

- GI biopsy

Diagnostic imaging

- Radiographs have limited diagnostic utility [1]
  - Obstructive pattern
  - 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



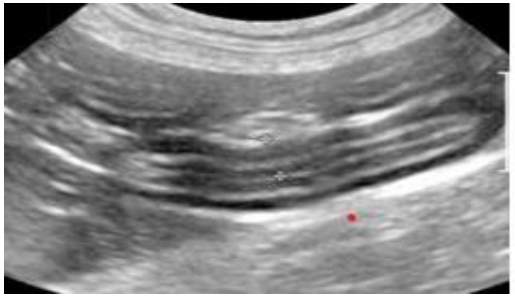
Normal jejunum, 2.7 mm

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

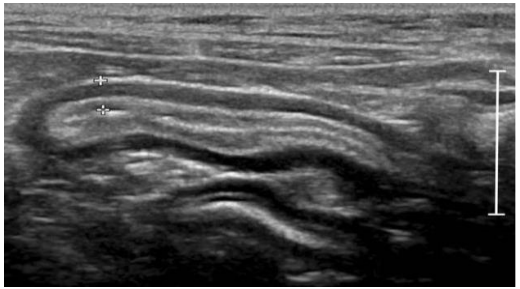
1.Marsilio et al., JVIM, 2023
2. Freiche et al., JVIMJ,2021 a
3. Di Donato et al., JFSM, 2014

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.

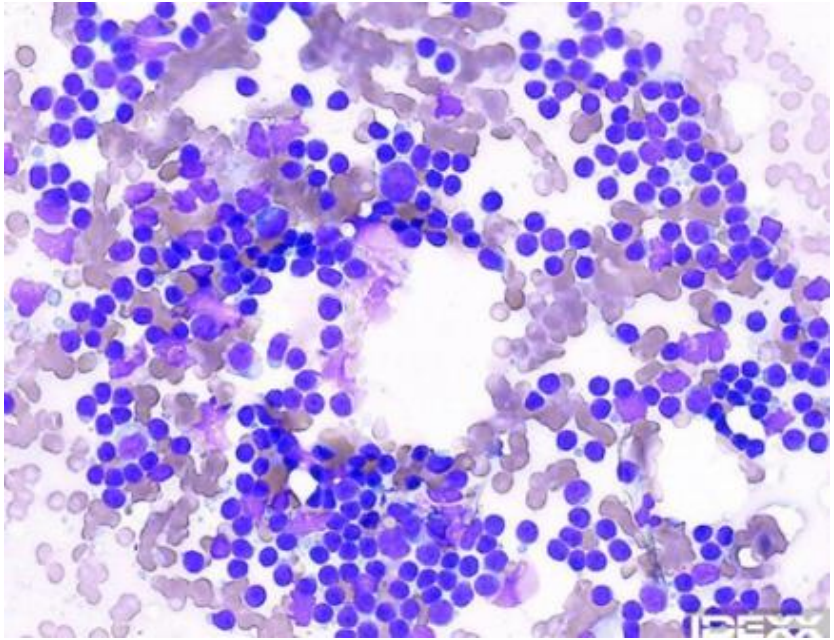


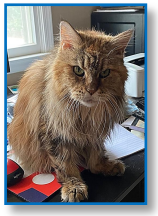
Marked muscularis thickening with LGAL (LGITL). Overall thickness normal 2.5 mm.

1.Marsilio et al., JVIM, 2023
2.Freiche et al.,JVIM, 2021a
3. Zwingenberger et al., JVIM, 2010

Cytology – helpful for GI disease?

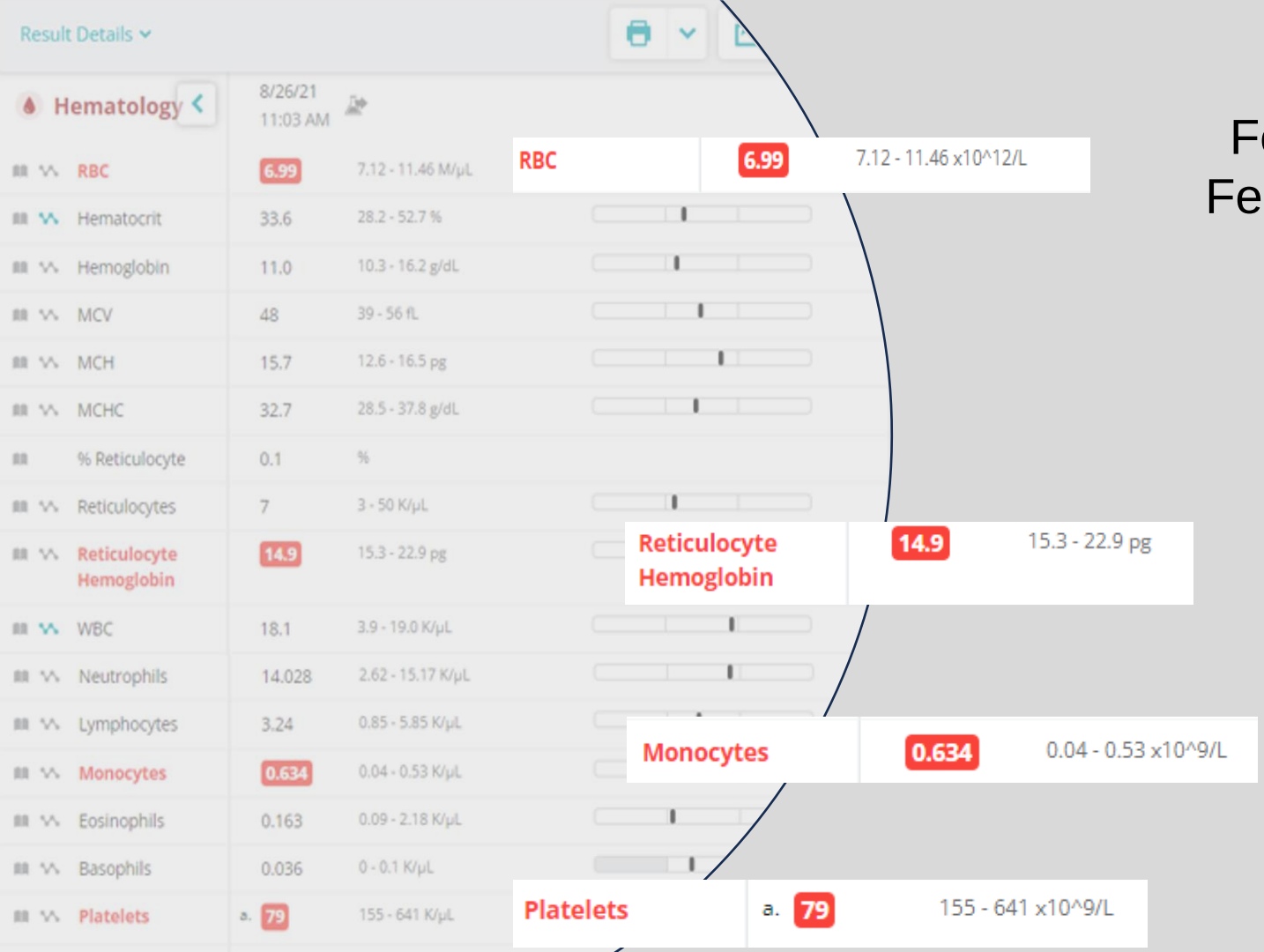
- Abdominal masses
- Lymphadenopathy
- Organomegaly
- Effusion
- Cystic structures
- Bloody diarrhea





