Chronic Diarrhea in the Dog and Cat

Jinelle Webb
DVM, DVSc, Dipl ACVIM
Treating the pet with diarrhea

- Many clients will present with their dog or cat, complaining of chronic diarrhea
- Many of these clients will have tried their own therapies at home already
  - Dietary modification
  - Over the counter or home remedies
    - Dewormers
    - Probiotics
    - Anti-diarrheals
Treating the pet with diarrhea

- The most effective way to treat chronic diarrhea is to determine an underlying cause, if possible
- History
- Therapies tried to date and response
- Physical examination including rectal examination
- Lab testing
- Further diagnostics
Causes of chronic diarrhea

Most common:

- Infectious disease
  - Parasites – worms, *Trichomonas*, etc
  - Bacteria – *Salmonella*, *Campylobacter*, etc
  - Viruses - not common
  - Fungi – specific geographic areas
- Dietary intolerance
- Inflammatory bowel disease
- Intestinal lymphangiectasia
- Neoplasia
Causes of chronic diarrhea

Most common continued:
- Intestinal dysbiosis (previously SIBO, ARD)
- Ulcerative colitis
- Idiopathic chronic diarrhea (undiagnosed?)

Less common:
- Breed related enteropathies
- Systemic disease
  - Pancreatitis, hyperthyroidism, exocrine pancreatic insufficiency, hypoadrenocorticism, etc
- Chronic intussusception
History

- Signalment (consider breed specific diseases)
- Housing, interaction, outdoor activities
- Travel history
- Deworming history (including heartworm prevention)
- Diet history (thorough!) including treats, access to other pet’s food, human food, indiscretion
- Therapies to date, including at-home and OTC
- Vomiting
- Activity level, perception of weight
- Describe the diarrhea (in detail)
- Skin coat
Diarrhea

Small intestinal
- Larger volume
- 3-5 times per day
- Melena
- Vomiting
- Weight loss
- Borborygmus
- Flatulence

Large intestinal
- Smaller volume
- More frequent
- Tenesmus
- Frank blood
- Mucous
- Flatulence
Physical examination

- Assess mentation
- Level of hydration
- Cachexia, muscle loss
- Skin coat
- Thoracic auscultation
- Abdominal palpation
- Rectal palpation
- Lymph node palpation
Initial diagnostic testing

- Complete blood cell count
- Biochemical profile
- Urinalysis
- Fecal examination for ova and parasites
- Consider microscopic examination of fecal material and/or distal colonic scraping
  - Ideally above testing in all patients
  - Consider patient – puppy may start with just O/P
Complete blood count

- Microcytosis, decreased hemoglobin, thrombocytosis associated with gastrointestinal blood loss
- Macrocytosis if recent, regenerative anemia, cats with hyperthyroidism or FeLV
- Eosinophilia with parasitism, eosinophilic IBD, hypereosinophilic syndrome, hypoadrenocorticism, some cases of lymphoma and mast cell tumour
- Neutrophilia with inflammatory and infectious conditions
- Lymphopenia with stress, PLE
- Lymphocytosis in hypoadrenocorticism or young pets
Biochemical profile

- ↑K and ↓Na with hypoadrenocorticism, Whipworms, *Salmonella* and GI ulceration
- Increase in ALT can be due to hyperthyroidism and GI disease (up to about 500 IU/L)
- Hypocholesterolemia with PLE and EPI
- Hypoalbuminemia and hypoglobulinemia most consistent with PLE (panhypoproteinemia)
- Hypoalbuminemia and hyperglobulinemia more consistent with PLN, liver disease, systemic inflammatory disease, neoplasia, some breed-related enteropathies
Further diagnostic testing

- Clinical disease activity indexes, fecal scoring
- TLI/cobalamin/folate
- Fecal DNA testing (such as *Giardia, Tritrichomonas*)
- Culture for fecal pathogens
- Fecal occult blood
- Thyroid testing (cats)
- ACTH stimulation test (usually dogs)
- cPL or fPL
- FeLV/FIV testing (cats)
CIBDAI and CCECAI

- **CIBDAI** - Clinical Inflammatory Bowel Disease Activity Index Jergins et al 2003, JVIM

- **CCECAI** – Canine Chronic Enteropathy Clinical Activity Index Allanspach et al 2007, JVIM

**CIBDAI and CCECAI:**
1. Attitude/activity
2. Appetite
3. Vomiting
4. Stool consistency
5. Stool frequency
6. Weight loss

**CCECAI only:**
7. Albumin
8. Ascites/peripheral edema
9. Pruritus

- Most useful for response to treatment?
Fecal scoring

Fecal Scoring System

Score 1 — Very hard and dry; requires much effort to expel from body; no residue left on ground when picked up. Often expelled as individual pellets.

Score 2 — Firm, but not hard; should be pliable; segmented appearance; little or no residue left on ground when picked up.

Score 3 — Log-like; little or no segmentation visible; moist surface; leaves residue, but holds form when picked up.

Score 4 — Very moist (soggy); distinct log shape visible; leaves residue and loses form when picked up.

Score 5 — Very moist but has distinct shape; present in piles rather than as distinct logs; leaves residue and loses form when picked up.

Score 6 — Has texture, but no defined shape; occurs as piles or as spots; leaves residue when picked up.

Score 7 — Watery, no texture, flat; occurs as puddles.
Levels reflect dietary intake, ability to uptake, bacterial utilization and production, body losses
Consider dietary intake and supplementation
Low cobalamin with EPI, PLE, intestinal dysbiosis, lymphoma, in Giant Schnauzers/Shar Peis
Low folate with severe jejunal disease, lymphoma, some Irish Setters with a gluten-sensitive enteropathy
High folate is seen with EPI, PLE, intestinal dysbiosis and some Irish setters with a gluten-responsive enteropathy
Changes seen with some hepatic/pancreatic disease
Fecal culture

- Indicated in acute hemorrhagic diarrhea, neutrophils on rectal cytology, pyrexia, +/- inflammatory leukogram
- Rarely helpful in chronic diarrhea
  - *Salmonella* spp
  - *Campylobacteria jejuni*
  - *Clostridium difficile* and *perfringens* – enterotoxin? significance?
- Many bacteria will need PCR probe to determine whether a pathogenic strain
# IDEXX Diarrhea Panel

<table>
<thead>
<tr>
<th>Canine Comprehensive Diarrhea Panel</th>
<th>Feline Comprehensive Diarrhea Panel</th>
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<tbody>
<tr>
<td><em>C. perfringens</em> Enterotoxin A</td>
<td>Feline Coronavirus</td>
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<tr>
<td>69%</td>
<td>79%</td>
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<tr>
<td><em>Giardia</em> sp</td>
<td><em>C. perfringens</em> Enterotoxin A</td>
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<td>24%</td>
<td>48%</td>
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<tr>
<td><em>Cryptosporidium</em> sp</td>
<td><em>Trichomonas foetus</em></td>
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<tr>
<td>14%</td>
<td>13%</td>
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<tr>
<td>Canine Enteric Coronavirus</td>
<td><em>Cryptosporidium</em> sp.</td>
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<tr>
<td>14%</td>
<td>10%</td>
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<tr>
<td><em>Campylobacter jejuni</em></td>
<td><em>Giardia</em> sp.</td>
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<td>8%</td>
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<td><em>Canine Parvovirus 2</em></td>
<td><em>Campylobacter jejuni</em></td>
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<tr>
<td>4%</td>
<td>3%</td>
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<tr>
<td><em>Salmonella</em></td>
<td><em>Salmonella</em></td>
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<tr>
<td>3%</td>
<td>1%</td>
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<tr>
<td><em>Campylobacter coli</em></td>
<td>Feline Panleukopenia Virus</td>
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<tr>
<td>2%</td>
<td>1%</td>
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<tr>
<td>Canine Distemper Virus</td>
<td><em>Campylobacter coli</em></td>
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<tr>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td><em>Toxoplasma gondii</em></td>
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<td></td>
<td>&lt;1%</td>
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</table>

1/3 of samples are co-infected; data courtesy of IDEXX CANADA.
Homer

- 6 month old MI Cavalier King Charles
- Poorly trained but very cute
- Rescued from breeder for suspected heart disease
- Parvovirus at 2 months
- Stools never fully formed after recovery
- Full blood work and UA normal
- Abdominal ultrasound normal
- No response to Fortiflora
- Oh wait, did I submit a fecal O/P?
Homer

- IDEXX results
- Fecal O/P negative
- Repeat fecal O/P:
  - Ova & Parasites - Sedimentation / Concentration
    - Isospora ohioensis oocysts
- Treated with S-250
- Normal stool after treatment
FISH testing

- Fluorescence in-situ hybridization
- Identifying and localizing various bacterial species within lesions in the mucosa (16s rRNA probe)
- Formalin fixed tissue

Indications:
- Boxer ulcerative colitis
- Cases with bacterial invasion of mucosa on histopathology
- Cases with significant neutrophilic component to inflammation
- Geographical cases
- Cases previously very responsive to antibiotics (especially if to antibiotics other than tylosin/metronidazole)
Fecal occult blood

- Blood/muscle component in food with heme product intact
- Depends also on test used to detect fecal occult blood
- O-tolidine – few false positives
- Guaiac test – more false positives
- Most labs use the guaiac based test
- Some diets cause a false positive
  - Likely based on meat component
  - z/d can cause false positive based on VIN discussion
Fecal occult blood

- Patients should not ingest food or vitamins, which can cause false-positive or false-negative test results, for at least 48-72 hours.

**False Positives:**
- Red meat (beef, liver and lamb)
- Non-steroidal anti-inflammatory drugs
- Corticosteroids, phenylbutazone, reserpine, anticoagulants, antimetabolites, and cancer chemotherapeutic drugs
- Diets rich in fresh vegetables
- The application of povidone/iodine mixture

**False Negatives:**
- Vitamin C in excess of 250 mg per day
- NOTE: Dietary iron supplements will NOT produce false-positive test results.
Spec cPL/fPL

- Assessment for pancreatic inflammation
- Issues with sensitivity and specificity, but no gold standard (even with pancreatic biopsy)
- Elevated in many cases of GI disease
- Not clear if due to GI disease-associated chronic pancreatitis, or non-pancreatic elevation
- Associated with a worse outcome in dogs with IBD (2009 study, 47 dogs)
- Elevated in some PLE cases (3/29), but not food responsive diarrhea cases (0/18) (2015 study, 47 dogs)
<table>
<thead>
<tr>
<th></th>
<th>cPL</th>
<th>TLI</th>
<th>Amylase</th>
<th>Lipase</th>
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<tr>
<td>(mild)</td>
<td>43</td>
<td>30</td>
<td>7</td>
<td>54</td>
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<tr>
<td>(mod/sev)</td>
<td>71</td>
<td>29</td>
<td>14</td>
<td>71</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
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<tr>
<td>(mild)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>43</td>
</tr>
<tr>
<td>(mod/sev)</td>
<td>86</td>
<td>100</td>
<td>100</td>
<td>43</td>
</tr>
</tbody>
</table>
Tests specific to GI disease

- Gastrointestinal permeability testing
- Evaluation of intestinal protein loss
- Markers of gastrointestinal inflammation and damage
- Assessment of intestinal function and pathology
- Assessment of intestinal dysbiosis
GI permeability testing

- Oral exogenous nonmetabolizable markers
  - Polyethylene glycol, mono/disaccharides, radioactive
- Increased presence of marker in blood or urine indicates increased GI permeability
- Only saccharide-based probe helps distinguish between different areas of GI tract
- Only useful if histopathology normal, and trying to prove increased permeability
- Theoretical use, not necessarily practical use
Markers of protein loss

