Canine and Feline Exocrine Pancreatic Insufficiency

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Who am I?

- Grew up in central MA (Upton)
 - Summering in Cape Cod since 1996
- Currently live in Plymouth with my wife, 3 cats and Golden Retriever
- Special interests include immune-mediated, gastrointestinal, urinary and endocrine diseases









Education

- University of New Hampshire
 - Bachelors of Science (Biomedical Science) 2016
- Atlantic Veterinary College
 - Doctor of Veterinary Medicine 2020
- Atlantic Veterinary College
 - Masters of Veterinary Science (Defending Spring 2025)







Advanced Training

- Cape Cod Veterinary Specialists
 - Emergency and Critical Care Internship (2020 - 2021)
- Atlantic Veterinary College
 - Small Animal Internal Medicine Residency (2021 - 2024)
 - Board-certification in small animal internal medicine (2024)





Publications

Idiopathic cervical abscesses in dogs follow seasonal trends and geographic risk factors, predominantly affecting young, large breeds: a case-control study of 67 dogs in New England Bryan T. Welch, Raphael Vanderstichel, Rebecca Quinn, Lauren Toleson. Journal of the American Veterinary Medical Association, August 2024. Volume 262(10).

Hyperglycemic Hyperosmolar Syndrome Case Example

American Society for Veterinary Clinical Pathology Case Discussion Session. 2024. Matthew Yeung, Noel Clancey, Cornelia Gilroy, Sandra McConkey, **Bryan T. Welch**.

Decompressive craniectomy surgery in a dog with intracranial extradural hematoma following blunt force trauma Ciaran C. O'Carroll, **Bryan T. Welch**, Meagan A. Walker, Adam T. Ogilvie, Lorrie Gaschen, Katie L. Hoddinott. Canadian Veterinary Journal, May 2024. Volume 65(5). Pg 437.

Cricopharyngeal and thyropharyngeal myectomy for surgical management of cricopharyngeal achalasia in a 6-monthold coton de Tulear dog Bryan T. Welch, Adam T. Ogilvie, Ian Porter, Emilia Bourassi. Canadian Veterinary Journal, July 2023. Volume 64(1). Pg 633.

Ionized hypercalcemia in cats with azotemic chronic kidney disease (2012-2018) (article review) Bryan T. Welch, Sheri Ross. Clinician's Brief "in the literature" reviews. October, 2022.

Active Manuscripts/Research

Prospective comparison of biochemical and hematologic parameters on blood samples collected via traditional venipuncture and peripheral intravenous catheters in 70 hospitalized dogs

Successful medical management of subdural empyema causing intracranial hypertension secondary to a retrobulbar penetrating injury in a dog

Multi-center retrospective descriptive study of combined canine SRMA and IMPA in dogs

Tonight's Outline

- Test your knowledge!
- Functional anatomy and physiology of the pancreas
- What is EPI?
- Classic EPI presentation
- Achieving an EPI diagnosis
- EPI treatment
- Nutritional topics
- Lipase-specific EPI
- Feline EPI cats are not small dogs
- Comorbidities
- Case examples



Test Your Knowledge: Which has EPI?

Patient 2:

9m FI French Bulldog

Patient 1: 8m MI Great Pyrenees Mix

| Gastrointestinal L Test (Fasting) Cobalamin | aboratory - Canine Results and Int Result 271 | terpretation Control Range 251 - 908 ng/L | Test (Fasting) Cobalamin | Result >1000 | Con 251 - 908 ng/L |
|--|--|---|---------------------------------------|-----------------|------------------------------|
| Interpretation: | | | Interpretation: | | |
| 5 -1-4- | | 77.014 | Folate Interpretation: | 23.1 | 7.7 - 24.4 ug/L |
| Folate | 4 | 7.7 - 24.4 ug/L | Pancreatic-Lipase Immunoreactivity | <30 | < or = 200 ug/L |
| Pancreatic-Lipaso | e <30 | <or 200="" =="" l<="" td="" ug=""><td>Interpretation:</td><td></td><td></td></or> | Interpretation: | | |
| Interpretation: Trypsin-Like | 20.8 | | Trypsin-Like Immunoreactivity | <1 | |
| | | | | | |

Control Range

200 ug/L

Pancreatic Functional Anatomy

- Endocrine pancreatic islets
 - Secrete directly into the blood
 - Alpha cells (25%)
 - Produce glucagon
 - Beta cells (60%)
 - Produce insulin and amylin
 - Delta cells (10%)
 - Produce somatostatin
 - PP cells (5%)
 - Produce pancreatic polypeptide
- Exocrine pancreatic acini
 - Secrete digestive enzymes
 - Excreted into pancreatic duct
 - Empties into duodenum



https://s3-us-west-2.amazonaws.com/courses-images-archive-read-only/wj content/uploads/sites/403/2015/04/21031221/1820_The_Pancreas.jpg

