Dr. Sandra Diaz (DVM, MS DACVD) is a Diplomate of the American College of Veterinary Dermatology. She is an assistant professor-clinical in the Dermatology and Otology Service at the College of Veterinary Medicine at The Ohio State University. Previously, she was an assistant professor of dermatology in the Department of Small Animal Clinical Sciences in the Virginia-Maryland College of Veterinary Medicine (VMCVM) at Virginia Tech. Dr. Diaz received her DVM from the Universidad Santo Tomas in Santiago, Chile, and an MS from the University of Minnesota where she also completed her residency. Prior to joining the faculty of the VMCVM, she was on staff at the NYC Veterinary Specialists and Cancer Center in New York City. Her research interests are disorders of hair and hair growth, canine and feline allergic disorders, and feline and canine otitis.
New Drugs in Veterinary Dermatology

Sandra Diaz, DVM, MS, DACVD
Assistant Professor – Clinical Dermatology & Otology Service

Outline
- Review of new drugs or old drugs with new dermatological applications in dogs and cats
- Trade names and classification
- Specific indications
- Dosages
- Adverse reactions
- Monitoring

Oclacinib

Trade Name
- Apoquel

Classification
- selective Janus kinase (JAK1 and 2) inhibitor
  - It specifically inhibits interleukin-31 signal transduction
  - JAK1-dependent cytokines involved in allergy and inflammation (IL-2, IL-4, IL-6, and IL-13) as well as pruritus (IL-31)

Oclacinib

Interleukin-31 is a key cytokine for neuronal itch stimulation
Activated T cells and keratinocytes release interleukin-31
IL-31 binds transmembrane receptors on cutaneous neurons, and through JAK activation triggers an action potential that results in a pruritic response, known as neuronal itch stimulation

Oclacinib

The interleukin-31 receptor is also present on peripheral blood mononuclear cells and keratinocytes
- Activation by interleukin-31 promotes the release of pro-inflammatory cytokines
Apoquel Indications in Dogs

Apoquel is labeled for the control of pruritus associated with allergic dermatitis in dogs.

Oclacinib

Side Effects
- Side effects reported in initial studies affected less than 3% of dogs:
  - vomiting, diarrhea, anorexia, and polydipsia
- May increase risk of opportunistic bacterial or fungal infections, including demodicosis
- May exacerbate neoplastic conditions
- Minimal effects on cytokines that did not activate the JAK1 enzyme (erythropoietin and granulocyte/macrophage colony-stimulating factor)

Dosage
- Label recommendations: 0.4 to 0.6 mg/kg orally twice daily for up to 14 days, and then once daily
Oclacitinib

Precautions/Contraindications

- Should not be administered in place of other immunosuppressive therapy, such as glucocorticoids or azathioprine
- Oclacitinib should not be administered to animals less than 12 months of age or those with severe infections

Further independent and long-term studies are needed to fully appreciate the effectiveness and safety of this drug

Canine Atopic Dermatitis Immunotherapeutic (CADI)

Trade Name
- Not available yet

Classification
- Immunotherapeutic
- Monoclonal antibody that specifically targets and neutralizes IL-31

CADI Application in Dogs

Relief from the itching associated with atopic dermatitis in dogs of any age

CADI

Dosage:

- SQ injection, 2 mg/kg body weight. Repeat monthly, as needed
- Supplied in 1-mL vials

Efficacy

Vomiting, diarrhea and lethargy, usually self limiting

Long term safety

- Well tolerated in laboratory safety study in which injections were administered at 3.3 mg/kg or 10 mg/kg monthly for 7 months
  - Laboratory Beagles, 12 dogs per group

Side Effects
Fluranalor

Trade names
- Bravecto®

Classification
- Systemic ectoparasiticide

Cost
- Bravecto medium dog 22-44 Lb ~ $50

Fluranalor indications in Dogs and Cats

- Bravecto is indicated for the treatment and prevention of flea infestations and the treatment and control of tick infestations for 12 weeks

Bravecto off label

Efficacy of orally administered fluralaner (Bravecto™) or topically applied imidacloprid/moxidectin (Advocate®) against generalized demodicosis in dogs

Results: After a single dose the mite numbers in skin scrapings were reduced by 99% on day 28, and by 100% by day 56 and 84.

Conclusions – Single oral administration of Bravecto is highly effective against generalized demodicosis, with no mites detectable at 56 and 84 days following treatment.

Fouka et al. Parasite & Vector. (2013) 8:106
DOI: 10.1186/s13071-013-0733-4

Bravecto

Dosage
- 25 mg/kg

<table>
<thead>
<tr>
<th>Body Weight Ranges (lb)</th>
<th>Fluranalor Content (mg)</th>
<th>Chews Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4 – 9.3</td>
<td>112.5</td>
<td>One</td>
</tr>
<tr>
<td>&gt;9.3 – 22.0</td>
<td>250</td>
<td>One</td>
</tr>
<tr>
<td>&gt;22.0 – 44.0</td>
<td>580</td>
<td>One</td>
</tr>
<tr>
<td>&gt;44.0 – 88.0</td>
<td>1000</td>
<td>One</td>
</tr>
<tr>
<td>&gt;88.0 – 123.0*</td>
<td>1400</td>
<td>One</td>
</tr>
</tbody>
</table>

* Dogs over 123.0 lb should be administered the appropriate combination of chews.

Precautions:
- Bravecto has not been shown to be safe in puppies less than 6 months of age
- Bravecto is not effective against Amblyomma americanum ticks beyond 8 weeks after dosing

Adverse Reactions:
- The most frequently reported adverse reaction is vomiting
Osurnia® (florfenicol-terbinafine-betamethasone acetate)

Trade names
- Osurnia® (Novartis)

Classification
- Otic gel- antibacterial, antifungal, anti-inflammatory
  - 10 mg florfenicol, 10 mg terbinafine, and 1 mg betamethasone acetate per mL

Cost
- 2 tubes (1 ml) ~ $30

Osurnia Indications

For the treatment of otitis externa in dogs associated with susceptible strains of bacteria (Staphylococcus pseudintermedius) and yeast (Malassezia pachydermatis)

Osurnia Dosage:
- OSURNIA should be administered in the clinic
  - Clean and dry the external ear canal before administering the initial dose of the product
  - Administer one dose (1 tube) per affected ear(s) and repeat administration in 7 days
  - Do not clean the ear canal for 45 days after the initial administration to allow contact of the gel with the ear canal

Osurnia Effectiveness

Study design: Randomized, double masked, placebo controlled, multi-center field study
- 235 cases: 159 Osurnia, 76 placebo
- Dogs were evaluated for pain, erythema, exudate, swelling, odor and ulceration and given a score, using a 12 point score system
- Success was defined as total score ≤2 at day 45