- Fecal $\alpha_1$-PI (proteinase-inhibitor)
  - Increased in cases of GI protein loss, but not in cases with other causes of protein loss (PLN, liver disease)
  - Useful if trying to differentiate, or if PLN/hepatic disease ruled out, and no symptoms of GI disease
  - Does not differentiate causes of PLE (lymphoma, IBD, lymphangiectasia, etc) so often not useful in cases of diarrhea

- Radiolabelled albumin is gold standard, but rarely used due to need for radioactivity
Markers of inflammation

- Fecal calprotectin/calgranulin C
- N-methylhistamine
- C-reactive protein
- Serum pANCA
- Fecal occult blood testing
- Breath hydrogen test
Markers of inflammation

- Fecal calprotectin/calgranulin C
  - Increased in humans with inflammatory bowel disease
  - Promise in canine IBD, early stages
  - Likely can use assay in cats, not validated yet
- N-methylhistamine
  - Correlates with disease activity in humans
  - Increased in Norwegian Lundehunds with chronic GI disease
  - Needs more study
C reactive protein

- Acute phase protein released by hepatocytes in response to tissue damage and/or inflammation
- Validated in dogs but not cats
- Not specific for GI damage/inflammation
- Measurement correlated with clinical disease activity
- Significantly increased in mod to severe IBD
- Successful therapy associated with significant decrease
pANCA

- Perinuclear antineutrophil cytoplasmic antibody
- Highly specific marker for IBD in dogs, low sensitivity
- Higher with diet responsive diarrhea (62%) vs IBD (23%)
  
  Luckschander et al, 2006

- Diagnostic marker PLE in SCWT?
  - Occurrence preceded hypoalbuminemia by 2.4 years
  - Association with clinical disease activity not been demonstrated

- No significant difference in expression between IBD and lymphoma
  
  Mancho et al, 2010
Breath hydrogen test

- Academia only
- Carbohydrate fermented by intestinal bacteria is variably absorbed based on intestinal permeability
- Increase detected 4-6 hrs after eating, or within 1-2 hrs with bacterial overgrowth / intestinal dysbiosis
  - Healthy dogs: fasting hydrogen 0.9 ppm
  - Chronic SI disease: fasting hydrogen 5.3 ppm
  - EPI: fasting hydrogen 3.3 ppm
  - Healthy dogs: peak 1.4 ppm 8 hrs after feeding
  - Chronic SI disease: peak 72.2 ppm 7 hours after feeding
  - EPI: peak 28.8 ppm 6 hours after feeding
Additional Markers

Intestinal function:
- Cobalamin and Folate

Intestinal dysbiosis:
- No definitive test
- Combination of clinical signs, ↓ cobalamin, ↑ folate
- Response to antibiotic? Non-specific, some antibiotics can cause intestinal dysbiosis
- Serum unconjugated cholic acid (SUCA), 13C-xylose absorption test, urinary indican test, hydrogen breath test
  - All non-specific
- D-lactate in cats – link to increase with dysbiosis?
Abdominal Radiography

Often will not provide that much information in chronic diarrhea cases

- Plain radiography
  - Ascites
  - Gas or fluid pattern
- Contrast radiography
  - Filling defects
  - Evidence of obstruction
  - Delayed emptying
  - Foreign objects

Washabau and Day, 2013
Abdominal Radiography

Plain radiographs, dog with evidence of obstruction

Washabau and Day, 2013
Abdominal Radiography

Contrast radiographs, dog with evidence of obstruction

Washabau and Day, 2013
Abdominal Radiography

Gastric mass, creating filling defect

Washabau and Day, 2013
Abdominal Radiography

Diffuse small intestinal lymphoma, creating an irregular mucosa

Washabau and Day, 2013
Abdominal Ultrasound

- Gastrointestinal masses
- Mesenteric lymphadenopathy
- Ascites
- Intussusception
- Chronic foreign bodies
- Ileus
- Thickened gastrointestinal wall
- Loss of layering
- Corrugation
- Speckling/striation (small intestine)
- Hyperechoic mesentery (lymphangiectasia?)
- Fluid in stomach, small intestine, colon
- Pancreatitis
- Dilated bile duct/gall bladder (rare)
Abdominal Ultrasound

Thickened small intestine, prominent serosal layer

Typical finding in feline small cell intestinal lymphoma

Washabau and Day, 2013
Abdominal Ultrasound

Similar finding in sagittal, often prominent in ileum

Ileocolic junction
Colon
Ileum

Washabau and Day, 2013
Abdominal Ultrasound

Speckling/striations supportive of lymphangiectasia

Washabau and Day, 2013
Abdominal Ultrasound

Corrugation – non-specific could represent neoplasia, severe inflammation, foreign body

Washabau and Day, 2013
Intussusception

Washabau and Day, 2013
Abdominal Ultrasound

Foreign body

Washabau and Day, 2013
Obtaining histopathology

Many cases will require biopsies:

- Endoscopic
- Surgical
- Laparoscopic
Endoscopy

- Upper (stomach and duodenum)
- Lower (colon and may include ileum)

Pros:
- Minimally invasive
- Inspect inside of organ
- Less cost
- Shorter anesthetic time
- Numerous biopsies/site
- Biopsies of colon
- Safer if hypoproteinemia

Cons:
- Do not biopsy jejunum
- Cannot biopsy other organs (LN, liver, pancreas, etc)
- Biopsies not full thickness
Exploratory laparotomy

Pros:
- Full thickness biopsies
- Biopsies of other organs (LN, liver, pancreas, etc)
- Resection of abnormal sections of intestine, masses
- Inspect all levels of gastrointestinal tract

Cons:
- Do not biopsy colon (can blindly with forceps)
- Invasiveness, especially if pet has hypoproteinemia
- Higher cost
- Higher risk (dehiscence, especially when biopsying abnormal intestine)
- Delayed therapy
Laparoscopy

