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Chronic intestinal disease (enteropathy) causing poor appetite, recurrent colic, diarrhoea and weight loss is a common presentation in equine practice. Other signs might include dependent oedema, skin disease and dysphagia. In the early stages of disease deterioration in athletic performance may be the only sign. This lecture will focus on inflammatory bowel disease (IBD), malabsorption and diarrhoea and complements those on Equine Gastric Ulcer Syndrome and A Practical Approach to the Diagnosis and Management of Weight Loss. Here the author will discuss some aspects of diagnostic testing and treatment based on the literature, clinical experience and results from general practice. Primarily surgical conditions will not be addressed.

**INTESTINAL STRUCTURE AND FUNCTION**

A basic understanding of intestinal structure and function is necessary to appreciate some of the difficulties in diagnosing and managing horses with chronic intestinal inflammation, infiltration or neoplasia. Such processes can result in malabsorption / malassimilation / maldigestion and protein, fluid and electrolyte losses. The intestine provides a massive surface area for the digestion and absorption of food. Conversely when there is mucosal injury a similarly massive area can be compromised leading to hypersecretion, malabsorption, protein exudation as well endotoxin absorption and bacterial translocation.

The small intestine has a greatly folded mucosal surface which is further folded creating surface villi and crypts which are in turn lined by enterocytes with numerous microvilli. Thus villous atrophy for example seriously compromises normal function. The large intestine has a flattened surface with multiple mounds & crevices covered by a thin mucosal layer containing multiple glands lined with goblet cells and granular cells with microvilli with both secretory and absorptive function as in the small intestine. The normal large intestinal recover more than 100L of fluid daily. Microbial fermentation drives carbohydrate digestion producing volatile fatty acids that supply 75% of the horse’s energy requirements. The normal large intestinal microflora also act to inhibit adhesion and colonisation by pathogenic bacteria including producing antibacterial factors. Normal VFA products are toxic to some pathogenic bacterial strains e.g. coliforms. Inflammation, invasive bacteria & intestinal parasites can all alter motility patterns which also affect movement of bacterial populations and absorptive function.

Diarrhoea is defined as an increase in the frequency, fluidity and volume of faeces with 14 days duration considered as chronic.Diarrhoea generally indicates disruption of colonic function through either large intestinal involvement in the primary disease process or delivery of abnormal carbohydrate substrates from a dysfunctional small intestine resulting in abnormal fermentation, a fall in pH (< 6), disruption of normal luminal microflora, increased osmolarity, increased osmotic
load and net secretion exceeding absorptive capacity. Although inflammation is central to most cases of diarrhoea, abnormal motility (including stress and excitement) affecting bowel transit time, a change in osmotic load (dietary change to carbohydrates and/or lipid, oral medications), increased capillary hydrostatic pressure (heart failure), reduced oncotic pressure and defective lymphatic drainage (neoplasia or inflammation) can all be causes. Caecal and colonic secretion of water and electrolytes and protein loss can rapidly lead to massive deficits. Significant intestinal malabsorption syndromes are uncommon in the horse and typically associated with small bowel disease but significant caecal and colonic pathology can result in malabsorption of both water and carbohydrate fermentation products. Mucosal injury disrupts normal villous crypt base enterocyte proliferation ablating villous secretory function with subsequent chronic malabsorption as there are no maturing enterocytes to migrate toward the tip of the villi (the primary sites for absorption). Absorption mechanisms include both active and passive transport processes and although our understanding of these has grown greatly in recent years as yet we are unable to manipulate these mechanisms for clinical use.

**CLINICAL EXAMINATION**

Poor body condition and diarrhoea may be obvious. There are four important questions to ask in such cases: is there clinical evidence of systemic disease (fever, endotoxaemia), colic, hypoproteinaemia and/or hypovolaemia as these factors may need immediate treatment. Also look for and question the owner regarding any evidence of chronic skin disease, mucosal inflammation or peripheral lymphadenopathy. Fever is a non-specific sign and can be caused by invasive mucosal infection (*Salmonella* spp., proliferative enteropathy), larval cyathostominosis or neoplasia. A rectal examination may detect thickened bowel but this rare, enlarged mesenteric lymph nodes or intra-abdominal masses. Small red L4 cyathostomin larvae may be seen on the rectal sleeve in cyathostominosis cases. Faeces can be collected.