Discovery, 18 yo, FS, Maine Coon

Diagnostic plan and results

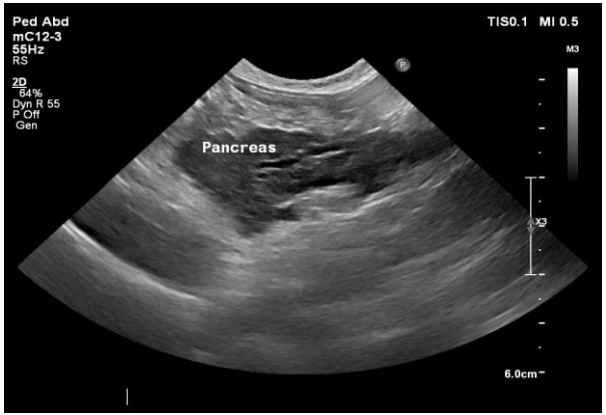


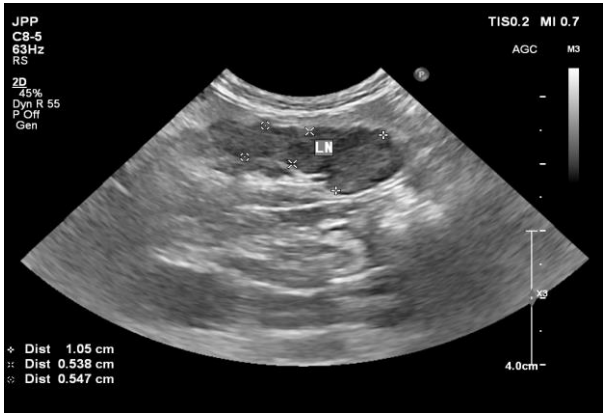
"Discovery"
Feline, Maine Coon
Female Spayed, 18y

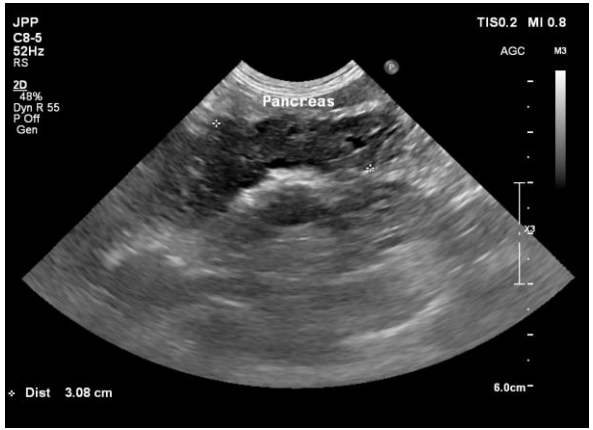
Complete Blood Count

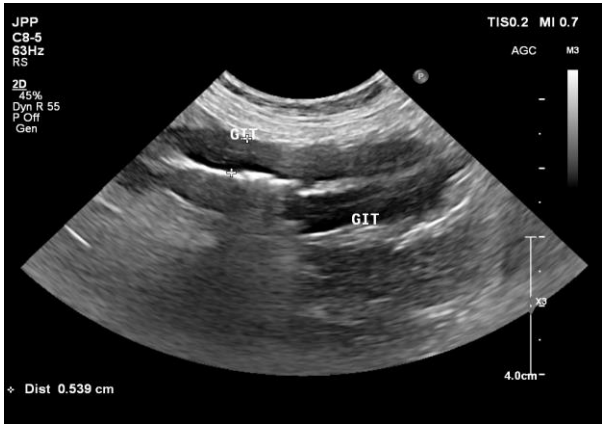
"Discovery"

Chemistry
IDEXX SDMA®
Electrolytes
Spec fPL®
Total T4

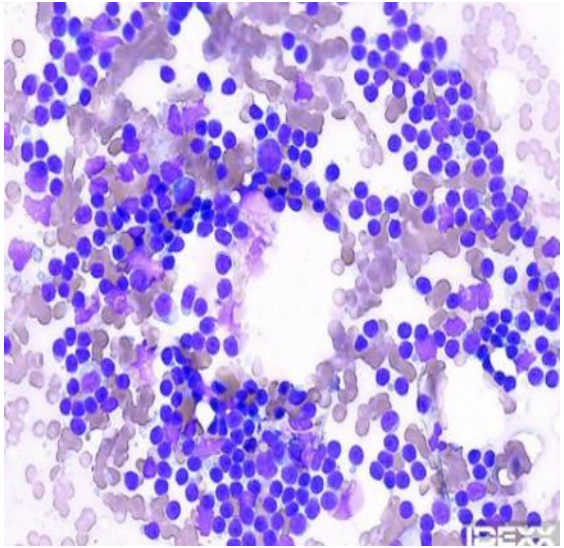




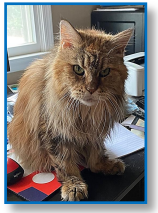




AUS images courtesy of Atlantic Veterinary Internal Medicine & Oncology, Annapolis, MD



Cytology of FNA of mesenteric lymph node



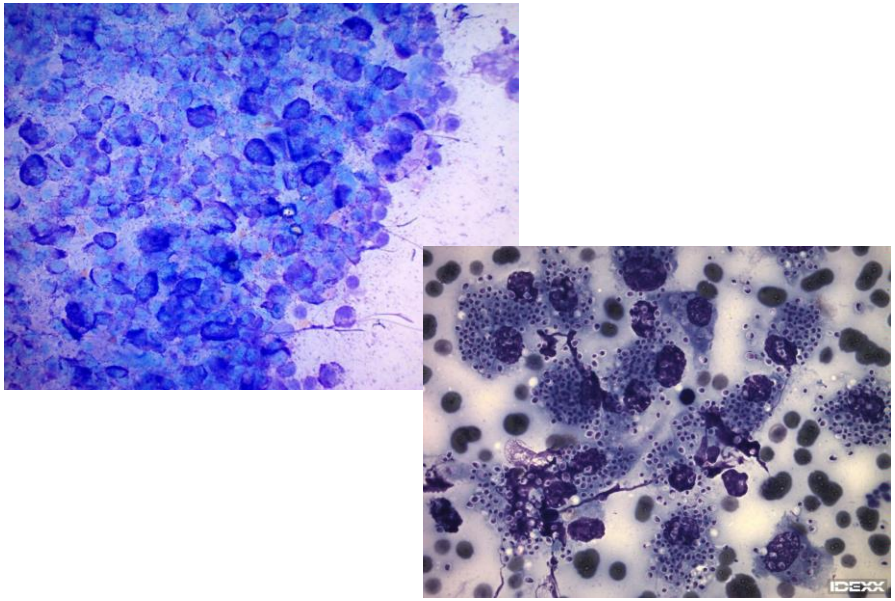
Discovery, 18 yo, FS, Maine Coon

Assessment and Management

- Diagnoses
  - Probable small cell lymphoma
  - Pancreatitis
  - Mild nonregenerative anemia
  - Mild monocytosis
- Plan
  - Prednisolone 5mg q24 hrs
  - Chlorambucil 20mg/m^2 q 14d (compounded to 5.8 mg for 0.283m^2)
  - Maropitant 8mg qd prn for nausea and vomiting
  - (Mirtazapine for appetite)
  - Recheck with CBC 3 weeks, sooner if needed

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 vs endoscopy
- Sample variables affecting diagnostic quality
  - Source
  - Number
  - Processing
- Pathology assessment

Marsilio et al., JVIM, 2023

Histologic criteria

- Villi
- Epithelium
- Lamina propria
- Crypts
- Monomorphism
- Depth of infiltration
- Fibrosis

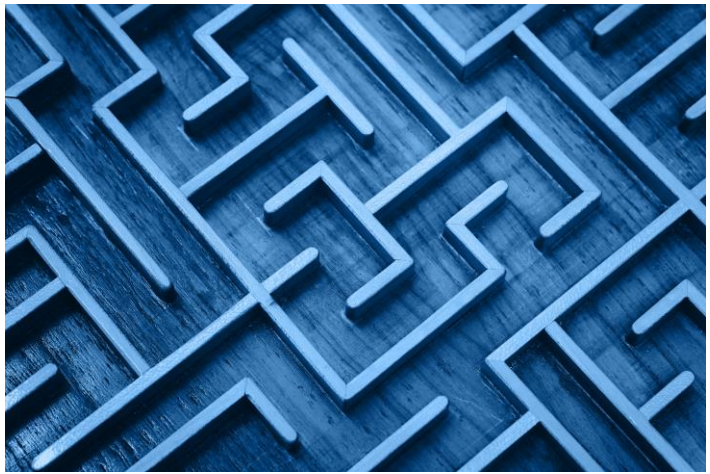
LGITL

- Marked infiltration of epithelium and LP with small monomorphic T-cells
- Lymphocytic cryptitis
- Villous atrophy
- Apical to basal gradient
- Deep fibrosis
- Concurrent LPE (45%)

Freiche et al., JVIM, 2021

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]