Pros:
- Ability to obtain full thickness biopsies
- Biopsies of other organs (LN, liver, pancreas, etc)
- Inspect all levels of gastrointestinal tract
- Less invasive
- Lower cost

Cons:
- Do not biopsy colon (can do blindly with forceps)
- Invasiveness, especially if pet has hypoproteinemia
- Higher risk (dehiscence, especially when biopsying abnormal intestine)
- Longer anesthesia than scope
- Delayed treatment (?)
Histopathology

- Pathologist dependent – find someone you trust, with who you can discuss case
- WSAVA has been attempting to standardize gastrointestinal histopathology in small animals
- Even with strict guidelines, it will be difficult to standardize interpretation between all pathologists
- Use of PARR (PCR for Antigen Receptor Rearrangements) in cases of possible lymphoma versus severe LP-IBD
- Feel comfortable asking for a second opinion if unsure
Treatment strategies

Most effective if targeting a known disease process

Infectious disease:
- Treat underlying infection, if possible
- This is sometimes a challenge (*Tritrichomonas*, etc)
- Consider whether the infection is likely the primary problem, or is secondary to an underlying gastrointestinal disease
- For example, an overgrowth of *Clostridium*, or the presence of clostridial enterotoxin, is often secondary to an underlying gastrointestinal disease
Tritrichomonas foetus

- Flagellated protozoan
- Cause of diarrhea in cats; not known where it came from (not thought to be from cattle)
- Transmission most commonly fecal oral
- Most common in catteries and exotic breeds
- Large bowel diarrhea, often malodourous, flatulence, hematochezia, mucous; can be asymptomatic
- Similar microscopic appearance to Giardia
- Diagnosis via PCR or special culture (visualization)
**Trichomonas foetus**

- Treatment is via Ronidizole 30 mg/kg PO q24h x 14d
- Do not give to sick cats (most cats with *Trichomonas* are healthy other than diarrhea)
- Instruct that there are potential human health hazards
- Side effects: lethargy, inappetence, ataxia, or seizures
- Most side effects resolve if medication stopped immediately, may take a few days to cease
- Do not give with metronidazole
- Occasional cases that are resistant; no other treatment options
**Trichomonas foetus**

- If untreated, approximately 90% of cats will clear infection within 2 years.
- During this time potential for infection of other cats.
- Organism is not very viable in environment, so routine cleaning should kill organisms.
- Can be costly to treat an entire cattery as ronidazole is expensive.
- Reinfection if not eradicated from all animals.
- Potential for zoonoses but only one documented case.
Dietary intolerance / IBD

- Different types classified by main inflammatory cell present
- Therapy varies but usually includes one or all of:
  - Dietary modification
  - Anti-bacterial treatment
  - Immunosuppressive therapy
  - Vitamin $B_{12}$ supplementation or monitoring
- Minimal objective data on efficacy
- Staged approach recommended
Lymphocytic-plasmacytic IBD

- Most common type
- Lymphocytic-plasmacytic inflammation can be seen in other organs
  - Pancreas
  - Liver
  - ‘Triaditis’ in cats
- Some difficult to differentiate from lymphoma, especially small cell lymphoma in cats
- Use of PARR in inconclusive cases
Mild to moderate cases

- Mild to moderate clinical disease, mild to moderate inflammation on histopathology, normal albumin
  - Deworm if not performed yet
  - Typically start with dietary modification; adequate length, strict diet trial
  - Some cases managed long term with diet +/- tylosin, metronidazole or probiotics
  - Initiate glucocorticoids if poor response
Moderate to severe cases

- Moderate clinical disease, moderate to severe inflammation on histopathology, low albumin
  - Deworm if not performed yet
  - Dietary modification (adequate length, strict diet trial), along with glucocorticoids and often metronidazole or tylosin short term
- If inadequate response, consider dexamethasone, addition of azathioprine or cyclosporine (chlorambucil in cats)
Eosinophilic IBD

- Second most common type
- Rule out parasitism, hypereosinophilic syndrome, hypoadrenocorticism
- Most <5 years age
- Boxer, GSD, Doberman, Rottweiler
- Mucosal erosion and ulceration
- More likely to present with hematemesis, melena and/or hematochezia
Eosinophilic IBD

- More likely to require multimodal therapy
- Prophylactic deworming in all cases
- Mild cases can try dietary modification alone
- Some cases managed long term with diet +/- antimicrobial (tylosin or metronidazole)
- Most cases will require immunosuppression
  - Prednisone/prednisolone (and vitamin B₁₂)
  - +/- Cyclosporine, Azathioprine, Chlorambucil
Demon

- 6 yo MI Rottweiler
- Chronic diarrhea, large and small bowel but with periods of tenesmus, hematemesis and hematochezia
- Intermittent cough
- Skin allergies
- Periods of lethargy and inappetence
- Chronic, persistent peripheral eosinophilia
Demon

- Mild diffuse bronchointerstitial lung pattern
- Abdominal ultrasound irregular small intestinal mucosa
- Negative O/P, numerous deworming
- Bronchoscopy, bone marrow biopsy, upper and lower gastrointestinal endoscopy
- Eosinophilic bronchitis, eosinophilic IBD, eosinophilia in bone marrow
- Hypereosinophilia syndrome
Hypereosinophilia Syndrome

- Uncommon to rare
- Rottweilers predisposed
- Eosinophils may be in liver, spleen, LN, GIT, lung, bone marrow (etc?)
- No cause found – immune system issue?
- Treatment with glucocorticoid, often requires additional immunosuppression
Neutrophilic IBD

- Uncommon type
- Causes
  - Bacterial infection
  - Bacterial invasion secondary to mucosal disruption from another primary gastrointestinal disease
- Culture, special stains, FISH
- Antimicrobial therapy initially, usually broad spectrum
- Glucocorticoid not recommended initially
Granulomatous Enteritis