**FAECAL ANALYSIS**

When diarrhoea is present fresh faeces should be submitted for worm egg count, wet smear examination for cyathostomin ("redworm"), bacteriology (including selective media for *Salmonella* spp.) and sedimentation to assess sand content. Anaerobic culture for *Clostridia* spp. (perfringens and difficile) and toxin analysis is appropriate in acute cases. PCR analysis for *Lawsonia intracellularis* and *Salmonella* spp. may be appropriate in certain animals. In chronic diarrhoea cases isolation of *Salmonella* spp. or a positive faecal PCR does not indicate causation; indeed horses with diarrhoea are more likely to shed *Salmonella* spp. *Aeromonas* spp. have been linked to diarrhoea but the importance of other species is questionable but there are likely to be regional variations.

**HAEMATOLOGY AND CLINICAL CHEMISTRY**

Leucopaenia may occur with chronic invasive intestinal bacterial infection and leucocytosis with both larval cyathostominosis and neoplasia. Anaemia of chronic disease may be present and occasionally immune-mediated haemolysis can be associated with lymphoma cases. Elevated fibrinogen levels give only non-specific evidence of inflammation. Hypoproteinaemia and hypoalbuminaemia characterise malabsorption syndromes; the smaller albumin molecule usually being lost preferentially. Serum globulin levels may be normal, elevated or low in protein-losing enteropathy. In a retrospective study of 36 weight loss cases in which transendoscopic duodenal biopsies were harvested because inflammatory bowel disease was suspected (Brazil 2009 JVIM 23: 432) a number of diagnostic tests were examined to determine whether any test
could help predict outcome of these cases. Survival rates of 95% in the 21/36 horses with normal serum albumin (30 g/L), 66% in the 9/36 (25%) with moderate hypoalbuminaemia (<30 & > 20 g/L) and 66% in the 6/36 (16.6%) with severe hypoalbuminaemia (< 20/gL) were reported. Thus the severity of hypopalbuminaemia does not predict survival.

PERITONEAL FLUID ANALYSIS

This is a low yield technique in most chronic enteropathy cases. Protein levels may be elevated but there is value in collecting a sample to assist the detection of the rare exfoliating intestinal / mesenteric neoplasia case.

ORAL GLUCOSE ABSORPTION TESTS (OGAT)

This will document malabsorption but abnormal results do not correlate well with either serum albumin nor the histological degree of intestinal inflammation. In the author’s retrospective study, survival rates of 89% in the 9/17 with normal absorption, 83% in the 6/17 with partial malabsorption and 0% in the 2/17 with complete malabsorption were reported.

RECTAL BIOPSY

Although a low yield diagnostic technique it is always worth performing as it may reveal a diagnosis. Recent work from Leroux et al (2011, JVIM, 25) revealed new insights into the technique when studying 7 horse with weight loss and diarrhoea and 5 with non-GIT disease. Biopsies were harvested from each horse at 15 & 30cm from anus and compared with necropsy histology of more proximal bowel (ileum, duodenum, caecum, colon & rectum). The 2 O’clock position was best for a right handed clinician. At 30 cm, 91% samples were cranial to peritoneal reflection and 48% at 15 cm. The mucosa was sampled in 100% of specimens and the submucosa in 95%. Inflammation scores of the mucosa were equal to those of the sub-mucosa. The inflammatory infiltrate in the caecum/colon was always greater than that in the rectum and was always greater at 30cm than 15 cm from the anus. Thus we should consider taking more proximal samples, perhaps endoscopically. Encysted cyathostomin larvae may be detected in rectal mucosa in some cyathostomosis cases.