Anatomic Differences Between Dogs and Cats

- Sonographic appearance
 - Cats
 - Body and left lobe most commonly visualized
 - Pancreatic duct more readily identified
 - Dogs
 - Body and right lobe most commonly visualized
- Pancreatic duct
 - Canine pancreatic ducts open discretely at the level of the major (and separately through the minor) duodenal papilla
 - Major duodenal papilla is common opening of pancreatic and common bile duct in cats
 - Cats lack minor papilla



The Exocrine Pancreas

- Large reserve capacity → signs of maldigestion not seen until <u>90% capacity</u> <u>lost</u>
- Pancreatic lipase → hydrolyzes fat into fatty acids
- Trypsin → splitting of proteins into polypeptides
- Pancreatic amylase → hydrolyzes starches and glycogen
- Phospholipase → splits fatty acids from phospholipids
- Cholesterol esterase → hydrolysis of cholesterol



https://basicmedicalkey.com/wpcontent/uploads/2016/06/m_Ham007_Fig_15-02.png

Exocrine Pancreatic Insufficiency

- **EPI:** syndrome characterized by insufficient synthesis and secretion of digestive enzymes from the exocrine pancreas
- Most common cause = absolute lack of acinar cells
 - Chronic pancreatitis (~50%)
 - Older patients
 - Depletion of acinar cells due to acinar atrophy (~50%)
 - Young to middle-aged
 - Pancreatic aplasia/hypoplasia → suspected when EPI diagnosed at very young age
 - No cases definitively diagnosed
 - Infrequent: pancreatic duct obstruction, pancreatic neoplasia
- Female predisposition (56% of cases)

Exocrine Pancreatic Insufficiency

- Consequence of EPI \rightarrow Maldigestion of intralumenal nutrients
 - Insufficient production of pancreatic digestive enzymes
 - Altered intestinal mucosal enzymes
 - Impaired intestinal function
- Additional consequences
 - Impaired cobalamin absorption
 - Cobalamin malabsorption and cellular deficiency
 - Small intestinal bacterial overgrowth (SIBO)

EPI – Pancreatic Acinar Atrophy



- Almost exclusively demonstrated in GSD, Rough-coated Collies and Eurasians
- PAA → inherited as autosomal recessive (partly)
- Realistically polygenic condition
 - Breeding of affected male with affected female → 2/6 puppies affected

EPI - Pathogenesis

- Acinar cells secrete digestive enzymes
 - Clinical signs of EPI not noted until >90% of exocrine pancreatic (acinar) function lost
- Lack of digestive enzymes \rightarrow maldigestion
- Maldigestion → undigested food in intestine → osmotic diarrhea, SI dysbiosis, weight loss
- Malabsorption + dysbiosis → lack of trophic factors that maintain GI mucosa

EPI - Pathogenesis

- Exocrine pancreas major source of intrinsic factor (dogs and cats)
 - In contrast to humans (gastric mucosa major source)
- Hypocobalaminemia
 - >80% of dogs
 - Lack of intrinsic factor
 - +/- concurrent ileal disease



https://azmilk.b-cdn.net/wp-content/uploads/2023/02/FUNCTIONS-OF-VITAMIN-B12.png

Intrinsic Factor

- Glycoprotein
 - Combines with B12 to make it available for absorption
- Intrinsic factor is REQUIRED for B12 absorption
 - Binds B12 \rightarrow protects from digestion
 - While bound, binds again to receptor sites in **ileum**
 - B12 transported to blood via pinocytosis
- Humans:
 - Produced by parietal cells of gastric glands
- Dogs and cats:
 - Produced exclusively by the pancreas



https://ars.els-cdn.com/content/image/1-s2.0-S1090023313000488-gr1.jpg



- 1) Ingested food includes B12
- R protein combines with B12 to protect from digestion in stomach
- Pancreas produces intrinsic factor and releases into duodenum
- 4) B12 released from R protein and combines with intrinsic factor
- 5) Intrinsic factor + B12 combo required for absorption in ileum

EPI – Clinical Presentation

- GSD, Eurasians, Rough-Coated Collies predisposed
 - Can happen in ANY breed

Most common clinical signs

- Weight loss
- Often poor hair coat and loose "pulpy" stool
- Borborygmus and increased flatulence
- Increased appetite
- Coprophagia
- Pica
- Watery diarrhea uncommon
- Can be subclinical!



https://shepherdshoperescue.org/wp-content/uploads/2020/12/EPI_before.jpg

EPI - Diagnosis



- Routine hematology and biochemical testing
 - Typically unremarkable
 - Abnormalities usually indicate concurrent/complicating disease
- Abdominal imaging
 - Ultrasound is preferred imaging modality
 - Pancreatic thickness may be reduced
 - Normal size does NOT rule out EPI
 - Small intestinal changes are common
 - Consistent with chronic enteropathy

https://www.catholichealthli.org/sites/default/files/styles/article_hero/public/2023-01/gettyimages-1300036735.jpg?h=95aa2365&itok=Bv4ohv25