- GSD over-represented, male, ~5 years age
- Potential causes
  - Infectious (*Trichuriasis, Yersinia, mycobacterium, fungal*)
  - Foreign body reaction
- Thickened, obstructive lesions often in ileum
- Treatment
  - Surgical resection
  - Anti-inflammatory medications
- Prognosis guarded
Ulcerative colitis

- Inflammation with macrophages in the colon
- Hematochezia, tenesmus, weight loss
- Most commonly seen in young Boxer dogs and (less common) French Bulldogs
- Previous therapy with immunosuppression did not often result in remission
- Possible underlying cause of invasive *E. coli*
- Remission seen in some cases using enrofloxacin; otherwise poor prognosis
Intestinal lymphangiectasia

- Abnormal distension of intestinal lymphatic vessels
- May also have lipogranulomas in mesentery
- Usually primary (genetic), can be secondary to lymphadenopathy, portal hypertension
- Result is exudation of protein-rich lymph into the intestine, severe malabsorption of fats
- Crypt cysts and abscesses often seen
Intestinal lymphangiectasia

- Most commonly seen in the Yorkie (10 x incr), SCWT, Norwegian Lundehund
- Clinical signs include chronic diarrhea, vomiting, ascites, edema, chylothorax
- May have no symptoms until severe hypoalbuminemia
- Decrease in albumin, globulin, cholesterol, potassium, chloride (calcium but not when corrected)
- Anemia, thrombocytosis, lymphopenia
Intestinal lymphangiectasia

- Diagnosis via biopsy, mild cases may need surgical biopsy, occasional cases not diagnosed on initial biopsy
- Increased risk with surgical biopsy in cases with severe hypoproteinemia, thrombocytosis, ascites, cachexia
- Discussion about whether prolonged fasting decreases the chance of detecting dilated lymphatics
Intestinal lymphangiectasia

- Treatment is via severely fat restricted diet
  - MCRC GI Low Fat diet, Hill’s i/d Low Fat diet, Rayne Low Fat/Novel Protein diet
  - Home cooked diet formulated appropriately
  - Weight control diets are NOT appropriate
- Prednisone can be useful in poorly responsive cases (± cyclosporine)
- Vitamin $B_{12}$ supplementation or monitoring
- Prognosis very variable
Sasha

- 5 yo FS Mixed Breed (Golden X)
- Presented to veterinarian for annual vaccination
- Physical examination prior to vaccination revealed edema in all four limbs
- Blood work performed, albumin 12 g/L (RR 27-39 g/L), cholesterol and lymphocyte count mildly decreased
- No proteinuria and normal bile acids
Sasha

- Endoscopy revealed marked dilation of lacteals
- Histopathology confirmed lymphangiectasia
- Low fat diet and prednisone resolved edema, albumin increased to 22 g/L
- Stable, however long term prognosis variable
Breed associated enteropathies
Basenji Enteropathy

- Severe, hereditary form of LPE
  - Mode of inheritance unknown
  - Both sexes, 3 years age
- Clinical signs: vomiting, small intestinal diarrhea, alopecia and hyperpigmentation of the skin
- Severe hypoalbuminemia with hyperglobulinemia
- Concurrent hypothyroidism, glomerulonephritis
- Progressive, perforation with severe cases
- Prognosis guarded
  - Early aggressive combination treatment
SCWT – PLE and PLN

- Genetic basis, mode inheritance unknown
  - Common male ancestor identified
  - Middle-age, female predisposed
- Immune-mediated pathogenesis likely
- Signs of PLE precede PLN
  - Vomiting, diarrhea, weight loss, +/- effusions
- Panhypoproteinemia
  - Risk of thromboembolism
  - Fecal α₁-protease inhibitor (PI) test
- Dietary therapy important
Irish Setter

- **Gluten/gliadin-sensitive enteropathy**
  - Familial lines of Irish Setters
    - Autosomal recessive, younger than 1 year
  - Histopathology similar to LPE
    - Abnormal processing of dietary antigens
  - Treatment gluten-free diet
Lundehunds - lymphangiectasia

- Starts at an early age, often puppy
- Inflammatory cell infiltrate with lymphangiectasia
- Panhypoproteinemia
  - 49% abnormal fecal $\alpha_1$-PI concentration
- Treatment with ultra low fat diet, vitamin B12, immunosuppression
- Poor prognosis
Enteropathy in Shar Peis

- IgG deficiency? Poorly understood
- Chronic diarrhea & weight loss
- IBD and intestinal dysbiosis
- Cobalamin deficiency proven
  - Autosomal recessive
  - Relation to enteropathy unknown, could be cumulative problem
Intestinal dysbiosis

- Alteration in the normal microorganism population in the gastrointestinal tract (GIT)
- Little is known about the healthy population in the canine and feline GIT
- Dogs with gastrointestinal symptoms:
  - Decreases in bacterial groups within the phyla Firmicutes and Bacteroidetes
  - Increases within Proteobacteia
  - Reduction in the diversity of Clostridium clusters XIVa and IV
Intestinal dysbiosis

- Little is known about what causes a shift from a healthy to unhealthy population
  - Antibiotic use
  - Genetics
  - Environment
  - Systemic disease (Exocrine pancreatic insufficiency, Pancreatitis? Diabetes? Immunosuppression?)
  - Primary GI disease (IBD, neoplasia, lymphangiectasia, etc)
Neoplasia

- <10% of all tumours in dogs and cats
- Gastrointestinal large cell lymphoma
- Small cell intestinal lymphoma
- Adenocarcinoma
- Leiomyosarcoma
- Predispositions in older animals, Siamese cats, and male dogs for leiomyosarcomas (80%) and GI lymphoma (90%)
GI lymphoma – large cell