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Success (Score ≤ 2)</th>
<th>Failure (Score &gt; 2)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSURNIA</td>
<td>103</td>
<td>56</td>
<td>159</td>
</tr>
<tr>
<td>Placebo Control</td>
<td>33</td>
<td>43</td>
<td>76</td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>99</td>
<td>235</td>
</tr>
</tbody>
</table>

Osurnia Reported Adverse Events

The following adverse reactions were reported during the course of the field study:

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Osurnia (n=159)</th>
<th>Placebo (n=94)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Alkaline Phosphatase</td>
<td>15 (7.5%)</td>
<td>3 (3.2%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (3.7%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Elevated AST, ALT, ALP*</td>
<td>2 (1.1%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Weight loss (&gt;10% body weight)</td>
<td>1 (0.5%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Hearing Decrease/Loss</td>
<td>1 (0.5%)</td>
<td>1 (1.1%)</td>
</tr>
</tbody>
</table>

Claro

Trade names
- Claro® (Bayer)

Classification
- Otic solution- antibacterial, antifungal, anti-inflammatory
  - 15 mg florfenicol, 15 mg terbinafine, and 2 mg mometasone furoate per mL

Cost
- ??
Claro Indications

CLARO is indicated for the treatment of otitis externa in dogs associated with susceptible strains of yeast (Malassezia pachydermatis) and bacteria (Staphylococcus pseudintermedius).

Claro Dosage

- CLARO is available in a single dose pre-filled laminate dropperette with a tapered tip; supplied in cartons containing 2, 10, or 20 dropperettes
- Administer one dose (1 dropperette) per affected ear
- The duration of effect should last 30 days

Claro Effectiveness

- Clinical Evaluation: The primary clinical effectiveness endpoint was based on the otitis externa score on day 30
- A clinical score was calculated for erythema, exudate, swelling, and ulceration
- The individual clinical scores were assigned based on the severity of that sign
  - 0 = none; 1 = mild; 2 = moderate; 3 = severe

Claro effectiveness

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Success</th>
<th>Failure</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLARO</td>
<td></td>
<td></td>
<td>120</td>
</tr>
<tr>
<td>Vehicle Control</td>
<td>NADA 141-440</td>
<td></td>
<td>63</td>
</tr>
</tbody>
</table>

Claro Reported Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>CLARO N = 140</th>
<th>Control N = 70</th>
</tr>
</thead>
</table>
Imiquimod Indications in Dogs and Cats

**These indications are mostly anecdotal**

- Actinic keratosis
- SCC in situ (Bowen’s disease)
- Herpes dermatitis
- Papillomatosis
- Pigmented epidermal plaques

**Imiquimod**

**Dosage**
- Three times a week
- Duration and frequency may need to be adjusted upon clinical response and adverse reactions

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**Use of imiquimod 5% cream (Aldara™) in cats with multicentric squamous cell carcinoma in situ: 12 cases (2002–2005)**


Department of Veterinary Clinical Science, New York University, NY, USA

Abstract

Multicentric squamous cell carcinoma in situ (SCC in situ) results from multiple independent SCC in dogs and cats. Occasionally, the tumors may involve more than one body region. This report describes a multicentric SCC in situ in a cat. The goal of this in vivo study was to evaluate the efficacy and adverse effects of Imiquimod 5% cream in a cat with multicentric SCC in situ. Imiquimod 5% cream was applied topically to the lesions four times a week. No adverse effects were observed. The response to therapy varied. In some lesions, the lesions regressed within 3 months, while in others, the lesions remained unchanged. The response to therapy varied. In some lesions, the lesions regressed within 3 months, while in others, the lesions remained unchanged. The response to therapy varied. In some lesions, the lesions regressed within 3 months, while in others, the lesions remained unchanged. The response to therapy varied. In some lesions, the lesions regressed within 3 months, while in others, the lesions remained unchanged.

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**CASE REPORT**

Apparent clinical resolution of pinnal actinic keratoses and squamous cell carcinoma in a cat using topical imiquimod 5% cream

Jeanine Postles-Kennedy, David W Scott, and William H Miller

Department of Small Animals, Marine, and Coral Reef Health, University of Florida, Gainesville, FL, USA

Abstract

Imiquimod applied for 12 weeks in a cat with multiple pinnal SCC in situ resulted in clinical resolution of all lesions.

---

**After 82 days of therapy**

Fig. 1. Photograph of the 15-year-old, spayed female, European shorthair cat with actinic keratoses and squamous cell carcinoma of the right pinna and a presumed spindle cell squamous cell carcinoma of the left pinna. Imiquimod was applied topically four times a week for 82 days. The cat is shown in the clinic after 82 days of therapy. The lesions were not visible and the cat was comfortable.

---
**Imiquimod**

**Precautions/Contraindications**
- Clients should wear gloves
- Do not allow the animal to groom/lick the treated site(s) for at least 30 min after application
- Do not use occlusive dressings
- Avoid sun exposure during treatment

**Adverse effects**
- Local skin reactions
  - Erythema, burning, tenderness, itching, swelling, pain, oozing/exudation, crusting, erosion
- Secondary infections may occur
- Depigmentation and hair loss – sequelae

**Monitoring**
- Response to therapy and adverse effects

**Mycophenolate Mofetil**

**Trade name**
- Cellcept®, generic

**Classification**
- Immunomodulatory, immunosuppressant

**Cost**
- Cellcept: ~$150/month (30 kg dog)
- Generic: ~$30-130/month (30 kg dog)

**Pemphigus foliaceus**

This indication is mostly anecdotal

Often used as a glucocorticoid sparing agent

**Dosages (anecdotal)**
- 20-40 mg/kg/day PO divided q8h-12h for 3-4 weeks
- Then dose can be tapered to 10-20 mg/kg/day q12-24h

**Reported success rate of 50%**
- Most dogs requires concurrent glucocorticoid therapy

**Precautions/Contraindications**
- Patients hypersensitive to the drug
- Patients with renal/liver dysfunction may require dose adjustment
- Avoid live or attenuated vaccines during treatment
Mycophenolate Mofetil

Adverse effects
- Vomiting, diarrhea, anorexia, lethargy, pyoderma, malassezia dermatitis
- Minimal risk of myelosuppression
- Typical: mild lymphopenia – does not prohibit therapy

Monitoring
- Efficacy and adverse effects
- CBC: baseline and after 1 month of therapy, then quarterly

Terbinafine Hcl

Trade name
- Lamisil®, generic

Classification
- Antifungal

Cost
- Generic: $4/30-250 mg tablets (generic prescription-target)

Terbinafine Hcl Indications in Dogs and Cats

- Dermatophytosis
- Malassezia dermatitis
- Blastomycosis
- Sporotrichosis

Precautions/Contraindications
- Patients with hypersensitive to the drug
- Avoid use in patients with renal failure and chronic or active liver disease