EPI - Diagnosis

• Serum TLI = test of choice for dogs and cats (highly Se and Sp)

- Trypsinogen and trypsin rapidly excreted by the kidney
 - Only detectable if pancreas is functioning
- In patients with EPI trypsinogen released into blood decreased
 - Diagnosis cutoffs:
 - Dog: 2.5 mcg/L
 - Cat: 8.0 mcg/L
- Bear in mind: this is a progressive condition
- Exceptions to the rule
 - Lipase-specific EPI (isolated lipase deficiency)
 - Developing EPI (it is often a progressive process)
 - Obstructed pancreatic duct
- Fecal elastase → marketed as alternative to TLI
 - PPV <60%; 23% false positive
 - May have utility in cases with pancreatic duct obstruction

EPI – Diagnosis (Other Tests)

- Serum amylase and lipase \rightarrow NO value in diagnosing EPI
- Spec PLI → minimal value
 - Cannot be used to diagnose lipase-specific EPI
 - Will be below the detectable range
 - Can be used to help build clinical picture of diagnosis
- Other tests have been shown to have minimal to no utility
 - Microscopic fecal examination, bentiromide absorption, etc
- Histopathology \rightarrow minimal utility
 - EPI is a functional condition
 - Can identify acinar atrophy

A Hidden Diagnosis: Lipase-specific EPI

- Previously considered very rare (2017 TVIM reported a single case report), but becoming increasingly recognized
- Not all pancreatic enzymes are deficient
 - TLI will be NORMAL
- PLI will be below detectable limit
 - WILL BE INTERPRETED AS
 NORMAL
 - Considered normal for general population

J Vet Intern Med 2007;21:1113-1116

Suspected Isolated Pancreatic Lipase Deficiency in a Dog

Panagiotis G. Xenoulis, Jonathan M. Fradkin, Steven W. Rapp, Jan S. Suchodolski, and Jörg M. Steiner

Case Report J Vet Intern Med 2013;27:588-591

Suspected Isolated Pancreatic Enzyme Deficiencies in Dogs

K.R. Viviano and V. Ziglioli

A Hidden Diagnosis: Lipase-specific EPI

- Clinical signs will be consistent
- TLI interpretation will not include EPI as a differential
- PLI WILL be below the detectable limit
 - This is considered within the normal range
- This is a diagnosis of largely assumption and response to therapy
 - There is currently no commercial test for lipase-specific EPI
- Huskies and other arctic breeds appear predisposed

Subclinical EPI (SEPI)

- No clinical signs consistent with EPI
- TLI repeatedly subnormal
- Considered likely to develop
 clinical EPI in future
 - Duration varies from months to years
 - Recommend repeat TLI every 3-6 months



https://avmajoumals.avma.org/view/joumals/javma/262/2/full-javma.23.09.0505.fig_02.jpg

EPI – Treatment (Dried Pancreatic Extract)

- Mainstay: digestive enzyme therapy
 - Pancreatic enzyme replacement
 - Dried pancreatic extract from pork pancreas most common
- Starting dose: 1tsp dried extract per 10kg body weight at each meal
 - Dosage varies with different products
 - Adverse effects: oral bleeding (rarely)



Exocrine Pancreatic Insufficiency

EPI – Treatment (Dried Pancreatic Extract)

Jan 2022 Revised & work in progress updated list:

| Enzyme powder with approx Std 71,400 USP units of Lipase, 388,000 USP units Protease, 460,000 USP units Amylase | High Potency Enzyme powder with approx 110,000 USP units of Lipase, etc | Enzyme pills/capsules (some with lesser potency) multiple pills needed | Enteric coated Enzymes | Raw enzymes |
|--|--|---|------------------------|------------------------------|
| Biocase (discontinued) | EnzymeDiane 8x | Chemeyes | CREON | Green Cuisine 4 Pets |
| EnzymeDiane 6x | | Enzymax Tablets | Cotazym | GreenTripe Raw Beef Pancreas |
| EpiZyme | | Pancrea Plus | Lypex | Hare Today |
| Nextmune | | | | |
| Panakare Plus | | Pancrea Tabs Plus | Pancrealipase | Raw To Go |
| Pancreatic Enzyme Concentrate | | Pancreoflat | Pancrex | |
| Pancrezyme | | | Protexin | |
| PancrePlus | | | WeNzymes | |
| Pank-Aid | | | | |
| Panzquin | | | | |
| Pan-Tenex | | | | |
| Viokase | | | | |

EPI – Treatment (Dried Pancreatic Extract)

- Sprinkle onto (moistened) food and allow ~20 minutes to absorb
- Most animals do not require >2tsp per cup of food
 - If required, assess for concurrent chronic enteropathy
- Improvement in stool typically seen within a few days
 - May take 2-4 weeks
- Weight gain and coat improvement seen over several months
 - Monitoring weight and body condition is crucial in assessing response