- Aggressive malignancy
- No correlation to FeLV status
- Can be B or T cell
- 80% of cats and 25% of dogs have spread outside the GIT
- Surgery if solitary mass, chemotherapy if diffuse or post op for most solitary masses
- Very little information in the literature, MST 77 days; 5-7 months
GI lymphoma – small cell

- Almost exclusively feline cases
- Older cats, can have diarrhea, some cases just weight loss, slow progression
- Diagnosis usually via endoscopy, some cases require surgical biopsy
- Many cases recover poorly from surgery, therefore endoscopy preferred
- Almost exclusively in the small intestine, therefore this must be biopsied (+/- ileum?)
GI lymphoma – small cell

- Treatment is with prednisolone and chlorambucil (Leukeran), Vitamin B<sub>12</sub>
- Appropriate precautions for owners to administer chlorambucil (wear gloves, keep in refrigerator)
- 95% response rate
- Average remission is 1.5-2 years
- Relapse can be treated with cyclophosphamide protocol
Adenocarcinoma

- Typically focal mass, but often metastasize
  - 40-50% metastasize to local lymph nodes
  - 30-40% metastasize to liver
  - 10-20% metastasize to distant sites
- Survival 4-10 months with surgery
- Improved survival with no LN involvement
- Suggested use of chemotherapy post-operatively, very few studies to assess
Leiomyosarcoma

- Typically focal mass
- Anemia, hypoglycemia, polyuria, polydipsia
- MST of 21.3 months (range 0.1-72.5 months)
- 1- and 2-year survival rates 75 and 66%
- Good prognosis if they survive surgery
- Even if LN involvement
- Very little data on chemotherapy
Systemic disease

- Hyperthyroidism
- Hypoadrenocorticism
- Pancreatitis
- Exocrine pancreatic insufficiency
- +/- Hepatic disease
Chronic intussusception

- Rare cause of diarrhea
- Surgical resection, may require resection of a fairly large amount of intestine
- May involve a lot of vasculature, mesentery, lymph nodes if chronic
- Possibility for short bowel syndrome depending on how much intestine removed
- Always send for histopathology and check for parasites, in case of an underlying cause
What if I have normal biopsies?

- Causes of chronic diarrhea with normal biopsies
  - Intestinal dysbiosis
  - Dietary intolerance
  - Chronic idiopathic diarrhea (but did we miss the cause?)
  - Patchy disease (IBD, lymphangiectasia, neoplasia, etc)
  - Mild intestinal lymphangiectasia
  - Undiagnosed systemic disease
Porter

- 7 yo MN Greyhound
- Blood donor at OVC, adopted
- Chronic diarrhea from adoption, varied from soft with no form, to formed
- Blood work normal
- Ultrasound normal
- Fecal examination normal
- Endoscopy normal
Porter

- Diet trial
- Endoscopy normal
- Metronidazole trial
- Endoscopy normal
- Tylosin trial
- Endoscopy normal
- Long term managed with diet and tylosin
- These days – fecal transplant?
Therapy for chronic diarrhea

- Dietary modification
- Anti-bacterial treatment
- Vitamin B\textsubscript{12} supplementation or monitoring
- Probiotics
- Fecal biotherapy
- Immunosuppressive therapy
- Supportive care
Dietary Modification

- Two options - Highly digestible or Exclusion diet (MUST be strict)
- Gradual introduction over 4-7 days
- Improvement within 2-4 weeks
- Most avoid gluten (ie sensitivity Irish Setters)
- Fat restriction?
- Modification of n3:n6 fatty acid ratio
- Response to diet ~50 to 88% dogs
Exclusion diet

Common dietary antigens
- Wheat gluten, soy, corn, lactose, beef and chicken

1. Single source protein and carbohydrate
2. Hydrolyzed diet
  - Chicken or soy protein → chemical or enzymatic treatment → low molecular weight protein derivative
  - Less antigenic, supported in recent study
  - Improved digestibility
Single source – MCRC Dry

Dog
- **Hypoallergenic** – duck, rice, oat flour
- **Sensitivity RC** – catfish, chicken fat, rice
- **Skin Support** – rice, fish meal, brown rice, chicken fat
- **Vegetarian** – oat, rice, potato, coconut oil, beet pulp, tomato, flaxseed

Cat
- **Hypoallergenic Selected Protein** – peas, duck, coconut oil, hydrolyzed soy protein, vegetable oil
- **Sensitivity VR** – venison, rice, fish oil, vegetable oil
Other options – MCRC Dry

Dog
- Skin Care Small Dog – corn, wheat, rice, tapioca, chicken fat, chicory
- Skin Care – corn, wheat, rice, tapioca, chicken fat, vegetable oil, beet
- GI Low Fat – rice, chicken, wheat, barley, beet pulp, chicken fat
- GI Mod Calorie – rice, chicken, corn, brown rice, chicken fat, beet, egg
- GI High Energy – chicken, brown rice/rice, chicken fat, corn, egg, beet

Cat
- GI Fibre Response – rice, chicken, corn, wheat, psyllium, chicory, egg
- GI Moderate Calorie – rice, chicken, corn, wheat, egg, beet pulp
- GI High Energy – chicken, rice, corn, wheat, egg, beet pulp
Dog

- **Hypoallergenic** – potatoes, duck, duck liver, fish oil
- **Sensitivity VR** – venison, rice, fish oil
- **Vegetarian** – soy protein, rice, rice flour, vegetable oil, brown rice, flax meal
- **GI Low Fat** – pork, rice, corn, cellulose, dried beet

Cat

- **Hypoallergenic Selected Protein** – duck, duck liver, pea, vegetable and fish oil
- **Sensitivity VR** – venison, rice, fish oil, vegetable oil
Other options – MCRC Canned

Dog
● GI Mod Calorie – pork, rice, chicken liver, chicken, beet pulp
● GI High Energy – pork, chicken, salmon, rice, vegetable oil