Terbinafine Hcl

Dosages

Dogs and Cats
- Dermatophytosis: 30–40 mg/kg PO q24h until 2 negative fungal cultures
- Malassezia dermatitis: 30 mg/kg PO q24h until 1 week past clinical resolution
- Systemic or deep mycosis: the most recently proposed dose is 30-35 mg/kg PO q8-12h until 30 days past clinical resolution

Adverse effects (overall well tolerated)
- Vomiting, lethargy, decreased appetite, mild lymphopenia and mild elevation in ALP and ALT
- Transient ocular swelling in dogs
- Facial pruritus, urticaria and macular/papular skin eruption were reported in cats

Monitoring
- Response to therapy and adverse effects
- Liver enzymes, CBC: baseline and during therapy if administered long-term
Approach to Diagnosing the Chronic Enteropathy

Speaker

Adam Rudinsky, DVM, MS, DACVIM

Dr. Rudinsky is the most recent addition to the Small Animal Internal Medicine service at The Ohio State University Veterinary Medical Center. He provides the service with a specialized interest, clinical perspective and clinically applicable research in gastroenterology, pancreatology, and hepatology. Dr. Rudinsky received his DVM degree from The Ohio State University, completed a small animal rotating internship at Purdue University, and then a combined residency in internal medicine and MS degree at The Ohio State University. He is now on faculty at Ohio State as a staff internist and research scientist as he completes his PhD program in gastrointestinal immunology. His current clinical and research interests include chronic enteropathies, pancreatic and hepatic disease, mucosal immunology, and the intestinal microbiome as it relates to small animal gastrointestinal disease pathophysiology and treatment. During his residency he received several teaching awards and hospital service awards.
Approach to Diagnosing the Chronic Enteropathy

Understanding ‘Chronic Enteropathy’

First and foremost, it is important that we all understand what a chronic enteropathy is in terms of a clinical entity. When I use this term, I am referring to a chronic gastrointestinal (GI) disorder resulting in GI clinical signs and inflammation. Diagnosing a chronic enteropathy is the mid-way point on the journey to correctly treating a chronic GI case. I prefer the term chronic enteropathy because the term IBD is a catch all for a variety of chronic enteropathies. If you tell me a patient has IBD, you are not necessarily incorrect but you may be able to be more specific. Saying IBD simply tells me that there is inflammation in the intestines. Whereas, the more important question is: Why is the inflammation present? Unfortunately, to date, the exact cause of ‘IBD’ is still unknown but likely involves 3 factors: the animal’s immune system, what is entering the GI tract (diet), and also who is living there (the microbiota). Conceptually, this is a very important idea as it forms the foundation for our therapeutic approach to this disease as you will see in subsequent lectures.

So that begs the question, how do we arrive at a diagnosis of chronic enteropathy? This simply means that a thorough evaluation of the patient was performed and differential diagnoses including infectious disease, parasitism, metabolic disease, endocrinopathies, etc... have been ruled out.

If chronic enteropathy is on your differential list, it is usually because your patient is presenting with signs or symptoms referable to the GI tract. Chronic enteropathy should then appear as a differential on your diagnostic approach as you plan for all options. The most traditional approach, and in my opinion the easiest, is to remember differentials both in the ‘GI’ category and the ‘non-GI’ category. Chronic enteropathy is typically a primary differential in the GI category for most chronic cases. However, even though it is common, it is still a diagnosis of exclusion and requires extensive diagnostics and treatments to confidently arrive at this end point.

Diagnostics

Therefore, if possible, it is advisable that all patients receive ‘tier 1’ diagnostics:

1. Dogs: CBC, Chemistry, UA, Fecal Analysis, Resting Cortisol
2. Cats: CBC, Chemistry, UA, Fecal Analysis, Thyroid Level (Cats over 6 years of age)

*If abnormalities are discovered during your ‘tier 1’ diagnostics, these should be evaluated to determine if they could be resulting in the clinical signs in your patient. If they are a potential explanation, these should be addressed prior to pursuing additional diagnostic evaluation. If no abnormalities are observed, the likelihood of diagnosing a non-GI cause of the symptoms is less likely.
*You also may be faced with the situation of cost benefit analysis with patients and client means. In general, the yield of all ‘tier 1’ diagnostics increase with age and you are more likely to find relevant information in your older populations. However, this is not an absolute rule and why it is still advisable to recommend these tests if feasible for your client! I prioritize fecal floatation, endocrine testing, and biochemical panels in my patients due to the greater likelihood of being a high yield diagnostic.

Depending on the signalment and presentation, ‘tier 2’ diagnostics can be quite variable in regards to what is warranted. Below are the more common presentations and warranted diagnostics:
1. Large Bowel Diarrhea (Dog) – Histoplasmosis Urine Antigen
2. Feline Large Bowel Diarrhea (Young) – Tritrichomonas foetus (T. foetus) PCR
3. Fecal Culture – rarely indicated
4. Fecal PCR – rarely indicated
5. Fecal Smear – rarely indicated
6. cPLI/fPLi – if signs consistent with pancreatitis
7. Pre and Post-Prandial Bile Acids – if suspicion of liver disease

At this point, if you are still pursuing diagnostics for a chronic enteropathy, imaging is the foundation of ‘tier 3’ diagnostics:
1. Abdominal Radiographs
2. Abdominal Ultrasound

*If the initial work-up is unremarkable and there are no indications for specific targeted diagnostics, it is advisable in many cases to proceed with advanced imaging.

*Abdominal radiographs, although routinely available in practice are unlikely to be helpful in the diagnosis of a chronic enteropathy. Instead, their value is most closely tied to ruling out potential problems (e.g. obstructed foreign body, abdominal mass, etc...).

*In the ideal situation, an abdominal ultrasound would be performed by a boarded radiologist. I cannot stress enough how important experience is regarding ultrasound imaging of the feline gut, pancreas, and liver, specifically, as it is highly susceptible to user interpretation.

*Abdominal ultrasound yield increases with age in both dogs and cats. It is much less frequently beneficial in young animals.

*It’s also important to remember that, even with ultrasound, you are still unlikely to be able to arrive at a definitive diagnosis unless you diagnose something other than chronic enteropathy. In most circumstances, chronic enteropathies (and lymphoma for that matter) will look completely normal or have subtle changes in intestinal wall layer thickness. Ultrasound is much more sensitive at identifying mass lesions or other subtle changes that would argue against a diagnosis of chronic
enteropathy. If significant abnormalities are noted on ultrasound, it has the added benefit of aiding in targeted acquisition of cytologic samples for pathology review.

Finally, ‘tier 4’ diagnostics are another consideration in diagnostic work-ups which are aimed directly (for all intents and purposes) at the GI tract.

1. Cobalamin and folate levels
   a. Cobalamin is a water soluble vitamin necessary for intestinal health and is often low in chronic enteropathy dogs and cats. Therefore, assessing for whether there is a deficiency and supplementing may drastically impact your ability to treat your patients. For owners that are willing, assessment of these vitamins should be performed in all animals.
   b. If cost is a concern, it is reasonable and safe to empirically supplement cobalamin or folate during empirical treatment. Further information regarding cobalamin deficiency and treatment can be found at http://vetmed.tamu.edu/gilab/research/cobalamin-information

2. Alpha-1 Protease Inhibitor
   a. Specifically targeted for protein losing enteropathies

In an ideal world, all of the above diagnostics are completed and if there are no other disease processes discovered, you may diagnose the patient with a ‘clinical chronic enteropathy’. However, in clinical practice, regardless of where we practice, many owners will be unable to complete an extensive diagnostic work-up. Therefore, you can proceed without the extensive list of diagnostics but must be certain to remind the client of the limitations of this approach and the fact that we may be missing the underlying diagnosis.

When to biopsy?

Following the initial work-up discussed above, if the owner wishes to be aggressive, this is the first time point where a biopsy should be offered. Combined with an unremarkable pre-biopsy work-up, this is the best method for definitive diagnosis of chronic enteropathy. However, remember this will only tell you that the chronic enteropathy is inflammatory (most commonly lymphoplasmacytic) in origin. Therapeutic trials will be required to sub-classify the inflammatory diagnosis by inciting cause (diet-responsive, antibiotic responsive, steroid responsive). Therefore, it is important the client knows that empirical trials will be recommended with or without the biopsy! See ‘Empirical Treatment of Chronic Enteropathies’ below.

So what is the benefit of the biopsy? In truth, it should be noted that this is not absolutely necessary in the majority of cases as the course of treatment will not be changed in most cases! On the other hand, the main benefits of biopsy include ruling out more severe disease (lymphoma), diagnosing diseases which require
specific treatment (Helicobacter, Enteroinvasive E. coli), procuring a definitive diagnosis of intestinal inflammation prior to empirical therapy, and potentially diagnosing non-inflammatory chronic enteropathies (IBS). This is vital information, especially if response to treatment is not as anticipated.

As the clinician managing a chronic enteropathy case in need of biopsies, you will need to decide what and how you will biopsy. First, ask yourself whether any of the pre-biopsy work-up results will warrant biopsies of either the pancreas or liver. There is some evidence that concurrent inflammation may occur in these organs and it may change how they are clinically managed (specific to cats). If either pancreatic or liver biopsy is warranted, surgical biopsies are required. The second consideration is which parts of the intestinal tract should be biopsied, regardless of whether other organs need sampled. The current general recommendation is that biopsies are acquired throughout the GI tract in all cases. However, in clinical practice many variables affect the feasibility of this recommendation. In those cases, that is where a good history and understanding of an animal’s clinical signs can target the best portions of the gut to go after. For example, a cat with chronic vomiting will benefit from gastric and small intestinal biopsies much more often than biopsies of the ileum or colon. The third consideration, if you haven’t already decided based on the first two questions, is whether to biopsy endoscopically or with an open surgical approach.

In my hands, I like endoscopic biopsies because it is minimally invasive, allows for direct assessment of mucosa and targeted biopsy of many areas. However, they also require significant training and skill to do. A large part of this is due to how small feline and some dog patients are and maneuvering of the endoscope without causing damage can be difficult. They are also limited in depth of biopsy and if not done correctly can result in inadequate biopsies for interpretation.

Surgical biopsies are preferred when multiple organs are targeted, allow for full thickness biopsies as well as full abdominal exploration, and for the general practitioner are a much easier skill to learn with greater likelihood of at achieving suitable samples for a diagnosis. Drawbacks to this method include limited numbers of biopsies easily obtainable and biopsies (full thickness) of the colon more invasive procedure with a higher risk of complication.

When a practitioner consults with me about GI biopsies, my recommendation the majority of the time is dictated by their experience. From past discussions with practitioners, surgical biopsies are much more commonly employed. An additional clinical note is that we VERY frequently see non-diagnostic biopsy reports on from inadequately sampled endoscopic biopsies submitted from cats, frequently due to the inexperience of the endoscope operator.

**Empirical Treatment of Chronic Enteropathies**
Empirical therapy is warranted for nearly all patients:

1. Patients unable to have a complete work-up but no other disease processes have been identified
2. Patients with a complete work-up, without biopsy, and no other underlying disease processes have been identified
3. Patients with a complete work-up, with biopsy, and no other underlying disease processes have been identified

The first two things I consider when deciding how to treat a patient with chronic enteropathy are:

1. How thorough has my diagnostic work-up been and have I adequately excluded potential differential diagnoses?
2. What is the animal’s current clinical status? BAR or sick?

In general, the more limited you are in your diagnostic work-up, the more crucial it is that you take adequate time to explain to the owners the pros and cons to empirical therapy. In addition, if a patient is sick, you may need to be more aggressive than in the relatively stable/BAR patient. The key to therapeutically diagnosing a chronic enteropathy requires time, patience, and a methodical approach. This is further complicated by the fact that each individual patient will require tailored therapy, specific for their condition, which is not known.

Regardless of the patient, a thorough history, examination, and potentially empirical treatment for helminths should be performed in each patient. In select cases, additional treatments and/or diagnostics for other parasitic diseases, such as giardia or T. foetus, may be performed. In general, I most commonly use Panacur (fenbendazole) (50 mg/kg PO SID for 5 consecutive days) if I am performing an empirical deworming. This will also cover for parasitic disease which would not be noted on fecal examination, such as Physaloptera.

From this point, you can safely begin empirical therapy trials. The traditional approach being:

- First - Dietary Management
- Second - Flora Modification
- Third/Last - Immunomodulation

The reason for this order is because the majority of chronic enteropathies will respond to diet (66%) or flora modification (11%). This is such a key point to remember and a major reason why you shouldn’t immediately place patients on immunosuppressants! Most animals referred for evaluation of IBD/Chronic enteropathy will respond to dietary or flora modification therapy alone! In these cases, it is highly preferred to control their chronic entropathies with these therapies rather than immunomodulatory drugs as they have less side effects! The remaining dogs either respond to immunomodulation (20%) or are non-responders (3%).
A final point to remember is that it is advisable to procure intestinal biopsies, if this has not already been performed, prior to empirical use of immunomodulatory drugs. This is especially important for instances where misdiagnosis is possible, as these drugs may change biopsy results (i.e. lymphoma, IBS).