TRANSCUTANEOUS AND TRANSRECTAL ABDOMINAL ULTRASONOGRAPHY

This is useful to detect thickened intestine but does not appear to predict survival. In the author’s retrospective study survival rates of 82% in the 11/27 with ultrasonographically normal small intestine and 75% in the 16/27 with thickened small intestine (> 4 mm wall thickness) were documented. Colonic and caecal thickening may also be noted. Although apparently rare in Europe right dorsal colitis may be tentatively confirmed ultrasonographically. Other thickened large bowel segments (caecum and colon) may be found in small numbers of cases with weight loss, hypopalbuminaemia and/or chronic diarrhoea.

DUODENOSCOPY

This facilitates examination of the proximal duodenal mucosa, bile duct papillae and harvest of transendoscopic duodenal mucosal biopsies for histology. In the author’s study 36 sets of biopsies were harvested. Inclusion criteria were partial or complete malabsorption on OGTT, thickened small intestine on abdominal ultrasonography (> 4mm small intestinal wall thickness at ≥3 sites), low serum albumin suggestive of protein-losing enteropathy (< 30 g/L) or subjective visual abnormality of proximal duodenum as well as clinical signs of chronic enteropathy (weight loss ± diarrhoea ± recurrent colic). Biopsy histology was categorised as normal (10/36, 27.8%), a mild (13/36, 36.1%), moderate (10/36, 27.8%) or severe (2/36, 5.5%) lymphocytic-plasma-
cystic infiltrate (LPI) and lymphoma (1/36, 2.8%). The following survival rates were noted: normal biopsy or mild LPI (82.6%), moderate LPI (90%), severe LPI (50%), lymphoma (0%). A duodenal lymphocytic-plasmacytic infiltrate may be part of a more generalised lymphocytic-plasmacytic enterocolitis but at least at mild to moderate levels may be a non-specific mucosal immune reaction to antigenic stimulation chronic enteropathy. Lymphoma has been recognised. Thus again although this may be a low yield diagnostic technique, it is relatively cheap and minimally invasive, hence justifying its inclusion in the diagnostic protocol.

EXPLORATORY SURGERY & BIOPSY

A definitive diagnosis of a chronic eneteropathy may require diagnostic laparoscopy and/or laparotomy and the collection of multiple full thickness biopsies from all intestinal segments and associated lymph nodes via a flank or midline celiotomy. Often there is minimal gross pathology. Avoidance of a laparotomy is preferred in a profoundly hypoproteinaemic animal.

CAUSES OF PROTEIN-LOSING ENTEROPATHY / CHRONIC DIARRHOEA

—Post acute colitis
— Cyathostomins
—NSAID toxicity
—IBD
—Lymphoma
—Sand
—Antibiotic-associated / bacterial overgrowth

NON-SPECIFIC OR UNDIFFERENTIATED DIARRHOEA

—Dietary
— Sand
—Motility
—? IBD
—? Bacterial

MANAGEMENT AND PROGNOSIS FOR INFLAMMATORY BOWEL DISEASE

IBD is categorised by the nature of the inflammatory infiltrate identified histologically; lymphocytic-plasmacytic, eosinophilic, granulomatous and mixed. Eosinophilic or mixed infiltrates are most common. Eosinophilic infiltrates can be part of generalized eosinophilic inflammatory disease (multisystemic eosinophilic epitheliotropic disease, MEED), may diffusely involve the bowel alone or occur as focal nodules or bands. The latter form typically presents with obstructive colic. Lymphoma is the most common neoplasia that clinically mimics IBD. Prognosis is always guarded but there is variation based on the nature of the inflammatory infiltrate identified histologically from full thickness biopsy specimens. However many cases would be treated and the response to therapy assessed before making a decision for euthanasia. The mainstay of treatment is corticosteroids. Bear in mind that little is known about the bioavailability of oral drug in animals with defective small intestinal malabsorption. Prednisolone (1-2 mg/kg once daily PO) or dexamethasone (0.05-0.1 mg/kg once daily PO or IM) is often required for 2-6 months, possibly longer. Once a minimal effective dose is found this may need to continue for 2-6 months, sometimes longer. Azothioprine (3 mg/kg once daily PO) is a viable alternative and can be used alone or in combination with corticosteroid allowing a lower dose. A recent retrospective study (Durham et al., 2010, Proceedings BEVA Congress) found a 61% (34/56 horses) survival rate at 12 months but the nature of the inflammatory infiltrate did affect outcome; Diffuse eosinophilic enteritis and mixed eosinophilic infiltrates had a better prognosis (70% survival) than lymphocytic-plasmacytic enteritis (55%). These survival rates are better than much of the published data.