Cat
● GI Mod Calorie – pork, chicken, chicken liver, corn
● GI High Energy – chicken, chicken liver, corn, rice, pork, fish oil
Single source – Hills Dry

Dog
- **d/d duck and potato** – duck, potato, pork fat, soybean/fish oil
- **d/d salmon and potato** – salmon, potato, pork fat, soybean/fish oil
- **d/d venison and potato** – venison, potato, pork fat, soybean/fish oil

Cat
- **d/d duck and green pea** – green and yellow peas, duck, pork fat, chicken liver flavor, fish oil
- **d/d venison and green pea** – green and yellow peas, venison, pork fat, chicken liver flavor, fish oil
Other options – Hills Dry

Dog
- i/d – corn, rice, egg, chicken, corn, pork fat, cellulose, chicken liver
- i/d low fat GI restore - corn, rice, wheat, chicken, chicken liver, flaxseed, oat, barley, beet pulp, ginger root, soybean oil

Cat
- i/d - chicken, rice, corn, pork fat, chicken liver flavor
Single source – Hills Canned

Dog
• d/d duck and potato – duck, potato, duck liver, soybean oil
• d/d salmon and potato – salmon, potato, soybean/fish oil
• d/d venison and potato – venison, potato, soybean/fish oil

Cat
• d/d duck – duck, duck liver, green pea, soybean/fish oil
• d/d venison – venison, venison liver, green pea, soybean oil, fish oil
Other options – Hills Canned

Dog
● i/d chicken and vegetable stew – chicken, pork, rice, carrots, corn, soybean oil, egg
● i/d GI health – turkey, egg, pork, rice, corn, beet pulp, flaxseed
● i/d low fat chicken and vegetable stew – pork, rice, carrots, corn, chicken, egg, flaxseed, beet
● i/d GI low fat restore – turkey, pork, rice, egg, rice, corn, flaxseed, beet, oat
Cat
● i/d GI health – pork, chicken, wheat, corn, rice, beet
● i/d chicken and vegetable stew – chicken, pork, carrots, wheat, corn, rice
Rayne Diet - dog

- **Novel Protein RSP dry** – Rabbit, sweet potato, potato
- **Low Fat Novel Protein KSP dry** – kangaroo, potato, chick peas, pea, sweet potato
- **Low Fat Novel Protein KSP wet** – sweet potato, kangaroo, squash
- **Sensitive GI dry** – turkey, sweet potato, peas, tapioca, tomato, chicken fat
Rayne Diet - cat

- **Novel Protein RSP dry** – rabbit, sweet potato, potato
- **Novel Protein KGR wet** – kangaroo, sweet potato, potato
- **Growth/Sensitive GI dry** – turkey, sweet potato, peas, potato, chicken fat, tomato pomace
- **Growth/Sensitive GI wet** – turkey, potato, fish oil
Iams Veterinary Dry Diets

Dog
- **Iams KO dry** – oats, kangaroo, canola, animal fat, beet, fish oil
- **Iams Skin and Coat FP dry** – potato, herring, catfish, animal fat, beet
- **Iams Intestinal Plus Low Residue dry** – corn, rice, chicken, fish, beet, egg

Cat
- **Iams Intestinal Plus Low Residue dry** – chicken, corn, beet, egg, fish oil

Canned – only one dog hypoallergenic diet
Hydrolyzed Protein Diets

**MCRC - Dogs**
- **Hypoallergenic HP dry (+ small dog version)** – rice, hydrolyzed soy protein, chicken fat, beet pulp, vegetable oil, fish oil
- **Anallergenic dry** – corn, hydrolyzed poultry aggregate, coconut oil, soybean oil, chicory, fish oil
- **Hypoallergenic HP canned** – pea, hydrolyzed soy protein, vegetable oil, chicken liver hydrolyzate, fish oil

**MCRC - Cats**
- **Hypoallergenic HP dry** – rice, hydrolyzed soy protein, chicken fat, vegetable oil, beet pulp
Hydrolyzed Protein Diets

**Hill’s - Dog**
- **z/d dry** – starch, hydrolyzed chicken liver, soybean oil, hydrolyzed chicken
- **z/d canned** – hydrolyzed chicken liver, corn, soybean oil

**Hill’s - Cat**
- **z/d dry** – rice, hydrolyzed chicken liver, hydrolyzed chicken, soybean oil
- **z/d canned** – hydrolyzed chicken liver, corn, soybean oil
Hill’s

- **Hypoallergenic dog treats** – starch, hydrolysed Chicken liver, hydrolysed chicken, soybean oil
- **Hypoallergenic cat treats** – hydrolysed chicken liver, rice, starch, soybean oil, hydrolysed chicken

MCRC

- **Medi-treats dog** – oats, rice, apple, tomato, coconut oil, flaxseed, carrot
- **Medi-treats cat** – rice, fish, coconut oil, tomato, flaxseed
Pill Pockets (Greenies)

Dog

- **Original** – chicken, wheat, vegetable oil, corn syrup, cultured skim milk
- **Allergy formula** – duck, peas, vegetable oil, cultured skim milk

Cat

- **Chicken** – chicken, wheat, vegetable oil, corn syrup, chicken liver, cultured skim milk
- **Salmon** – chicken, wheat, hydrolyzed salmon, vegetable oil, corn syrup, cultured skim milk
Anti-bacterials

- Justification for therapy
  - Potential treatment of undiagnosed enteropathogens
  - +/- Immunomodulatory
- Metronidazole
  - Immunomodulatory and antimicrobial
- Tylosin
  - Antimicrobial, may be immunomodulatory
- No difference with oral prednisone and prednisone-metronidazole for IBD therapy in 54 dogs