These empirical therapies will be discussed in detail in the following sections.
Nutritional Management of Chronic Enteropathies

Speaker

Valerie Parker, DVM, DACVIM, DACVN

Dr. Parker received her DVM from Tufts University in 2007. She then completed a small animal internship at the Animal Medical Center in New York City, followed by a small animal internal medicine residency at Iowa State University and a clinical nutrition residency at Tufts University. She is a diplomate of both the American College of Veterinary Internal Medicine and the American College of Veterinary Nutrition. Dr. Parker is currently an Assistant Professor at The Ohio State University. Her primary areas of interest include kidney disease, gastrointestinal disease and endocrinology, as well as all aspects of nutritional management of disease.
Nutritional Management of Chronic Enteropathies

Valerie J. Parker, DVM, DACVIM, DACVN
January 23, 2016

Objectives
- Review common chronic enteropathies
- Nutritional management
  - Various diets
  - Other dietary factors

Defining chronic enteropathy
- ≥ 2-week history of vomiting and/or diarrhea
- Must exclude other causes of vomiting/diarrhea
  - Endocrine
  - Pancreatic
  - Hepatic
  - Neoplasia
  - Neurologic

Characterizing diarrhea
- Small intestinal
  - Large volume
  - Melena
  - Weight loss
  - +/- Vomiting
- Large intestinal
  - Small volume
  - Hematochezia
  - Mucus
  - Tenesmus
  - Increased frequency & urgency
  - No weight loss

Patient assessment
- Body composition
  - Body weight, body condition score, muscle condition
- Diet history
- Response to previous treatment
Diagnostic plan
- Minimum database
  - CBC, chemistry profile, urinalysis +/- T4
- Fecal examination

Diagnostic plan
- Abdominal imaging
  - Radiographs, ultrasound
- Additional tests
  - GI panel
    - Cobalamin, folate, trypsin-like immunoreactivity (TLI)
    - Resting cortisol +/- ACTH stimulation test
  - Biopsies

Common chronic enteropathies
- Inflammatory bowel disease (IBD)
- Lymphangiectasia
- Food intolerance vs. food allergy

Inflammatory bowel disease
- Umbrella-term
  - Food-responsive
  - Antibiotic-responsive
  - Immunomodulatory-responsive
- Often multi-modal therapy required

Diagnosis
- Diagnosis of IBD is one of exclusion
- Minimum database may be normal
- Some diagnostics may yield indirect support
  - ↓ cobalamin, ↓ folate
  - Abdominal ultrasound

Cobalamin & folate
- Folate absorbed in proximal small intestine
- Cobalamin absorbed in distal small intestine
Diagnosis

- Biopsies may support clinical diagnosis
  - Lymphoplasmacytic inflammation most common
- Histopathology does not necessarily dictate how an individual animal will respond to therapy

Management

- Step-wise approach
  - Diet trial
  - Antibiotic trial (e.g., metronidazole)
  - Fiber supplementation
  - Immunomodulatory medications
- May require some trial and error

Lymphangiectasia

- Form of protein-losing enteropathy (PLE)
  - Primary or secondary
- Definitive diagnosis requires intestinal biopsy
  - Many animals are presumptively diagnosed
    - Signalment
    - Clinicopathologic findings
    - Abdominal ultrasound

Food allergy vs. intolerance

![Diagram showing allergies and intolerances]

Diagnosis of food intolerance

1. Feed elimination diet for several weeks
2. See resolution of clinical signs
3. Challenge animal with original diet to see relapse

Diagnosis of food allergy

1. Feed elimination diet for several weeks
2. See resolution of clinical signs
3. Challenge animal with one ingredient at a time to document the food(s) to which animal reacts
Most common food allergens

- Dog
  - Beef, dairy, wheat
- Cat
  - Beef, dairy, fish

If no response

- Consider these factors
  - Animal has atopic dermatitis
  - Lack of compliance
  - Diet was not truly novel
- No good reason to perform multiple novel ingredient diet trials

Nutritional management

- No single best approach for every case
- May require some trial & error
- Concurrent medical therapy is often needed

Diet trial

- Why change the diet?
  - Reduce antigen delivery to intestine
  - Increase digestibility
  - Modify intestinal flora
- Nutrients affect intestinal disease
  - Not just specific ingredients!

Diet trial options

- Novel ingredient diet
- Hydrolyzed diet
- Highly digestible diet
  - Aka ‘bland diet’
- Low-fat diet
- Home-cooked diet
Novel ingredient diet
- Novel protein AND novel carbohydrate sources
- "Limited ingredient" diet
- May not be able to identify commercially-available novel ingredient diet for all animals
- Typically highly digestible
- Variable nutrient profiles

Novel ingredient diets
- Veterinary products

Novel ingredient diets
- OTC diets

Hydrolyzed diet
- Reduced protein size → reduced allergenicity
- Some diets use intact carbohydrate sources
- Typically highly digestible

Hydrolyzed diets

Highly digestible diet
- Formulated to be highly digestible (~90%)
- Typically low-to-moderate in fat (canine)
- NOT novel ingredient or hydrolyzed
Highly digestible diets

- Highly digestible
- Fat concentration
  - Canine diets: 1.8-2.3 g/100 kcal
  - AAFCO minimum – 1.4 g/100 kcal
- Useful in dogs with fat intolerance
- Certain protein-losing enteropathies

Low-fat diets

- Highly digestible
- Fat concentration
  - Canine diets: 1.8-2.3 g/100 kcal
  - AAFCO minimum – 1.4 g/100 kcal
- Useful in dogs with fat intolerance
- Certain protein-losing enteropathies

Home-cooked diet

- No inherent benefit
- Most recipes online or in books do not provide complete & balanced nutrition
- Can formulate novel ingredient diet
- Typically excellent digestibility
- Consult with veterinary nutritionist

Getting help

- www.acvn.org/directory
- www.BalanceIT.com
Million dollar question

Which diet is best???

There is no “best” diet

- Consider client & pet preferences
- Compare nutrient profiles
- Concurrent medical therapy is often necessary
- Good client communication is imperative

Additional factors to consider

- Fiber
- Cobalamin
- Probiotics
- Prebiotics

Fiber

- Component of dietary carbohydrate
- Resists enzymatic digestion in small intestine

Characteristics

- Solubility
- Fermentability

Soluble fiber

- Useful in management of diarrhea
- Binds excess water in intestine
  - Reduces water content in stool
  - Increases viscosity
- Short-chain fatty acids
  - Benefit colonocytes

Fiber supplementation

- 1 teaspoon Metamucil = 3 g fiber
- ½ cup canned pumpkin = 3.6 g fiber
Fiber supplementation

- Metamucil = psyllium
  - Unflavored, sugar-less
- Dose
  - Start with 1-2 tsp per meal
  - Titrate to effect
  - Up to 1-4 tbsp per day

Cobalamin (vitamin B₁₂)

- May be decreased with chronic enteropathies
- Cobalamin deficiency itself can contribute to intestinal disease
  - Villous atrophy
  - Mucosal inflammation