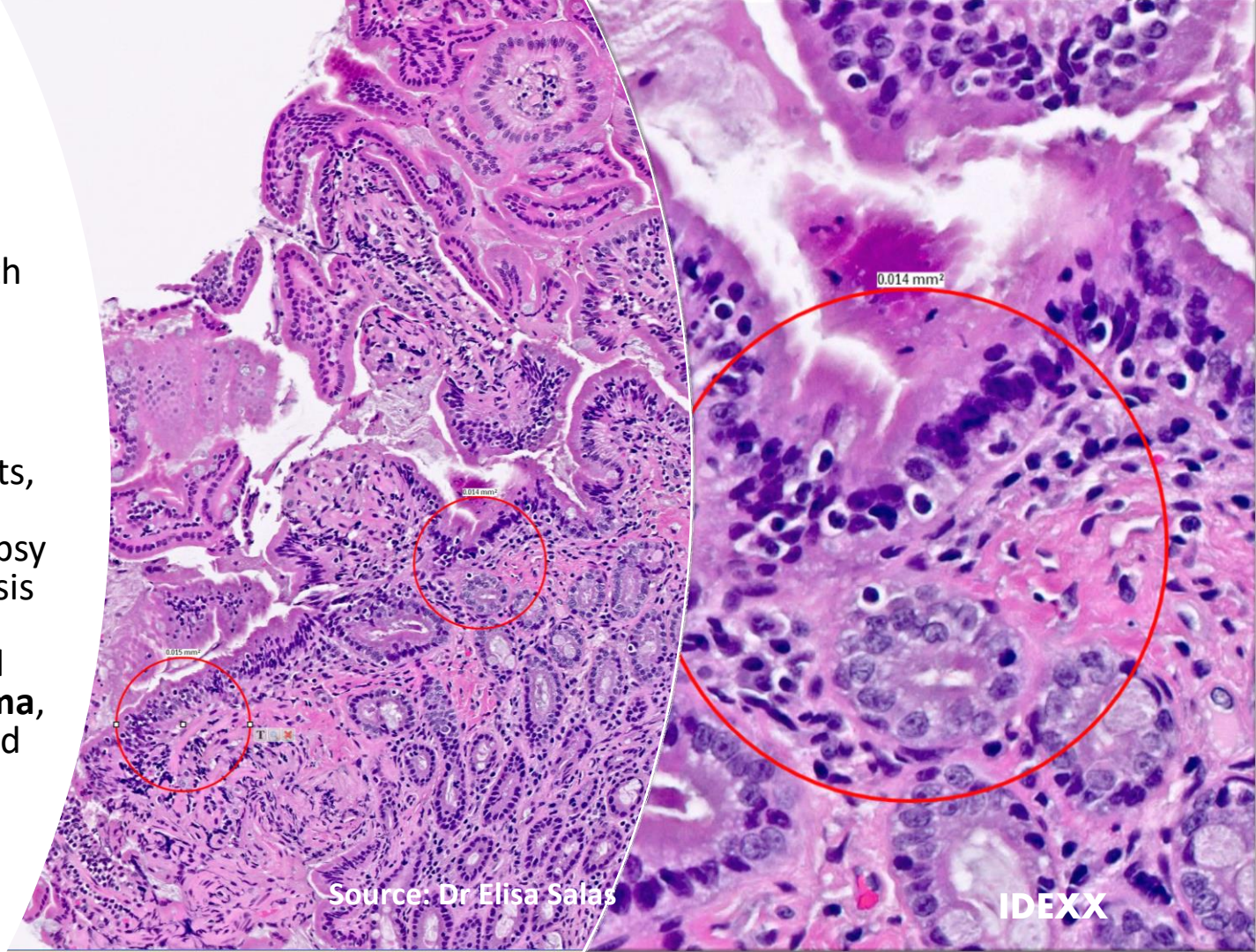
1.Marsilio et al., JVIM, 2020
2.Marsilio et al., SciRep, 2019
3. Riggers et al., Vet Sci, 2023

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)

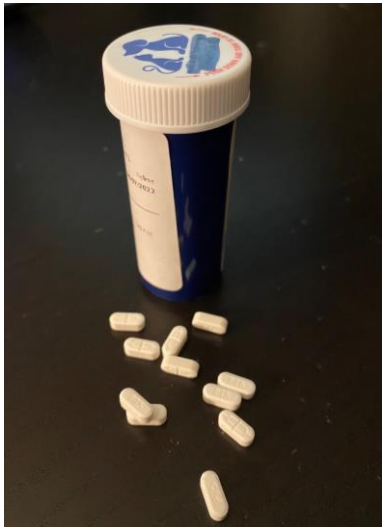


What about Discovery?

- Findings consistent with LGITL +- chronic pancreatitis
  - Geriatric cat with chronic course
  - AUS and lymph node cytology
- Opportunities
  - Diet trial
  - Cobalamin
  - GI biopsies
- Responded well to treatment for 2 + years !

Management

- Discriminating between LPE and LGITL may not drive primary treatment
  - Diet
  - Corticosteroids
    - Prednisol**one**
    - Budesonide
    - Dexamethasone
  - Chlorambucil



Marsilio, Vet Clin NA, 2021

Dietary management

- Novel ingredient (protein)
- Hydrolyzed diet
- Highly digestible
- Home-prepared

1.Guilford et al., JVIM, 2001
2.Perea et al., Fr Vet Sci,2017

Adjunctive treatment

- Antiemetics
- Appetite stimulants
- **Cobalamin**
- Folate
- Probiotics
- Feeding tube?
- Fecal transplantation

Texas A&M University Veterinary Medicine & Biomedical Sciences, Gastrointestinal Laboratory. *Cobalamin Information*. GI Lab website. Accessed January 2, 2023. https://vetmed.tamu.edu/gilab/research/cobalamin-information.