EPI - Treatment (Pancreatic Enzyme Capsules)

- Study results:
 - No difference in response or outcome
- Commonly available formulations:
 - Creon, Cotazyme
- Potential benefits
 - Generally consistent availability
 - No need to sprinkle on food and allow absorption
 - Extended effects
- Downside
 - MUCH more expensive
- Dosing
 - Back-calculate based on targeted powdered extract dose – each product has different potency



Standard Article 👌 Open Access 💿 😧 😒

Randomized placebo controlled clinical trial of an enteric coated micro-pelleted formulation of a pancreatic enzyme supplement in dogs with exocrine pancreatic insufficiency



EPI – Treatment (Fresh Raw Pancreas)

- Fresh raw pancreas
 - 1-3 ounces (30-90g) of raw pancreas = 1 tsp dried extract
 - Finely chopped, divided into meal-sized portions and immediately frozen
 - Maintains enzymatic effects for long periods of time (storage not of concern)
 - Concerns regarding transmission of infections disease (BSE, pseudorabies)
 - More academic concern than reality
 - Powdered formulations carry identical (negligible) risk



https://static.wixstatic.com/media/8c5669_fd5cf7927fdc4235a461660c7d52bf61~mv 2.png/v1/fill/w_520,h_520,al_c,q_85,usm_0.66_1.00_0.01,enc_auto/8c5669_fd5cf7 927fdc4235a461660c7d52bf61~mv2.png

EPI – Treatment (Animal Alternatives)

REVIEW Open Access © (C) A review: Pancreatic enzymes in the treatment of chronic pancreatic insufficiency in companion animals

TERINARY INTERNAL MED

JOURNAL OF

- Plant and microbial product enzymes are being investigated
- Promising alternative to animal-derived enzymes
- Studies in humans and animals
 - Results show similar response
- Not currently commercially available
- Potential benefits
 - Lab culture grown
 - High quality control
 - Not reliant on animal supply

EPI – Cobalamin Deficiency

- 2 most common causes of hypocobalaminemia
 - EPI \rightarrow lack of intrinsic factor
 - Chronic ileal disease \rightarrow reduced number of cobalamin receptors
 - Concurrent chronic enteropathy common
- Every dog with EPI should be evaluated
 - Majority (>80%) deficient
- Methylmalonic acid (MMA) → more accurate indicator of cobalamin on cellular level
 - More expensive and limited testing availability; not routinely performed
- When to supplement
 - < 400 ng/L → benign therapy, I will often consider it in the low 400s as well



The Veterinary Journal Volume 191, Issue 3, March 2012, Pages 306-311



Methylmalonic Acid

Association between serum cobalamin and methylmalonic acid concentrations in dogs

Nora Berghoff 😤 🖾, Jan S. Suchodolski, Jörg M. Steiner

- More accurate indicator of cellular cobalamin levels
 - Serum cobalamin does not necessarily reflect cellular cobalamin
- Production of MMA occurs when cellular adenosyl-cobalamin inadequate
 - Cobalamin required cofactor for methylmalonyl CoA mutase
 - Altered metabolism pathway with hypocobalaminemia → production of MMA
- Hypocobalaminemia correlates well with MMA
 - Serum cobalamin <251 ng/L significantly higher MMA (p<0.05)
 - Trend of increasing MMA with decreasing cobalamin (P<0.0001)

Consequences of Hypocobalaminemia

- Cobalamin is a cofactor involved in a wide range of cellular mechanisms
- Deficiency can be associated with:
 - Abnormalities in GI mucosal permeability (contributes to malabsorption)
 - Megaloblastic anemia
 - RBC size not shown to be consistent in dogs
 - Known cause of non-regenerative anemia
 - Pernicious anemia (in humans due to associated iron deficiency)
 - Degenerative myelopathy
 - Cardiovascular disease
 - Worsened outcome in chronic enteropathy, EPI, lymphoma

EPI – Cobalamin Supplementation

- Supplementation with SQ injectable or oral formulations
 - No clinical benefit of injectable formulation
- SQ protocol:
 - 1x weekly for 6 weeks, then 1 month later
 - Recheck levels 1 month after final dose
- Oral protocol:
 - Daily oral supplementation for 12 weeks
 - Recheck levels 1 month after final dose
- I tend to give clients option of retesting versus long-term oral administration



Journal of Veterinary Internal Medicine

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STANDARD ARTICLE 🖻 Open Access 💿 🛈
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Effect of oral or injectable supplementation with cobalamin in dogs with hypocobalaminemia caused by chronic enteropathy or exocrine pancreatic insufficiency

Chee-Hoon Chang 🔀, Jonathan A. Lidbury, Jan S. Suchodolski, Joerg M. Steiner


EPI – Treatment (Nutrition)