Cobalamin supplementation

- Must supplement parenterally
  - Recommended when cobalamin < 300 ng/L
- Dose once per week x 6 weeks
  - Then one dose after 30 days
  - Recheck cobalamin 1 month later
  - Adjust as needed

Probiotics

- Criteria for efficacy
  - Live microorganisms
  - Adequate amounts
  - Purported benefits
    - Establish healthy intestinal microflora
    - Compete with pathogenic bacteria to colonize intestinal mucosa
    - Support immune system

Commercial probiotics

- 25 products evaluated
  - 4 products met label claim of viable organisms
  - 2 products considered acceptable

Assessment of commercial probiotic bacterial contents and label accuracy

Probiotics
- FortiFlora
  - *Enterococcus faecium* (1 x 10^8 cfu/g)
  - Contains animal digest
- Prostora Max
  - *Bifidobacterium animalis* (1 x 10^8 cfu/g)
  - Contains skim milk, soy lecithin

Probiotics
- Proviable-DC
  - Several strains bacteria (5 x 10^9 cfu/g)
    - *Enterococcus, Streptococcus, Lactobacillus, Bifidobacterium*

Prebiotics
- What is a prebiotic?
  - Non-digestible dietary fermentable substance that enhances “good” intestinal flora
- Examples
  - Inulin
  - Fructooligosaccharides (FOS)

Meet Gabby
- 6.5-yo SF Collie
- 3-week history of loose stool & decreased appetite

Additional history
- No vomiting
- Normal drinking/urination
- Diet – Purina Pro Plan Sensitive Skin & Stomach
  - No treats; no dietary indiscretion
- Current on vaccines & flea/tick/heartworm prevention
Physical examination
- QAR; normal hydration, normal TPR
- BW – 50 pounds (23 kg)
  - BCS – 5/9; normal muscle condition
  - Normal cardiopulmonary auscultation
  - Abdominal palpation unremarkable
  - Soft yellow stool on rectal examination
  - Some ventral subcutaneous edema

Diagnostic plan
- Minimum database
  - CBC, chemistry profile, urinalysis
- Fecal examination
- Gastrointestinal panel
  - Cobalamin, folate, TLI, cPLI
- Abdominal ultrasound
  - +/- Endoscopy & biopsies

Results
- CBC – stress leukogram
- Chemistry profile
  - Severe panhypoproteinemia
    - TP – 2.6 g/dl (5.2-7.1 g/dl)
    - Albumin < 1.0 g/dl (2.7-4.0 g/dl)
  - Hypocalcemia
  - Hypocholesterolemia
- Urinalysis
  - Negative for protein

Results
- Fecal flotation – Many Isospora oocysts present
- GI panel
  - ↓ cobalamin, ↓ folate

Results
- Abdominal ultrasound
  - Normal GI wall thickness & layering
  - Mild volume of free peritoneal fluid

Now what?
- Biopsies?
  - Not a good candidate for full thickness biopsies
- Treat empirically?
Treatment plan
- Diet trial
- Cobalamin supplementation
- Sulfadimethoxine (eg, Albon)

Diet comparison

<table>
<thead>
<tr>
<th>Diet (dry)</th>
<th>Calories (kcal/cup)</th>
<th>Protein (g/100 kcal)</th>
<th>Fat (g/100 kcal)</th>
<th>Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pro Plan Sensitive Skin &amp; Stomach</td>
<td>418</td>
<td>7.2</td>
<td>4.7</td>
<td>Salmon, rice, cat meal</td>
</tr>
<tr>
<td>Hill’s d/d Potato &amp; Venison</td>
<td>371</td>
<td>4.5</td>
<td>4.0</td>
<td>Potato, venison</td>
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<tr>
<td>Royal Canin PV</td>
<td>286</td>
<td>5.7</td>
<td>3.2</td>
<td>Potato, venison</td>
</tr>
<tr>
<td>Iams Response KO</td>
<td>328</td>
<td>5.9</td>
<td>3.7</td>
<td>Kangaroo, oats</td>
</tr>
<tr>
<td>Royal Canin HP</td>
<td>335</td>
<td>5.2</td>
<td>4.7</td>
<td>Hydrolyzed soy, rice</td>
</tr>
<tr>
<td>Hill’s z/d Ultra</td>
<td>327</td>
<td>4.8</td>
<td>3.3</td>
<td>Hydrolyzed chicken, starch</td>
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<tr>
<td>Purina HA</td>
<td>311</td>
<td>5.2</td>
<td>2.6</td>
<td>Hydrolyzed soy, starch</td>
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<tr>
<td>AAFCO minimum</td>
<td></td>
<td>5.1</td>
<td>1.4</td>
<td></td>
</tr>
</tbody>
</table>

Follow-up – 1 week later
- Doing well at home
  - Good appetite, good energy
- No diarrhea, no vomiting

Follow-up – 1 week later
- Panhypoproteinemia improving
  - TP – 4.3 g/dl (5.2-7.1 g/dl)
  - Albumin – 1.7 g/dl (2.7-4.0 g/dl)
- Continue with current therapy
  - Monitor and adjust as needed

In summary
- Diet can be a useful tool in management of chronic enteropathies
- Consider each animal as an individual
- Some trial and error may be required to achieve best results

Questions?
- Contact information:
  - Email: parker.888@osu.edu
  - Phone: (614) 292-3551
Flora Modification & Immunomodulatory Drugs for Chronic Enteropathy

Speaker

Adam Rudinsky, DVM, MS, DACVIM

Dr. Rudinsky is the most recent addition to the Small Animal Internal Medicine service at The Ohio State University Veterinary Medical Center. He provides the service with a specialized interest, clinical perspective and clinically applicable research in gastroenterology, pancreatology, and hepatology. Dr. Rudinsky received his DVM degree from The Ohio State University, completed a small animal rotating internship at Purdue University, and then a combined residency in internal medicine and MS degree at The Ohio State University. He is now on faculty at Ohio State as a staff internist and research scientist as he completes his PhD program in gastrointestinal immunology. His current clinical and research interests include chronic enteropathies, pancreatic and hepatic disease, mucosal immunology, and the intestinal microbiome as it relates to small animal gastrointestinal disease pathophysiology and treatment. During his residency he received several teaching awards and hospital service awards.
Flora Modification and Immunomodulatory Drugs for Chronic Enteropathy

Remember, the term IBD is a catch all for a variety of chronic enteropathies. If you say a patient has IBD, you are not necessarily incorrect but you may be able to be more specific. Saying IBD simply says there is inflammation in the intestines. Whereas, the more important question when inflammation is present is: Why is the inflammation present? Unfortunately, to date, the exact cause of ‘IBD’ is unknown but likely involves 3 factors: the cat’s immune system, what is entering the GI tract (diet), and also who is living there (the microbiota). Conceptually, this is a very important idea as it forms the foundation for our therapeutic approach to this disease. In previous lectures, we have focused on the ‘what’s entering the GI tract’ variable with Dr. Parker’s review of nutritional and fiber management of chronic enteropathies. We will now change focus to a discussion of what to do if diet therapy is unsuccessful....