Prognosis for CIE (LPE)

- Retrospective
- For CIE, clinical remission reduced risk of death due to GI disease (n=54 cats)
  - 20 euth. for GI disease (37%), median survival 129.5 d (8-2970)
  - 25 alive, in remission (46%), median survival 916 d (78-2113)
- FRE most likely to achieve clinical remission
  - 16/25 food responsive
- Clinicopathological findings did not predict poor outcome

Bandara et al., JSAP, 2023

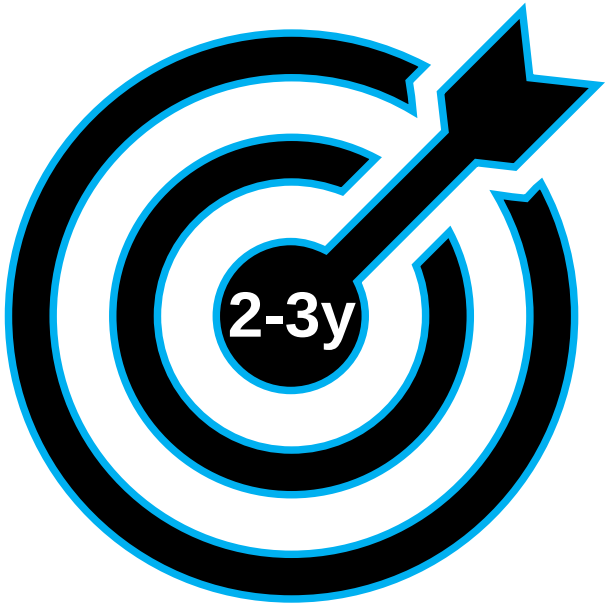
Prognosis for LPE vs LGITL

- Prospective cohort of 44 client-owned cats that failed food trials
- Laparotomy for surgical biopsy in most (41)
  - 3 of 44 cats died due to postop complications
- Treatment
  - 22 LPE treated with pred + diet
  - 22 LGITL treated with pred + chlorambucil + diet
- LGITL had shorter survival but not statistically
  - Median survival 719 days (range 4-1272)
  - Median not available for LPE
- In both more deaths from other conditions than recurrence

Freiche et al., JVIM, 2021b

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 2021 b

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

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

OC, 10 yo, FS, DLH

CC: Chronic partial anorexia, weight loss, sporadic watery diarrhea and vomiting

Hx:

- Partial anorexia and weight loss for 6 + months
- Constipation with sporadic watery diarrhea, yellow to tan, no blood or mucus, goes 1-2 daily
- Rare vomiting, partially digested food
- Chronic nasal dc and sneeze- antibiotic responsive
- No C/PU/PD
- No toxins
- Diet consistent- canned and dry, free fed
- Sole cat for 3 months
- Allergy immunotherapy; selamectin/sarolaner

PE:

- Difficult to examine, unthrifty
- Wt. 7.4#
- T 101°F, HR 200 bpm, RR 30
- BARH, MM moist, CRT <2s
- BCS 5/9; MCS moderate muscle loss
- Oral: Many missing teeth, gingivitis
- CV: Soft 1-2/6 left systolic murmur
- RESP: Nasal dc, inspiratory effort, normal bronchovesicular sounds
- ABD: Soft, doughy, no masses, organomegaly or fluid wave
- PLN: WNL

OC, 10 yo, FS, DLH

Problems:

- Vomiting, constipation, diarrhea, partial anorexia
- Weight loss 2# over 6 + months
- Heart murmur
- Chronic nasal discharge and sneeze, recent worsening
- Chronic gingivitis
- Allergic dermatopathy responsive to allergy drops
- High Fear Anxiety Stress (FAS)

OC, 10 yo, FS, DLH

Differentials:

- Chronic vomiting, diarrhea, constipation, anorexia
  - GI
    - **Feline chronic enteropathy**
    - Pancreatitis
    - Exocrine pancreatic insufficiency (EPI)
    - Parasites
  - Extra-GI
    - Hyperthyroidism
    - Kidney or liver disease
- Weight loss
  - GI
    - **Feline chronic enteropathy**
    - Pancreatitis
    - EPI
    - Parasites
  - Extra-GI
    - Hyperthyroidism
    - Kidney or liver disease
    - Diabetes mellitus
    - Cardiomyopathy

OC, 10 yo, FS, DLH

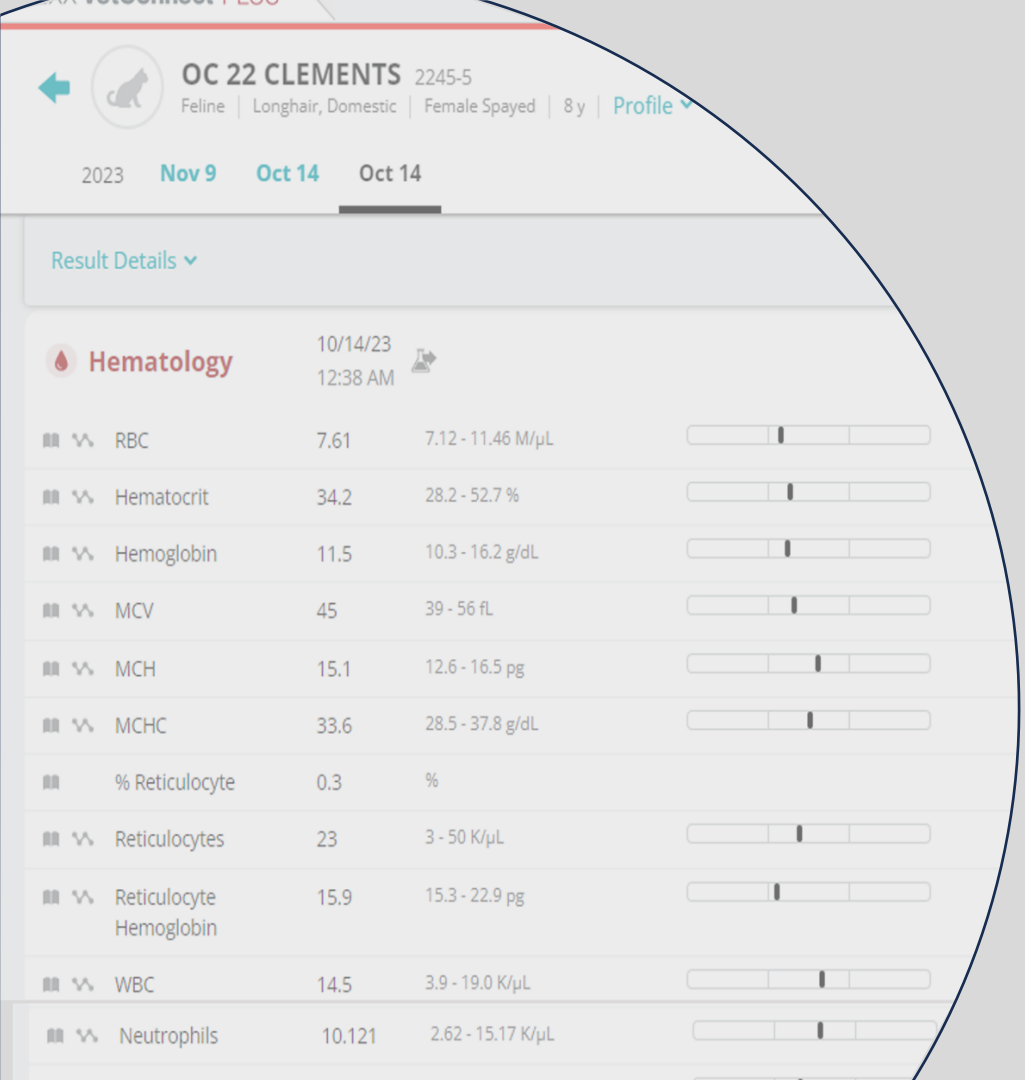
Differentials, continued:

- Heart murmur
  - Cardiomyopathy
  - Trivial
- Chronic upper respiratory signs
  - Allergic
  - Infectious
  - Cancer
  - Polyp
- Reduced muscle condition
  - **Feline chronic enteropathy**[2]
  - Cancer cachexia
  - Cardiac cachexia
  - Hyperthyroidism
  - Kidney or liver disease

1. Xifra et al., 2022
2. Marsilio et al., 2023

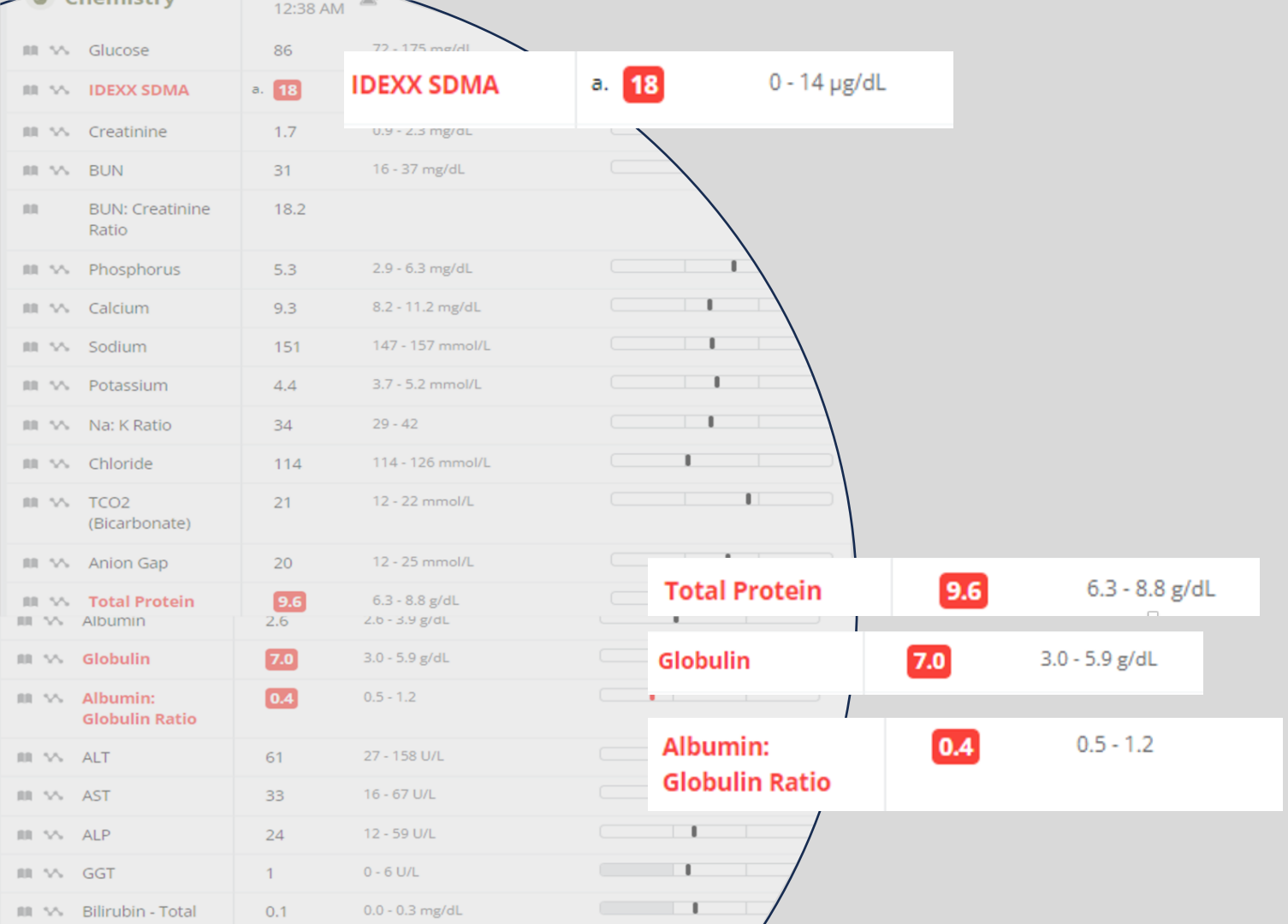
OC, 10 yo, FS, DLH

Diagnostic plan and results



“OC”
Feline, DSH
Female Spayed, 10y

Complete Blood Count



“OC”