- Some recommend low fat diet → not required; may not be recommended
 - Even with supplementation, normal fat digestion does not return
 - Restricting fat may risk deficiencies of fat-soluble vitamins and essential fatty acids
- Several studies have documented no benefit in specific diets
- AVOID high fiber diets → adversely affect fat soluble vitamin absorption and lack caloric density
 - Most of these animals have caloric deficit as it is



EPI – Fat-soluble Vitamins

DOI: 10.1111/jvim.15292

Journal of Veterinary Internal Medicine

STANDARD ARTICLE

Serum concentrations of lipid-soluble vitamins in dogs with exocrine pancreatic insufficiency treated with pancreatic enzymes

Patrick C. Barko 💿 | David A. Williams

- Retinol (vitamin A), alpha-tocopherol (vitamin E) and 25OHD (vitamin D)
- Human EPI
 - Documented correlation of EPI with vision loss, decreased bone density and coagulopathies
- Vitamin A and E levels significantly lower in dogs with EPI
 - Clinical significance unknown
 - Re-evaluate reference intervals?

EPI – Treatment Failure

- Causes of treatment failure:
 - Inadequate enzymatic supplementation
 - Assess type, dose, formulation and adjust accordingly
 - Concurrent, complicating conditions
 - Inflammatory bowel disease
 - Intestinal dysbiosis
 - Diabetes mellitus

EPI – Treatment Failure

- Consideration of tylosin trial
- Antacid therapy
 - Pancreatic lipase supplemented orally may be destroyed by gastric pH
 - Increased gastric pH → less degradation → improved therapeutic response
 - However, increased pH \rightarrow increased gastric lipase destroyed
 - For refractory cases, omeprazole therapy may result in significant improvement
- If all else fails: decrease dietary fat content (last resort)

EPI – Prognosis



Contents lists available at ScienceDirect

The Veterinary Journal



journal homepage: www.elsevier.com/locate/tvjl

Original Article

Serum cobalamin and folate as prognostic factors in canine exocrine pancreatic insufficiency: An observational cohort study of 299 dogs



N. Soetart^{a,*}, D. Rochel^a, A. Drut^b, L. Jaillardon^a

- Life-long treatment required
 - Pancreatic acinar cells generally considered to not regenerate
 - Experiments support some regenerative ability
- Isolated reports of patients who recover
- In general, normal quality of life and life expectancy
- Prognostic indicators
 - Negative prognostic indicator severe hypocobalaminemia
 - MST 1346 vs 2709 (p 0.012)
 - Male sex
 - Decreased appetite at diagnosis
 - Failure to supplement enzymes

EPI – Prognosis

- Overall good prognosis long-term
- Pancreatic enzyme replacement therapy efficacy
 - Complete response in 60% of dogs
 - Partial response in 17% of dogs
 - Poor response in 23% of dogs
- Incomplete response to treatment → chronic diarrhea most common



EPI dog just diagnosed (left) and 4 months later with proper treatment (right)



https://cooperpetcare.com/wp-content/uploads/2023/07/EPI-cats.png

- Feline EPI is much more common than once thought!
- Can occur at any age
- No sex predilection
- Identifying EPI in cats can be challenging
 - Weight loss is the most common clinical sign (up to 91% of cases)
 - Soft stool, poor hair coat, lethargy, vomiting and anorexia may also be seen
 - Weight loss may be ONLY sign
- 70-100% of cats are hypocobalaminemic
 - Supplementation as for dogs

- Concurrent conditions
 - Extremely common in cats
 - 82% in one study
 - Chronic enteropathy 59%
 - Pancreatitis 18%
 - Diabetes mellitus 14%
- Diagnostic imaging
 - Pancreas appeared normal in 39%
 - Limitations of feline pancreatic ultrasonography
 - Pancreatic duct dilation seen in 46%



STANDARD ARTICLE 🕆 Open Access 🛛 😨 🛞

Abdominal ultrasound and clinicopathologic findings in 22 cats with exocrine pancreatic insufficiency



Standard Article 🔂 Open Access 💿 🔅 😒

Feline Exocrine Pancreatic Insufficiency: A Retrospective Study of 150 Cases

- Treatment
 - Pancreatic enzyme replacement
 - Starting dose 1 tsp per meal
 - Lower fTLI and cobalamin supplementation associated with improved clinical response
- Prognosis
 - Long-term prognosis is good; requires life-long treatment
 - Pancreatic enzyme replacement therapy
 - 40-60% have complete response
 - 27-60% have partial response

Concurrent Conditions Seen With EPI

- EPI is often not an isolated condition
 - Abnormal metabolism of trophic factors and dysbiosis are part of EPI pathogenesis
- May see development of chronic enteropathic conditions
 - Chronic bacterial dysbiosis
 - Chronic enteropathy/inflammatory bowel disease
 - Micronutrient deficiencies