MANAGEMENT OF LARVAL CYATHOSTOMINOSIS

3 forms are seen:
- Hypoalbuminaemia, diarrhoea, depen dent oedema and weight loss
Hypoalbuminaemia and dependent oedema without diarrhoea
- colic

Some affected animals may have a good anthelmintic treatment history but drug resistance is increasingly common. The diagnosis may be confirmed immediately if red L4 larvae are seen on a rectal sleeve. Occasionally encysted larvae may be identified in rectal biopsy specimens.

In the short term intravenous synthetic colloid (Hetastarch 10 ml/kg daily) may be required to raise plasma oncotic pressure. Corticosteroids (see above) and larvicidal anthelmintics (Fenbendazole, 7.5 mg/kg daily for 5 days, repeated every 4 weeks followed by moxidectin 0.4 mg/Kg repeated every 13 weeks) should be used in combination to reduce bowel inflammation and eliminate emerging cyathostomin larvae.

Codeine Phosphate 1-3 mg/Kg one to 3 times daily may help to reduce diarrhoea.

**MANAGEMENT OF CHRONIC DIARRHOEA**

Chronic diarrhoea without systemic effects should be managed nutritionally initially by withholding concentrate, removing from pasture grass and supplying hay only. Many horses cannot tolerate haylage but are manageable on hay. In chronic diarrhoea hypovolaemia and electrolyte depletion is less of a concern but should be considered, especially potassium which is readily supplemented PO (30g KCL BID). If fluid therapy is required care should be taken in hypoproteinaemic animals, especially if dependent oedema is present which may require colloid support. The colloid osmotic pressure (COP) can be estimated from serum albumin (A) and globulin (G) concentrations (COP = -4.384 + [A x .5501] +[G x .2475] mmHg. In chronic disease reduced COP is better tolerated such that a COP <10 mmHg requires colloid therapy although COP <15 mmHg may be addressed depending on the clinical picture. Synthetic colloids (hetastarch 10ml/Kg, pentastarch 8ml/kg) are preferred in chronic disease but the above formula becomes invalid after their use.

**ANTIBIOTICS**

In the absence of systemic disease and negative faecal culture they have little role. Some animals respond well to metronidazole (15 mg/Kg, PO BID) which has anti-inflammatory effects beyond its antibacterial effect.

*Lawsonia intracellularis* proliferative enteropathy in weanlings is a unique scenario requiring 1-6 wks of therapy with either erythromycin (25 mg/Kg PO TID) or doxycycline (10 mg/Kg PO BID).

**INTESTINAL PROTECTANTS AND ADSORBENTS**

**Kaolin/Pectin & Kaolin and morphine**

Contraindicated in acute and/or severe diarrhoea as it may exacerbate malabsorption and electrolyte losses.

**Bismuth subsalicylate**

Bismuth subsalicylate has anti-endotoxic, weak antibiotic and antiprostaglandin activity. In acute diarrhoea it act to decrease endotoxin absorption, enteroocyte hypersecretion and stimulates fluid and electrolyte absorption. Dosing is speculative Adults up to 4 l/500Kg BID, Foals: 30 ml 6x daily. However most widely used combination therapy is Pepto-Bismol 1-2 ml/Kg BID

**Activated charcoal**

This may reduce toxin absorption in acute colitis if administered early (1g / Kg) but of little value in chronic cases.

**SMECTITE BASED ADSORBENTS**

**Di-tri-octahedral smectite**

*Diarsanyl* (Biosponge, PlatinumPerformance)

Loading dose of 3g/kg then 1g/kg TID. Aluminiumsium silicate binds digestive mucus and can adsorb exo and endotoxins. *In vitro* effective in neutralisation of C.difficile & perfringens toxins and did not effect activity...
of the acidic drug metronidazole. Anecdotally very useful.