Chemistry
Electrolytes
IDEXX SDMA®

“OC”

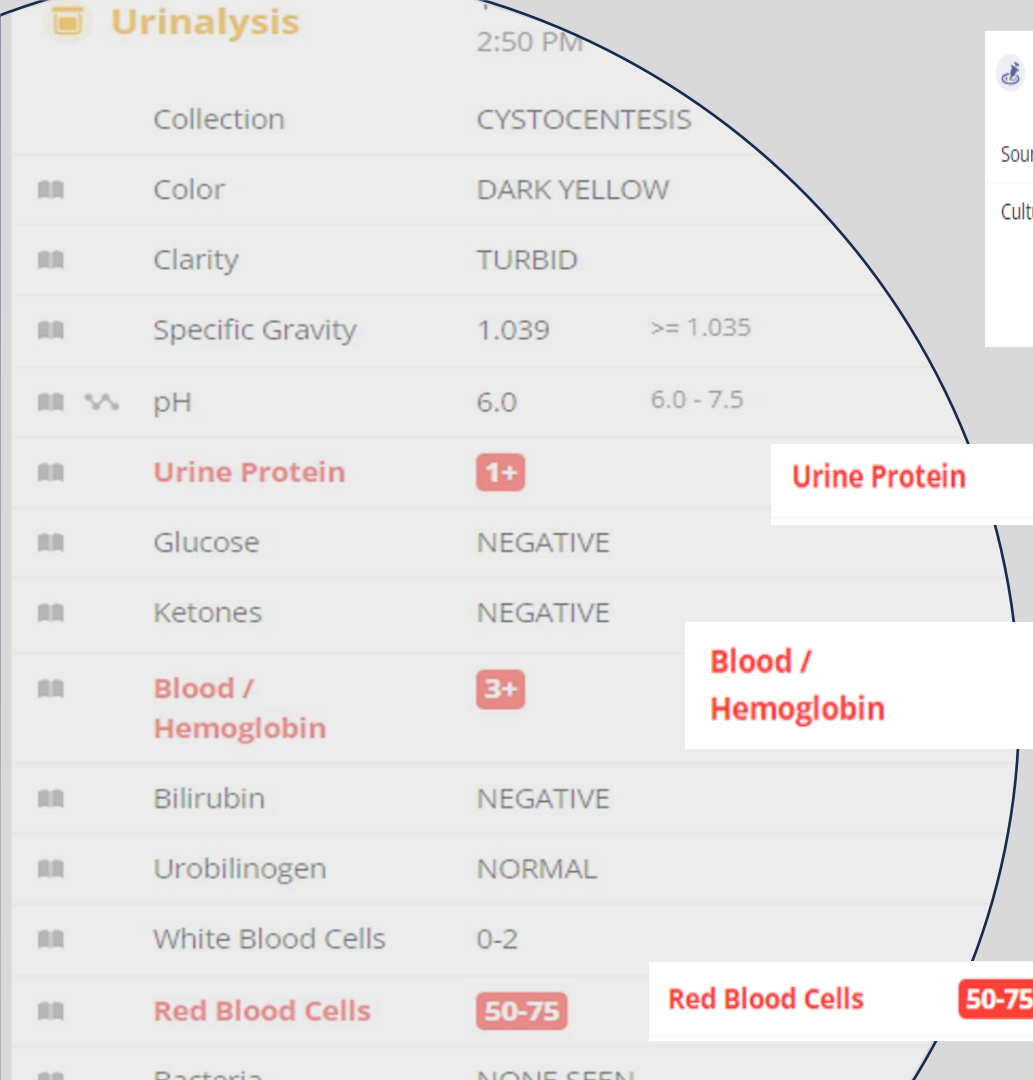
Spec fPL	1.8	0.0 - 4.4 µg/L	
Cobalamin (B-12)	d. 209	276 - 1,425 ng/L	
Folate	e. >24.0	8.9 - 19.9 ug/L	
Cardiopet proBNP (Feline)	f. 103	0 - 100 pmol/L	

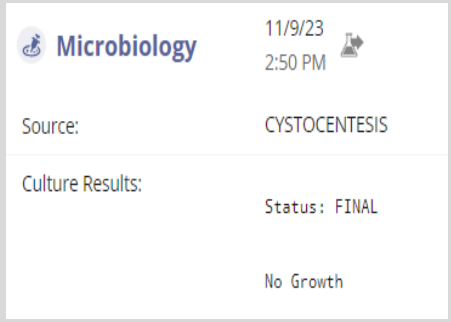
Spec fpl®
Cobalamin
Folate
Cardiopet® proBNP
Total T4

Endocrinology

10/14/23
12:38 AM

Total T4	a. 1.3	0.8 - 4.7 µg/dL	
Free T4 (ng/dL)	0.9	0.7 - 2.6 ng/dL	
Free T4 (pmol/L)	b. 11.6	9.0 - 33.5 pmol/L	





Urine Protein 1+

Blood / Hemoglobin 3+

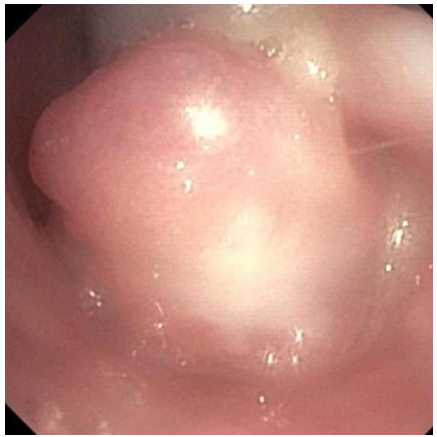
Red Blood Cells 50-75

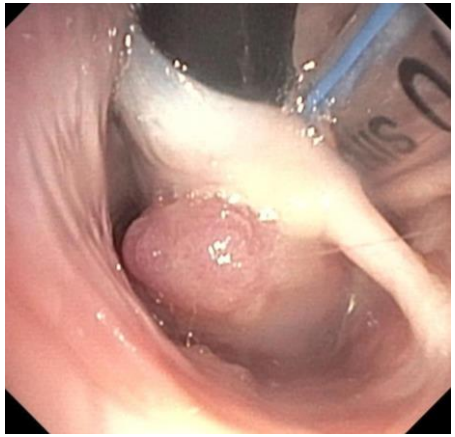
"OC"