EPI and Micronutrient Deficiencies

- Deficiencies in lipid-soluble vitamins are common in human EPI
- EPI dogs also have malabsorption of lipid-soluble vitamins
 - Persist after enzyme replacement therapy
 - Case report of vit K deficiency in cat with EPI
- Clinical significance unclear

•

- Vit A, D and E are vital in gastrointestinal health
- Supplementation of lipid-soluble vitamins is not common practice
 - Hypervitaminosis from lipid-soluble vitamins and resulting toxicity is possible
 - Accumulation within tissues
 - This is not seen with water-soluble vitamins (cobalamin)

EPI and Chronic Enteropathy





Article Ultrasonographic Findings of Exocrine Pancreatic Insufficiency in Dogs

Tina Pelligra 🔍, Caterina Puccinelli 🔍, Veronica Marchetti 🔍 and Simonetta Citi *

- Persistent clinical signs after enzyme replacement should raise suspicion
 - Clinical signs can be indistinguishable
- Concurrent chronic enteropathy is quite common
 - 20 >50% of cats with EPI have chronic enteropathy
 - 85% of dogs in one study had SI changes consistent with inflammatory bowel disease

Chronic Enteropathy – Diagnostic Approach

- If patient with EPI not responding as expected, CE must be considered
 - Particularly if titrating up pancreatic enzymes not effective
- Diagnostic investigation
 - AUS if not performed already
 - Full baseline bloodwork and urinalysis
 - Depending on timeframe from diagnosis of EPI, consider retesting full GI panel
 - DON'T FORGET A FECAL (Keyscreen PCR is a comprehensive consideration)
 - Consider fecal dysbiosis index (Texas A&M)

Chronic Enteropathy – Subtypes

- Chronic enteropathy (AKA inflammatory bowel disease) is a spectrum
- Not a specific diagnosis, but a clinical syndrome
- **Diagnosis of exclusion** with compatible clinical signs and diagnostic tests
- 3 classic subtypes
 - Diet-responsive → managed with diet-alone
 - Antibiotic-responsive → managed with antibiotic (tylosin) +/- diet
 - Steroid-responsive → Diet + immunomodulation (steroids) +/- adjunctive therapies

Chronic Enteropathy – Nutritional Approach

- All dogs with chronic enteropathy benefit from nutritional assessment
 - Response rate to dietary manipulation >50%
 - Some report even higher with time and patience
- Nutritional factors to consider
 - Previous diets
 - Protein source
 - Fat content
 - Digestibility
 - Energy requirements
 - Formulations
 - Feeding schedule

Dog Nutrition Chart



Practical Approach to Diet Trials



- Good diet history is KEY
 - Vast majority of immunologic response to diet is the PROTEIN source
 - Despite clever marketing of "boutique" diets, the grain content and processing of commercial diets is almost never to blame
 - EVERYTHING that passes dog's lips must be accounted for
 - Including monthly preventative medications
- Escalation of diets:
 - Novel protein → hydrolyzed protein → extensively hydrolyzed (ultamino)
 - Consideration for home-cooked diets for dogs who will not eat hydrolyzed or fail other options
 - STRONGLY recommend guidance from nutritionist

Practical Approach to Diet Trials

- My typical approach for **mild cases**
 - Easily digestible diet (GI Biome) → novel protein diet → hydrolyzed protein diet
- My typical approach for **severe cases**
 - Hydrolyzed protein diet → ultamino diet → home-cooked nutritionist-guided diet
- Important considerations:
 - Nexgard, Heartgard, etc are NOT hydrolyzed
 - Simparica Trio IS
 - 2-3 week STRICT diet trial to assess response
 - Immunologic response to ingesta today can persist for 2-3 weeks
 - Exception: if patient's signs get significantly worse after diet change

Nutritional Factors to Consider

- Some dogs do better with smaller, more frequent feedings
 - Particularly if regurgitation or bilious vomiting is seen
- Fat content can be very important
 - Fat restrictive diets can be extremely helpful
 - Particularly in cases of PLE (z/d Low Fat is my preferred diet for these cases)
- Digestibility
 - Highly digestible diets are beneficial
- Formulations
 - Not all diets come in canned and kibble formulations
 - Not all diets are formulated for growth
 - Purina HA Salmon IS
- Energy requirements
 - Malabsorptive conditions may lead to significant increase in caloric requirements