Once a patient has failed an appropriate diet trial (i.e. Food responsive enteropathy ruled out) the main differentials become antibiotic responsive, probiotic responsive, or a steroid responsive enteropathies. These enteropathies are commonly grouped together under the term IBD or ‘idiopathic inflammatory bowel disease’ and the classification that best fits with this term is ‘steroid responsive chronic enteropathy’.

In a non-sick patient (i.e. eating well and does not require hospitalization), empirical antibiotic therapy is preferred after a failed diet trial. However, in a sick patient, preference is given to immunomodulatory drugs (i.e. corticosteroids), which has an added benefit of appetite stimulation in some patients.

Antibiotic Responsive Chronic Enteropathy

The historical term, frequently confused with antibiotic responsive chronic enteropathy, is SIBO (small intestinal bacterial overgrowth). SIBO is a recognized disease in people but, due to limitations in the way it is characterized in veterinary medicine, it may or may not be a relevant topic. This overgrowth of bacteria typically results from a secondary disorder, which causes a loss of control mechanisms within the GI tract. Further studies are required to better characterize this phenomenon in dogs and cats.

Newer evidence points to GI dysbiosis (relative changes in bacterial populations within the GI tract) that lead to ‘antibiotic responsive enteropathy’. This syndrome is characterized by a chronic diarrhea responsive to antibiotic therapy.

Criteria for Diagnosis:
1. No other underlying diseases discovered on diagnostic work-up and GI biopsies
2. Failed appropriate diet trial
3. Response to antibiotic trial (metronidazole or tylosin; rarely oxytetracycline)
Tylosin - First choice
Metronidazole – Second choice
Oxytetracycline

4. Relapse with withdrawal of antibiotic therapy

Treatment:
1. Choose an appropriate antibiotic (tylosin or metronidazole; oxytetracycline in resistant cases)
2. Administer for initial 4-6 week trial to assess response
   a. If response is positive, titrate to lower chronic dose if possible
   b. If no response in first 2-3 weeks:
      i. Change antibiotic drug
      ii. Move to immunomodulatory drugs
3. Adjunctive therapies may be beneficial if done concurrently (dietary modification, cobalamin supplementation, etc...)

Probiotic Responsive Chronic Enteropathy

This is a difficult diagnosis, because it is rare that animals respond solely to probiotics. Currently, there is no conclusive evidence that supports the use of probiotics for chronic enteropathies in canine and feline patients. However, anecdotal success stories are reported in individual cases and limited research with the predominant probiotics show some promise. Furthermore, human and murine studies indicate that there is the potential to antagonize pathogenic bacteria and positively modulate the intestinal immune response.

At our institution, we believe probiotics are best used as an adjunctive therapy alongside more traditional management strategies. Unfortunately, despite some promising evidence in initial studies, we are currently clueless as to which probiotic is best and in what circumstances. Furthermore, as probiotics are not held to strict manufacturing standards, we recommend veterinary products with governing quality assurance standards with indicating some evidence of efficacy in veterinary species.

Our preferred probiotic options are:

   1. VSL #3
   2. Flortiflora
   3. Prostora
   4. Proviable

Steroid (Immunomodulatory) Responsive Chronic Enteropathy

This type of chronic enteropathy is associated with an immune mediated cause leading to an inappropriate inflammatory response. Over time, if left uncontrolled,
this inflammation can result in structural and/or functional issues within that GI system.

As no underlying cause is identified in these cases, we utilize immunomodulating medications to stop the inflammation.

Criteria for Diagnosis
1. Failed appropriate food and antibiotic trials
2. Thorough diagnostic investigation to eliminate other potential causes
3. Biopsy consistent and demonstrates significant inflammation

Treatment
1. Choose an appropriate drug therapy plan
2. First line therapy
   a. Corticosteroids
      i. Prednisone, Prednisolone (cats)
      ii. Budesonide
3. Secondary drugs
   a. Cyclosporine
      i. Based on side effect profile. My preference in cases of diarrhea.
   b. Mycophenalate
      i. Based on side effect profile. My preference in cases of vomiting.
   c. Azathioprine?? – when and why used compared to the others?
4. Adjunctive therapies may be beneficial if done concurrently (dietary modification, cobalamin supplementation, etc...)

**Chronic Enteropathy Pharmacology**

**Antimicrobial Drugs**

This is a large category of medications that we commonly encounter in practice. They can be dividing into drugs that target specific pathogens (anti-helicobacter antibiotics, anti-protozoals, or anti-helminths) or drugs that are used to modify the existing microorganism populations. This latter group will be the emphasis of discussion for management of chronic enteropathy cases. The two drugs, which dominate this category, are metronidazole and tylosin.

**Metronidazole**

Classically known for its anti-protozoal effects against organisms like Giardia, this drug also can improve cases of diarrhea not associated with this organism. This drug is believed to work from its antibiotic properties, modifying the resident bacteria populations and thereby decrease inflammation associated with these
organisms. There is significant evidence in both cats and dogs demonstrating the ability of metronidazole to alter GI flora populations. Alternatively, it may work through immunomodulatory effects by decreasing the cell mediated immune response.

Dogs and Cats: 7-10 mg/kg PO BID

Side Effects: neurologic disorders, lethargy, weakness, neutropenias, hepatotoxicity, hematuria, anorexia, nausea, vomiting and diarrhea

Duration: Most patients will respond partially in the first week, complete response may take 2-6 weeks

Tylosin

The other medication commonly employed for treatment of antibiotic-responsive diarrhea (Dysbiosis) is Tylosin. This drug is commonly sold as ‘Tylan Powder’ where one teaspoon holds approximately 3000 mg of drug. Therefore, most dogs are typically in the 1/8 to ¼ teaspoons range for normal dosing requirements. The benefit of Tylan powder is that it is inexpensive, however the down side is the powder has a taste that can be undesirable for some animals. I commonly have owners administer the powder in gelatin capsules to ease administration. This is particularly helpful in feline patients. Alternatively, in some instances you may be able to acquire tablets from some distributors. However, in my experience this has been less consistent for owners to obtain. The parenteral formulation should not be used.

Dogs and Cats: 10-15 mg/kg PO BID

Side Effects: gastrointestinal upset

Duration: Most patients will respond partially in the first week, complete response may take 2-6 weeks

**Immunomodulatory Drugs**

In our experience, choosing an immunosuppressant is best done based on what is important to you as a clinician and what is important to the owner. Specifically, as a clinician, time to action (i.e. how quickly does the drug work), side effects for the patient, and lastly evidence based medicine for each drug individually are important considerations. Commonly, owners care about the side effects for their pet as well as the cost of the medication. Therefore, there are some general rules for drug selection, however each drug plan must be tailored to your specific patient/client.