**Monmorillonite smectite (Diarsanyl)**

Another smectite product containing montmorillonite (smectite clay), which is claimed to have the capacity to absorb toxins, bacteria, viruses, enzymes and free radicals. Anecdotally useful in undifferentiated diarrhoea.

**MOTILITY MODIFIERS AND ANTISECRETORY AGENTS**

Contra-indicated in acute severe and suspected infective diarrhoea cases.

Codeine Phosphate (1-3 mg/Kg SID-TID to effect) has value to control chronic diarrhoea but must be withdrawn slowly and can cause colonic impaction at high doses. Loperamide (Lomotil) acts primarily as an antisecretory agent and may be useful in chronic diarrhoea in both foals and adults (0.04 – 0.2 mg/Kg, PO, BID).

**ANTI-INFLAMMATORY THERAPY**

Some recalcitrant undifferentiated diarrhoea that do not respond to dietary changes (reducing concentrate and changing to hay as roughage source) and medication above may respond favourably to oral anti-inflammatory agents (prednisolone 1mg/Kg PO SID am) and/or metronidazole (10-20 mg/Kg, PO BID).

**PSYLLIUM**

A source of fermentable fibre that is broken down by colonic bacteria to short chain fatty acids, particularly of butyrate, a major energy source for colonic enterocytes. This may act as a probiotic (see below). There is little evidence for its effectiveness in removing sand from the colon and it is not an alternative to appropriate grazing/dietary management. It has been recommended for right dorsal colitis (0.5-1g/kg in feed).

**TRANSFAUNATION**

Transfaunation can be an efficient method of repopulating the normal large intestinal flora. Administer omeprazole (Gastrogard) 4-6 h beforehand to increase gastric pH. Administer 5-6 L of preferably caecal liquor from a freshly killed, preferably Salmonella spp. negative horse by stomach tube. Alternatively one pile fresh faeces of a healthy individual on the same premises combined with warm water and grated potato (trypsin inhibitor), sieved through cheese given on 2-3 occasions. Variable but occasionally impressive responses are seen.

**PROBIOTICS & PREBIOTICS**

Probiotics are feed supplements containing live organisms that exert a benefit beyond nutritive value alone on ingestion of a specific number. Many products make spectacular claims as to their effects. Multiple trials in many species produce little or no concrete evidence for their efficacy. A minimum dose of 1 x 10⁹ has been suggested as a minimum dose. There are no controlled trials for any products on the UK market. Lactobacillus spp. have primarily been advised. Few probiotic products contain any recoverable live bacteria when placed in culture. Indeed detection of administered bacteria in faecal culture does not differentiate between colonisation and passive intestinal transit. The EU launched a directive for evaluation of their efficacy in 2002. Trials with commercially available probiotic supplements in the US failed to demonstrate any positive effects on salmonella spp. shedding or the prevalence of diarrhoea in hospitalised adult patients (Parraga et al 1997 JVIM 11 36-41). Lactobacillus rhamnosus strain GG shows promise. It appears to colonise the adult colon at very high doses but can produce persistent colonisation in foals (Weese et al 2003 Can Vet J 44 299). Screening of equine intestinal flora revealed Lactobacillus pentosus WE7 as a potential candidate for probiotic use and initial studies demonstrated ability to colonise the equine
gut and to inhibit common enteric pathogens in vitro (Weese et al 2004 EVJ 36 351). But subsequent trials in neonatal foals induced diarrhoea rather than preventing it (Weese et al 2005 JAVMA 226 2031). Non-pathogenic yeasts such as Saccharomyces boulardii (25g BID) may be valuable in supplying fibre and B vitamins as well attenuating bacterial enterocolitis. Supplementation did reduce severity and duration in horses with acute enterocolitis (Desrochers et al 2005 JAVMA 227 954). Prebiotics (non-digestible food ingredient that stimulates the growth and activity of beneficial bacteria already present in the colon) have received little attention in the horse but fibre such as psyllium and spent brewer’s grains has been suggested as potentially useful.