Nutritional Factors to Consider

REVIEW

Dietary management of chronic enteropathy in dogs

M. K. Tolbert ^{(0*,1}, M. Murphy[†], L. Gaylord[‡] and A. Witzel-Rollins[†]



Nutritional Factors to Consider

REVIEW

Dietary management of chronic enteropathy in dogs

M. K. Tolbert ⁽¹⁾*,¹, M. Murphy[†], L. Gaylord[‡] and A. Witzel-Rollins[†]

| Ideal Bodyweight If Underconditioned: Increase by 10% for each BCS below 5/9 BCS 1/9=40% Current BWx1.4 BCS 2/9=30% Current BWx1.3 BCS 3/9=20% Current BWx1.2 Resting Energy Reg 70x(ideal be Maintenance Energy R RERxL | Ideal Bodyweight If Over-Conditioned: (Current BWxCurrent % lean) 0.8* *Ideal percentage of bodyweight that is lean uirement, RER, in kcal/day = ody weight in kg) ^{0.75} Requirement, MER, in kcal/day = Lifestage Factor | |
|--|--|--|
| Nutritional Assessment Factor | Lifestage Factor | |
| Neutered adult | 1.2 to 1.6 | |
| Intact adult | 1.6 to 1.8 | |
| Inactive, obese prone | 1.0 to 1.2 | |
| Weight loss | 1.0 | |
| Growth | <4 months: 3.0 | |
| Malabsorptive disease | >1.8 | |

Chronic Enteropathy – Antibiotic-Responsive

- Antibiotic-responsive CE patients tend to have diarrhea as primary clinical sign
- Preferred: tylosin
 - Starting dose 20-25mg/kg PO q12-24hr
 - Taper to lowest effective dose
 - Dosing tip: 1 tsp = 2.5g; 1/8 tsp = 325mg
- Can be considered: metronidazole
 - For long-term treatment consider low-doses
 - 5-7.5mg/kg q12-24hr
 - Convincing evidence of long-term dysbiosis following treatment
 - In reality, the same issue likely exists with tylosin

Chronic Enteropathy – Steroid-Responsive

- Initially prednisone or prednisolone
 - Anti-inflammatory doses
 - Immunosuppressive doses RARELY more effective and associated with worse outcome
 - Taper to lowest effective dose (in some cases can be discontinued with dietary management)
 - Consider budesonide for long-term administration
- Occasionally other immunomodulatory medications
 - Cyclosporine
 - Azathioprine
 - Mycophenolate

Chronic Enteropathy – Adjunctive Treatments

- Numerous adjunctive treatments exist
 - Antacid therapy (PPIs for chronic administration)
 - Prokinetics (metoclopramide)
 - Pro/prebiotics
 - Preferred options: Proviable, Visbiome
 - Fecal microbiota transplantation
 - Replenishes Clostridium hiranonis



https://katygastro.com/wp-content/uploads/2021/08/bigstock-Vector Mographics The-Goo-427177235-1.jpg

Chronic Enteropathy – When To Biopsy?

- There are many times when to consider a biopsy
 - Loss of GIT layering on AUS
 - Focal mass/thickening
 - Lack of response to treatments
 - Prior to steroid therapy
- Important considerations for biopsies
 - Endoscopy has limitations!
 - Depth of samples (cannot reach muscularis layer)
 - Location of samples (cannot reach jejunum)
 - There are situation where surgical biopsies are preferred
 - Yes, even by an internist



https://www.circlehealthgroup.co.uk/-/media/circle/spotlights/inspotlights/in-article-images/everything-you-need-to-know-abou endoscopy_2.jpgalt=?rev=027672a0600841838f6a30798980 &hash=566EB34ACD3C87BE 09B7FEE 6807E95D5

EPI and Persistent Dysbiosis

EPI predisposes to SIBO

- Enzyme replacement therapy may correct dysbiosis
 - May persist despite therapy
- Fecal microbiome studies in dogs have documented persistent dysbiosis despite appropriate therapy
 - Dysbiosis is a differential for persistent clinical signs
- Probiotics and prebiotics may be considered, but are often ineffective
- Tylosin 25mg/kg q12-24hr for 2-4 weeks and tapered to lowest effective dose can be effective; may be continued indefinitely
- Fecal microbiota transplantation can be quite effective

Fecal Dysbiosis Testing



sinsmallanimal care.com/cms/asset/dca430ca-4f76-45b8-b8de-

- Fecal DI testing can provide valuable insight
 - Documentation of dysbiosis
 - Identification of unique sources of dysbiosis
 - Prediction of FMT efficacy
 - Screen fecal donor
 - Monitoring response to treatment
- I prefer Texas A&M
 - Quantitative fecal flora PCR
 → provides DI index
 - Other companies do similar testing, but are aiming to sell a product

Fecal Microbiota Transplantation

- FMT transplantation therapy is safe and effective
- Useful in both acute and chronic diarrhea
- Provides replenishment of organisms often not included in traditional pro/prebiotics
 - Clostridium hiranonis
- Colonic direct inoculation and oral capsule forms
 - Data comparing the two is lacking
 - Most studies with direct inoculation





Article

Clinical Effects of Faecal Microbiota Transplantation as Adjunctive Therapy in Dogs with Chronic Enteropathies— A Retrospective Case Series of 41 Dogs

Fecal Microbiota Transplantation in Dogs

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ACVIM JOURNAL OF VETERINARY INTERNAL MEDICINE

STANDARD ARTICLE 🔂 Open Access 💿 😧

Effect of a single rectal fecal microbiota transplantation on clinical severity and fecal microbial communities in dogs with chronic inflammatory enteropathy