Jergens et al, 2010
Immunosuppression

- **Glucocorticoids**
  - Most frequently used
  - Prednisone/prednisolone drug of choice
    - 2 mg/kg q 24 hours x 2-4 weeks, then taper slowly
    - Give with food, and gastroprotection at high dose
  - Some larger breeds are excessively symptomatic at this dose, and may need a reduction
  - Dexamethasone can also be used (0.25 mg/kg q 24 hours starting dose), and in some cases causes less side effects and/or remission in refractory cases
**Immunosuppression**

- **Budesonide** - Locally acting nonhalogenated corticosteroid
  - High hepatic clearance, resulting in high local and low systemic activity
  - Useful in cases that are very sensitive to prednisone, or contraindications such as diabetes mellitus
  - Highly effective in some cases, other cases have little to no response
  - 0.5 - 3 mg PER DOG/CAT (or can use 3 mg/m$^2$) q 24-48 hours, usually not tapered
Immunosuppression

- **Cyclosporine**
  - Induces rapid immunosuppression
  - Side effects in up to 50%
    - Vomiting, inappetence, diarrhea, alopecia, gingival hyperplasia, idiosyncratic hepatopathy, opportunistic infectious disease
  - 5 mg/kg PO q 12-24 hours
  - Expensive, should avoid certain formulations
  - Response in 12 of 14 dogs with steroid-refractory IBD
    - Allenspach et al, 2006
  - Many clinicians 2\textsuperscript{nd} treatment of choice
Immunosuppression

- Azathioprine
  - Induces slower immunosuppression
  - Side effects
    - Vomiting, inappetence, diarrhea, pancreatitis, hepatopathy, bone marrow suppression
  - Less expensive than cyclosporine
  - 1-2 mg/kg PO q 24 hours
  - Monitor CBC and liver enzymes
  - Do not use in cases with pancreatitis
  - Not recommended in cats - sensitivity of bone marrow
Immunosuppression

- Chlorambucil
  - Most commonly used in cats
  - Side effects
    - Vomiting, inappetence, diarrhea, bone marrow suppression
  - Less expensive than cyclosporine
  - Several dosing protocols
    - 2 mg PO q 48 hours (large cats)
    - 2 mg PO Mon/Wed/Fri (small cats)
    - 20 mg/m² every 14 days
  - Monitor CBC
Vitamin B\textsubscript{12} (cobalamin)

- Vit B\textsubscript{12} deficiency causes ill-thrift, poor appetite
- Evidence that having high normal to mildly elevated levels may be beneficial to GI health
- Many dosing protocols
  - We use \(~20\) ug/kg weekly for 4 weeks, then monthly
- Can otherwise monitor levels
- Less common to have folate deficiency, not usually supplemented
Probiotics

- Live microorganisms that can confer a health benefit when given in sufficient quantity
- Use supported in human/mice studies
  - Newborns in developing countries
  - Antibiotic associated human diarrhea
  - Positive response in human IBD
  - Improved immune response to *Giardia* in mice
- Minimal information on effectiveness for diarrhea in dogs and cats
Probiotics

- Study on quality of 25 veterinary probiotics (Weese et al CVJ 2011 52:43-6.)
  - 84% listed specific microorganisms
  - 60% listed expected bacterial numbers
  - 32% had misspelled organisms
  - 73% had less than # of organisms claimed on label
  - 8% (2 products) had an acceptable label

- Prostora Max – Iams®
- Fortiflora – Purina®
Fecal biotherapy

- Fecal microbiota transplantation or fecal biotherapy
  - previously stool transplant, fecal transfusion, fecal transplant, fecal enema, human probiotic infusion
- Transplantation of a large, healthy population of flora into the gastrointestinal tract
- Highly effective at treating *C. difficile* in humans, and more effective than vancomycin
- Promise in treating human IBD, although repeat infusions usually needed
The FDA nows lists human feces as an experimental drug

Treatment of non-GI disease being investigated:
- Autoimmune disorders
- Neurological conditions
- Female cystitis
- Obesity
- Diabetes
- Multiple sclerosis
- Parkinson’s disease
Fecal biotherapy

- Very easy to obtain and administer
- Fresh feces from healthy, recently screened donor
  - Parasites, pathogenic bacteria
- Blend with saline (evidence of higher relapse rate in humans if water used)
- Administer as an enema, we also infuse in duodenum at time of endoscopy
- Can also feed to dog (or cat?)
Fecal biotherapy
Fecal biotherapy

- Small number of cases treated at our hospital to date, but promising results
- Chronic diarrhea cases that had full resolution of symptoms long term
- Cases that had marked improvement, but required repeat transplantation
- Cases with improvement but required on-going additional medication
- Cases that had no improvement
Kona

- 3 yo MN German Shepherd
- Chronic small and large bowel diarrhea since puppy, also chronic skin allergies
- Markedly emaciated
- Numerous therapies tried, including antibiotics, diet trials, prednisone, cyclosporine
- Mild hypoproteinemia
- Normal abdominal ultrasound
Kona

- Upper and lower gastrointestinal endoscopy with biopsies normal
- Fecal transplantation performed, all medications stopped
- Bowel movements normalized within 2 days, gained weight back to normal BCS
- Maintained stools and skin allergies long term on diet and intermittent cephalexin
Supportive care

- Depends on severity
  - Metronidazole or tylosin intermittently
  - Cephalexin or enrofloxacin in some cases
  - Sulfasalazine
  - Probiotic
  - Bland diet, NPO
  - Loperamide, etc
  - Fluid therapy, colloids, iron therapy
Stem cell therapy

- Human inflammatory bowel disease
  - Promising early results
  - Not yet standard of care, usually in clinical trials
  - Mesenchymal stem cells safe but varying results
  - Hematopoietic stem cells very effective but associated serious adverse effects
    - pulmonary edema/deep vein thrombosis, splenic rupture, myocardial infarction; no increase in rate of cancer
- Anecdotal use in dogs and cats with inflammatory bowel disease (CSU study)
Questions?

“The Crappuccino”
(per Dr Scott Weese)