Urinalysis
Urine culture

Imaging and Endoscopy

- AUS: No significant findings
- Nasopharyngoscopy





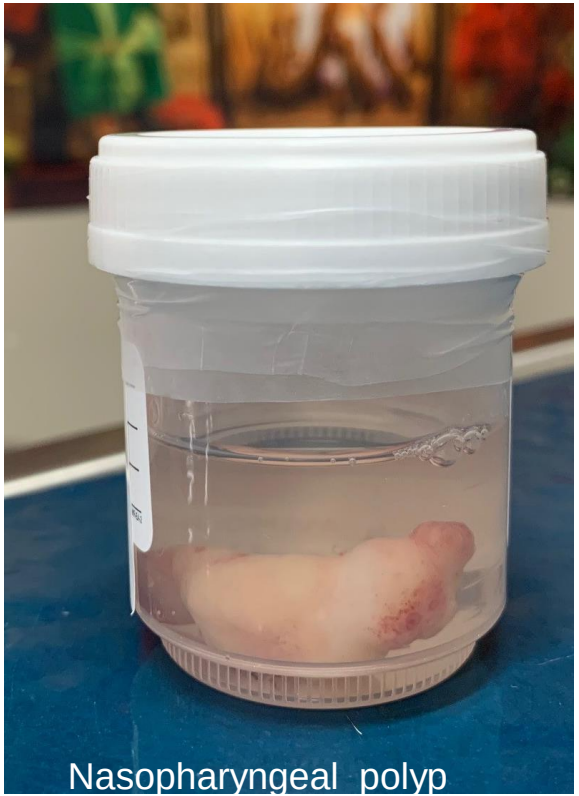
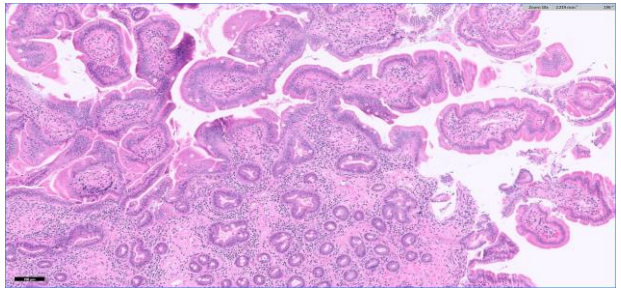
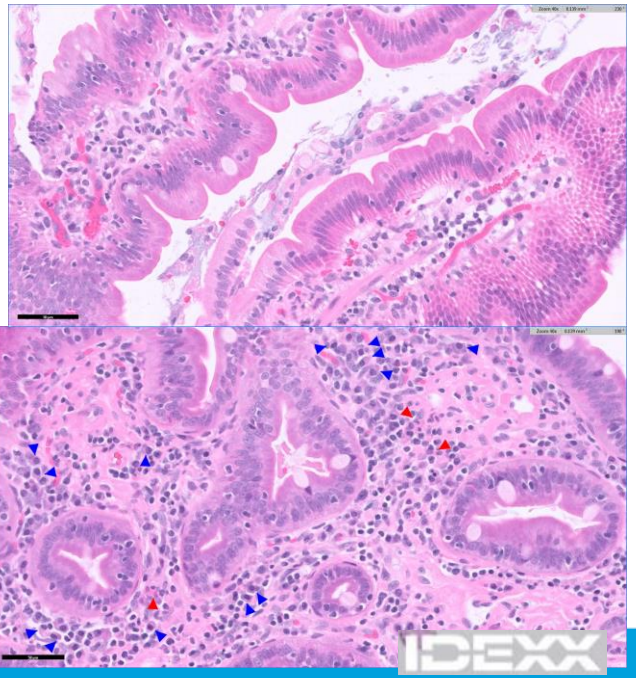


Image courtesy of Atlantic Veterinary Internal Medicine & Oncology, Annapolis, MD

Gastroduodenoscopy and Biopsy

- Grossly normal
- Histopathology
  - Stomach: Mild to moderate lymphoplasmacytic & mild eosinophilic gastritis with superficial spirochete bacteria
  - Duodenum: Mild plasmacytic and eosinophilic enteritis





OC - Assessment and Management

- Diagnoses
  - Chronic enteropathy
    - LPE
    - Food responsive?
  - Hypocobalaminemia
  - Nasal polyp- incompletely removed
- Plan
  - Prednisolone at tapering dose
  - Cobalamin supplementation SQ
  - Elimination diet
  - Monitor signs and weight

OC - Assessment and Management

- Consider additional diagnostics
  - fTLI
  - PCR for *Tritrichomonas*
  - Nasal imaging & rhinoscopy
  - More GI biopsies

- Dental consultation
- Top-loading carrier

Takeaways:

- Feline CE is common and weight loss may be the only sign
- Dietary management should be a priority
- Intestinal biopsy and histopathology is gold standard dx; even ancillary test results may be ambiguous
- Prognoses are similar for LPE and LGITL
- Spectrum of care may support human-animal bond and your patient

Thank you!

Questions?

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VMX
VETERINARY MEETING & EXPO

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, 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, prescoping scores did not differ between IBD, FRE
  - All 17 IBD patients (100%) complete remission after 3 weeks ≥75% reduction FCEIA

Jergens et al., 2010