Standard Article 🔂 Open Access 🛛 💿 🚯

Fecal microbiota transplantation in puppies with canine parvovirus infection

The Importance of Good Bacteria



 Faecalibacterium, Fusobacterium, Turicibacter, Blautia are short-chain fatty acid producers

- SCFAs: acetate, proprionate, butyrate
- Primary energy source for colonocytes
- Peptacetobacter (Clostridium) hiranonis is the main species responsible for the conversion of primary into secondary bile acid in dogs and cats
 - Regulate glucose and lipid metabolism
 - Energy production
 - Inflammatory signaling
- Diminished C. hiranonis strongly associated with severe dysbiosis and colonization with pathogenic bacteria

https://static.vecteezy.com/system/resources/previews/045/639/99 8/non_2x/cute-bacteria-and-virus-character-flat-cartoon-illustrationon-white-background-vector.jpg

Dysbiosis Index



Figure 5. A dog with persistent dysbiosis after long-term antibiotic administration. FMT as enema was performed, leading to normalization of the microbiota.

An update on Fecal Microbiota Transplantation (continued)

Box 1. FMT protocol (Dr. Jennifer Chaitman, VMD, Diplomate ACVIM at Veterinary Internal Medicine and Allergy Specialists)

- Screen donor stool for parasites, enteropathogens (via fecal flotations and PCR diarrhea panel), and for the normal microbiota (using PCR test for dysbiosis index)

- Optionally, at our clinic we place the donor dog on a limited ingredient hypoallergenic diet for six weeks prior to collecting stool for donation

- Use fresh or frozen stool. The recipient will receive 2.5 to 5 grams of donor stool per kg BW blended with 60 ml of saline (blender setting on high). For very large dogs a larger volume of saline may be needed to obtain a sufficiently liquefied stool

- Draw up the mixed stool/saline material into a 60 ml catheter tip syringe, and attach a 12 French red rubber catheter

- Push some of the material into the catheter until it comes out the tip so that no air will be introduced into the colon of the recipient
- Advance the catheter all the way in to the colon, then administer enema. The recipient dog does not need to be sedated

- If possible, do not feed the patient for 4-6 hours. Also, restrict the recipient dog's activity for 4-6 hours after the transplant to lessen the chance for a premature bowel movement



Case Example – Patient 1 (Kenji)

- 8m MI Great Pyrenees X
 - Referred for evaluation of fever, warm and painful joints and lethargy
 - Described as always having semi-formed stool and difficulty gaining weight
 - Diagnosed with IMPA, SRMA, <u>lipase-specific</u> EPI, hypocobalaminemia and diet-responsive chronic enteropathy
 - Treated with prednisone, azathioprine, tylosin, B12 injection protocol, Cotazyme (enteric-coated capsule), hydrolyzed protein diet

Case Example – Patient 1

| | Gastrointestinal Laboratory - Canine Results and Interpretation | | |
|---|---|--|---|
| 1 | Test (Fasting) | Result | Control Range |
| | Cobalamin | 271 | 251 - 908 ng/L |
| | Interpretation: | Result is at the low end of the reference interval. Suggestive of distal small intestinal disease (i.e., ileum), EPI, or dysbiosis. Check serum canine TLI concentration to rule out EPI (if this has not already been done). Oral or parenteral cobalamin supplementation is indicated Please see - http://vetmed.tamu.edu/gilab/research/cobalamin-information | |
| | Folate | 4 | 7.7 - 24.4 ug/L |
| | Interpretation: | Decreased serum folate concentration. Consistent with diseases affecting the proximal small intestine. Consider folate supplementation. http://vetmed.tamu.edu/gilab/research/folate-information | |
| | Pancreatic-Lipase | <30 | <or 200="" =="" l<="" td="" ug=""></or> |
| | Interpretation: | Result within the reference interval. It is unlikely that this dog has clinically relevant pancreatitis. Investigate for other diseases that could cause the clinical signs absented. | |
| | Trypsin-Like | 20.8 | 5.7 - 45.2 ug/L |
| | | | |

Case Example – Patient 1 (Before)



Case Example – Patient 1 (After)





Case Example – Patient 2 (Neen)

- 9m FI French Bulldog
 - Presented for evaluation of failure to thrive, chronic diarrhea, lethargy and hypoalbuminemia
 - Diagnosed with EPI (pancreatic acinar atrophy), inflammatory bowel disease and suspected portal vein hypoplasia
 - Clinical signs, pancreatic and intestinal biopsies
 - Treated with Pantenex (powdered pancreatic enzymes), oral cobalamin protocol, tylosin and hydrolyzed protein diet
Case Example – Patient 2









QUESTIONS?

Any additional questions may be directed to bryanwelch@capecodvetspecialists.com



NOTICE

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