**Glucocorticoids**
This class of drugs which include prednisone, prednisolone, and budesonide are the mainstay of immunomodulatory drugs due to their minimal expense and multifactorial effects on suppressing the immune system. They are able to decrease chemotactic factors, mediators of inflammation (cytokines), and inflammatory cell (i.e. T-cell) distribution. However, they have a predictable and extensive list of side effects, which may decrease owner satisfaction and animal comfort. It is also important to remember these can exacerbate/worsen other concurrent diseases such as proteinuria and diabetes.

The majority of your cases will be adequately controlled on monotherapy with glucocorticoids. However, the two biggest reasons for adding a secondary drug (see below) is to provide control in cases where monotherapy with a glucocorticoids is insufficient to provide disease symptom control or to reduce side effects associated with glucocorticoids. The latter is very important as therapy can lead to severe complications, the majority of which are related to iatrogenic hyperadrenocorticism.

Prednisone/Prednisolone (cats)

Dogs: 1-2 mg/kg/day PO

Cats: 2 mg/kg/day PO – Prednisolone is preferred in cats due to the poor oral bioavailability of prednisone

Budesonide

Dogs and Cats: 1-3 mg/m² PO SID

Side Effects: iatrogenic hyperadrenocorticism

Duration: Effect usually noted by 3-5 days, full response may take up to 2 weeks

**Cyclosporine**

This drug targets the immune system through lymphocytes (i.e. lymphocyte specific), preventing calcium dependent signal transduction. The added benefit of it being lymphocyte specific means that cytotoxicity and myelotoxicity does not occur as it does not affect other types of rapidly dividing cells. However, nephrotoxicity is a concern in, especially in cats and potentially dogs. Less severe side effects include gingival hyperplasia (which resolves after drug withdrawal), fibropapillomatosis, pyoderma, increased hair growth, and, theoretically, an increased risk for the development of neoplasia.

One side effect that many practitioners experience in the use of this drug is either GI intolerance (primarily vomiting) or dislike of the taste. Four options for mitigating
these side effects include freezing pills prior to administration, administration within a gelatin capsule, giving metoclopramide as a premedication 30-60 minutes prior to dosing, or dose escalation to reach your target dose over the course of a week.

Based on our knowledge of its performance, Atopica is still the best option for patients when the use of cyclosporine is desired. However, there is also interest in two other oral formulations available, Sandimmune and Neoral. It is extremely important to remember these drugs are not equivalent. Sandimmune is poorly bioavailable in veterinary species. Alternatively, Neoral is a microemulsification of cyclosporine that becomes microemulsified when in contact with GI fluids where it can then be absorbed directly through the gastrointestinal epithelium.

Follow in patients on this medication can be difficult. Ideally a trough level (12 hours post dose) should be greater than 500 ng/ml in dogs. Cats will usually be well controlled with lower trough levels as long as they are maintained above 250 ng/ml. Blood levels can be submitted through multiple commercial laboratories. Therapeutic levels should be measured 2 hours after dosing if it is indicated.

In cases where cost is a concern, you can decrease the dose by administering Ketoconazole concurrently. This will interfere with hepatic metabolism and increase serum levels of the drug. In some cases, we are able to reduce the cyclosporine dose by 30-50%. However, with this multimodal therapy you must also monitor for and be cognizant of side effects associated with azole therapy, which mainly include hepatotoxicity.

Atopica/Neoral

Dogs: 5 mg/kg PO BID

Cats: 5 mg/kg PO SID

Side Effects: vomiting, anorexia, diarrhea, gingival hyperplasia, hypertrichosis, excessive shedding, papillomatosis, hepato and renal toxicity unlikely

Duration: Effect usually noted by 3-5 days, full response may take up to 2 weeks

Ketoconazole:

Dogs: 5 mg/kg PO BID

Side Effects: vomiting, anorexia, diarrhea, hepatotoxicity, thrombocytopenia, dose related suppression of gonadal and adrenal steroid synthesis

Metoclopramide (IF necessary):
Dogs and Cats: 0.4 mg/kg PO BID

Side Effects: mentation changes, behavior changes, ideally avoided in patients with seizures or pheochromocytomas

**Azathioprine**

This drug is typically selected in cases where a secondary drug is needed to control clinical signs and/or cost is an issue. It is a purine analog which is metabolized into ribonucleotide monophosphates. They accumulate in cells and interfere with DNA coding and transcription. Humoral immunity is believed to be affected to a greater degree than cell-mediated immunity.

From a canine GI perspective, this has most commonly been used in the treatment of inflammatory bowel disease (Chronic enteropathies?), atrophic gastritis, and chronic hepatitis. This drug is much less commonly used in cats due to the more frequent occurrence of myelotoxicity. All patients should be monitored for bone marrow suppression, liver injury, pancreatitis, and hepatotoxicity. Although the side effects are severe they are, in general, uncommon and we have had good success with its use with minimal side effects.

Dogs: 2 mg/kg PO SID (strongly recommend taper down)

Cats: 0.3 mg/kg PO BID (highly controversial – toxicity)

Side Effects: bone marrow suppression, gastrointestinal upset, poor hair growth, acute pancreatitis, hepatotoxicity

Duration: 2-3 weeks for initial effect, 3-4 weeks for complete effect

**Mycophenolate Mofetil**

This drug is commonly referred to as ‘MMF’ for short and sold under the name ‘Cellcept’. It is another lymphocyte specific therapy which interferes with enzymatic processes necessary for purine formation. Side effects for this medication include leukopenia and GI side effects (anorexia, GI bleeding, and/or colitis).

This drug has emerging evidence of efficacy in canine chronic enteropathies. In our experiences, it is very well tolerated and has been used successfully in many canine patients.

Dogs: 10 mg/kg PO BID

Side Effects: diarrhea, vomiting, anorexia, lethargy, lymphopenia
Duration: Effect usually noted by 3-5 days, full response may take up to 2 weeks

**Alkylating Agents (Chlorambucil and Cyclophosphamide)**

These drugs are the most commonly used anti-neoplastic drugs in veterinary gastroenterology. The focus of this paper is oriented toward chlorambucil trade name ‘Leukeran’. Cyclophosphamide is less commonly used as a result of the risk of sterile hemorrhagic cystitis, and at our institution is reserved for refractory cases. The most common side effect that requires monitoring is bone marrow suppression. CBCs should be monitored during therapy and the frequency is dictated by the dosing regimen.

Dogs: 1.5 mg/m² PO EOD

Cats: 20 mg/m² PO every 2 weeks or 2 mg/m² PO EOD

Side Effects: myelosuppression, gastrointestinal toxicity, alopecia

Duration: typically rapid effect within the first week of therapy