The presence of clinical signs of gastrointestinal disease (diarrhoea, vomiting, weight loss and change of appetite) for longer than 3 weeks is consistent with a chronic enteropathy. This is a commonly encountered situation in practice and a logical approach to investigations is essential to facilitate accurate diagnosis and treatment.

There is some confusion regarding the descriptions used for this spectrum of diseases. The term chronic enteropathy (CE) is currently preferred to inflammatory bowel disease as it recognises the difference between the conditions seen in small animals compared to humans. Importantly the majority of dogs identified with a chronic enteropathy will not require immunosuppressant therapy (Dandrieux 2016). Chronic enteropathy can be subdivided based on response to treatment:

- **Food-responsive enteropathy (FRE)**
- **Antibiotic-responsive enteropathy (ARE) or small intestinal dysbiosis**
- **Immunosuppressant-responsive enteropathy (IRE)**

In dogs with normal serum albumin at diagnosis approximately 75% will be diet-responsive, 15% antibiotic-responsive and 10% immunosuppressant-responsive. Dogs with protein-losing enteropathy (PLE), have demonstrable enteric protein loss associated with more severe inflammatory disease, gastrointestinal lymphoma or lymphangiectasia. Hypoalbuminaemic dogs have a poorer prognosis as reports suggest that only 35% are likely to have their clinical signs controlled by diet alone, 35% will require long-term immunosuppression and 30% are likely to die or be euthanased due to their condition.

**Aetiology of Chronic Enteropathy**

The triggers for inflammation of the gastrointestinal tract and consequent chronic enteropathy remain poorly defined. The breakdown of immunologic tolerance to luminal antigens (including bacterial and dietary components) is likely critical and may result from disruption of the mucosal barrier, immune dysregulation (Burgener et al 2008), or disturbance of the intestinal microbiota (Xenoulis et al 2008). Genetic factors are also likely to play a significant part with specific mutations identified in some dog breeds.

**Diagnosis of Chronic Enteropathy**

A standardised diagnostic approach to chronic enteropathy has been described (Simpson 2012). This provides a logical method to investigating cases:

- Exclusion of extra-gastrointestinal disease
- Characterisation of the nature and severity of disease
- Selection of treatment based on this severity assessment

This approach can be further broken down into an adaptable diagnostic algorithm as follows:

1. Clinical history and examination
• Large intestinal localization (dyschezia, tenesmus, increased frequency of defecation, small volume of faeces, mucous, blood).
• Small intestinal localization (large volume diarrhoea, weight loss, vomiting).
• Melaena (suggesting upper GI bleeding/ulceration).
• Atypical signs suggestive of other system involvement (e.g. PUPD)

2. Detection of endoparasites and enteric pathogens or a therapeutic trial with a broad spectrum anthelmintic

   • Detection of non-GI disease
     i. Haematology
     ii. Biochemistry
     iii. Urinalysis
   • Detection & characterisation of GI disease
     i. TLI
     ii. Folate & Cobalamin

4. Diagnostic Imaging
   • Radiographs – structural GI disease.
   • Abdominal ultrasound – obstruction, intussusception, focal masses, thickening, intestinal layering, hyperechoic striations. Also, evaluation of organs intimately associated with the GI tract (pancreas, liver, biliary tract).

5. Clinical staging based on disease activity index
   • Several validated scoring systems are available including the Canine Chronic Enteropathy Activity Index (CCEAI) (Allenspach et al 2007). The overall severity score for the CCEAI is out of 27. Only a classification of very severe disease (>12/27) has been shown to be a predictor of a negative outcome.
   • Hypocobalaminëmia, hypoalbuminaemia, hypovitaminosis D and elevated c-reactive protein (CRP) have also been identified as negative prognostic markers

6. Therapeutic trials with diet +/- antibiotics.

For cases with a high CCEAI or that have failed to respond to appropriate diet trials (exclusion diet fed for 3 weeks) and antibiotic therapy (see below), acquisition of histologic samples may be pursued.

1. Endoscopic gastrointestinal biopsy:
   a. May be preferred if there is significant hypoalbuminaemia (wound healing)
   b. Samples obtainable from stomach, duodenum, ileum and colon

2. Surgical gastrointestinal biopsy

Biopsy samples are assessed for the severity of inflammation and any structural changes as well as the presence of malignancy (e.g. gastrointestinal lymphoma) or specific pathologies (histiocytic ulcerative colitis).
Treatment of Chronic Enteropathy

1. Exclusion diet trial  
   a. Commercial hydrolysed diet (consider choice of protein source)  
   b. Commercial novel protein diet  
   c. Home-cooked novel protein diet (ideally formulated by a nutritionist unless only fed for a short period of time)

2. Antibiotic therapy (trial)  
   a. Questionable antibiotic stewardship  
   b. May offer effective treatment for their clinical signs  
      i. Metronidazole (10mg/kg PO every 12 hours)  
      ii. Tylosin (25mg/kg PO every 12 hours)

3. Immunosuppression  
   a. Glucocorticoids, usually prednisolone (1-2mg/kg/day) considered first-line treatment  
      i. BUT: adverse effect profile including catabolic effects that can lead to further weight loss (especially muscle mass) in already cachexic patients.  
      ii. Consider budesonide, a glucocorticoid with extensive first pass metabolism and therefore reduced systemic side effects  
   b. Additional immunosuppressant medications can facilitate a more rapid taper  
      i. Ciclosporin (at 5mg/kg every 12 to 24 hours)  
      ii. Chlorambucil (at 4-6 mg/m²/day initially)  
      iii. Azathioprine (inexpensive but some evidence suggesting worse outcomes with the use of this drug (Dandrieux et al 2013)).

4. Cobalamin supplementation if hypocobalaminæmic  
   a. Injectable therapy  
   b. Oral supplementation may be effective in many cases (Toresson et al 2016).

5. Anti-thrombotics  
   a. Risk of thromboembolic disease in PLE  
      i. Ultra low dose aspirin or clopidogrel

6. Short-term supportive treatments  
   a. Antacids (omeprazole, ranitidine)  
   b. Anti-emetics (maropitant, metoclopramide, ondansetron)  
   c. Pro-kinetics? (efficacy difficult to document)  
   d. Mucosal protectants

Monitoring and Prognosis of Chronic Enteropathy

Close monitoring especially in the early stages permits effective dose adaptation. Treatment escalation or de-escalation can be guided by a number of factors including clinical response.
control of clinical signs, weight gain; clinical severity scoring (CCEAI); measurement of serum proteins (PLE cases). The value of monitoring other biomarkers such as c-reactive protein is uncertain.

If response to treatment is sub-optimal reassessment is advised to ensure this is not due to an unidentified complication (malignancy, hypcobalaminemia). With a favourable response tapering of immunosuppressive medication should be performed gradually over several months whilst monitoring clinical signs. Long-term (even lifelong) therapy may be necessary in some patients.

Overall 10-20% of pets with chronic enteropathy will die or be euthanased as a result of their condition.

Conclusions

Chronic enteropathy is a common presentation in practice but, with a logical approach to diagnosis and treatment, a positive response can be seen in most patients.

References:


