Diagnosis and treatment of cyathostominosis in horses

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Cyathostomins have become the most common cause of parasite-associated disease in horses[1] and with increasing reports of resistance of these parasites to anthelmintics in the UK[2],[3], clinical disease is only likely to become more common.

Life cycle

In excess of 50 species of cyathostomins may be parasitic to horses, although a small number of species tend to predominate the world over. Most are less than 1.5cm in length and less than 1mm in diameter.

The relative pathogenicity of individual species and details of their individual life cycles are not understood. Some species tend to parasitise the colon; others the caecum[4].

Grazing horses ingest L3 larvae, which penetrate the basement membrane of the epithelial cells of the tubular glands of the caecum, ventral colon, and to a lesser extent, the dorsal colon. Within two weeks the larvae become encysted in a fibrous capsule. Within the cyst the early L3 sequentially matures to a late L3, early L4 and then late L4. Late L4 larvae emerge from the cyst and migrate to the intestinal lumen, further developing into reproductive adults.

Maturation from ingested L3 to maturity may take as little as five to six weeks. Alternatively, maturation may arrest at the early L3 stage and the larvae may remain dormant for two years or occasionally longer[5]. Whether the arrested state is induced by the immune response of the host or by parasite factors is not known.

Eruption of a large proportion of the encysted population often occurs during late winter or spring, enabling the resultant adults to produce eggs during the warmer months of the year when conditions favour the subsequent hatching and moulting of larvae.

Larvae ingested early in the grazing season may develop through to maturity, resulting in a second generation of egg-laying adults in late summer. Those larvae that are ingested later in the grazing season are more likely to arrest their development and encyst until late winter or early the following spring, commencing a new cycle. This pattern of development probably confers a survival advantage, enabling parasites to evade cold periods by surviving in the host; in the southern hemisphere parasites adopt a similar strategy, but encyst to evade hot, dry periods.

Pathogenicity

The presence of early L3 larvae provokes a fibroblastic response, which magnifies as the larvae grow, resulting in the production of a capsule of fibroblasts and collagen.

The presence of larvae is associated with infiltration of lymphocytes, eosinophils and a lesser number of plasma cells and mast cells into surrounding tissues. The inflammatory response may be associated with

marked oedema, submucosal haemorrhage, dilation of lymphatics, focal necrosis, ulceration of the mucosa and, in severe cases, haemorrhage into the intestine.

Inflammation and loss of mucosal barrier function produces an increase in intestinal permeability[1] and protein loss to the intestinal lumen. The inflammatory changes in the intestinal mucosa, as well as alteration in microcirculation, may result in alterations in intestinal motility that can result in diarrhoea and abdominal pain[6].

Severe inflammation – and hence disease – is most likely to occur when large numbers of parasites erupt; however, disease is also possible if large numbers of larvae are ingested and invade the submucosa and mucosa simultaneously.

The species composition of cyathostomins and the host's immune response (which will be influenced by previous exposure) are also likely to be factors in susceptibility to clinical disease.

Clinical signs

A spectrum of clinical signs may be seen as a result of cyathostominosis, ranging from lethargy and weight loss through colic to peracute diarrhoea and rapid death. Signs may not be related specifically to the intestinal tract, with peripheral oedema and pyrexia being the only clinical signs in one case series[7]. Despite having a normal or increased appetite, weight loss can be dramatic.

Clinical disease is more likely in horses under five years of age[8], but may occur in animals of any age[9]. It is presumed protective immunity develops with age in response to exposure.

Classic larval cyathostominosis resulting from mass eruption of larvae is most likely to be seen in

the late winter or spring; however, cases may be seen all year round and in the author's hospital there is no obvious seasonal bias. Recent anthelmintic administration may be a risk factor for disease[10] – a phenomena thought to be related to the death of adult stages triggering mass eruption of encysted larvae.

Diarrhoea is not necessarily acute and may be chronic or even intermittent[9]. Non-specific mild colic is common with severe infestation; however, infarctions and intussusceptions have also been reported[11],[12].

Diagnosis

Haematological and blood biochemical analysis is invaluable in investigating suspected cases of cyathostominosis, although no pathognomonic findings exist. Almost all cases will develop a neutrophilia, which may be transient, but if there is high parasite burden with marked inflammation, it tends to be persistent.

Hypoalbuminaemia is a consistent finding that will be present if there is extensive intestinal inflammation. Less consistent findings are anaemia, hyperglobulinaemia and an increase in alkaline phosphatase concentrations. Perhaps contrary to popular belief, eosinophilia is an inconsistent finding[1] and serum protein electrophoresis is of little, if any, value in the diagnosis and monitoring of cyathostomin infection[13]-[15].

Cyathostominosis should be considered in any horse with a protein losing enteropathy – especially if it is young or the history of anthelmintic use is unknown or inappropriate. Establishing that hypoalbuminaemia is due to intestinal disease may not always be straightforward; however, marked protein losses as a consequence of hepatic or renal disease are rare in horses and the only other likely explanation for marked hypoalbuminaemia is an effusive process within the abdominal or thoracic cavities.

Ultrasonographic examination is helpful in ruling out the presence of an effusive process and in identifying whether there is thickening of the colon or caecum consistent with cyathostominosis.

Thickening of the small intestine would indicate another cause of intestinal disease, such as *Lawsonia intracellularis* infection or idiopathic inflammatory bowel disease, would be more likely.

An oral glucose absorption test may also be helpful in differentiating large and small intestinal disease. It should be remembered the intestine may appear thickened in the absence of primary intestinal disease if it becomes oedematous as a result of low colloidal oncotic pressure or in association with ascites.

Faecal analysis is often performed when cyathostominosis is suspected, but is of limited benefit. The presence of eggs confirms exposure to the parasite, but egg numbers do not correlate with

larval numbers.

Serological tests for the presence of cyathostomins are being investigated and may prove invaluable in confirming cyathostomin-associated disease; however, they are not yet commercially available.

Frequently, diagnosis is based on a compatible history and exclusion of other possibilities. In horses with a large cyathostomin burden, the administration of anthelmintics may result in large numbers of larvae being shed in faeces within a couple of days of treatment[16]; however, their absence does not eliminate the possibility of cyathostomin-associated disease.

Treatment

While luminal cyathostomins will be killed by ivermectin, moxidectin, pyrantel, fenbendazole and mebendazole, larval stages are more of a challenge to eliminate. Ivermectin has limited activity against late L3 and L4 larvae, while moxidectin will eliminate around 60 per cent to 90 per cent of these stages[17],[18].

Hypobiotic L3 larvae are more challenging to eliminate and reports of efficacy for both ivermectin and moxidectin are highly variable, ranging from 10 per cent to 90 per cent[17]-[21], with moxidectin generally considered to be more effective. Moxidectin is therefore preferred over ivermectin in the treatment of larval cyathostominosis.

The marked lipophilic nature of moxidectin has led to concern over its use in lean animals and hence a reluctance to use it in heavily parasitised animals that have lost bodyweight.

However, macrocyclic lactones are extremely safe in mammals and have a wide safety margin[22], so, provided they are not grossly overdosed, they should be safe to use in cases of acute or chronic cyathostominosis. Most of the reported adverse reactions have been associated with gross over-estimation of the horse's bodyweight by owners or from slippage of a faulty syringe locking mechanism[23].

Macrocyclic lactones potentiate the effects of the inhibitory neurotransmitter gamma-aminobutyric acid and where very marked overdoses have been administered, toxicity has resulted in neurological signs such as blindness, ataxia, reduced mentation and even death[24],[25].

Fenbendazole administered at the standard dose rate daily for five days is also licensed for the treatment of horses with larval cyathostominosis. Duncan (1998)[26] reported this regimen eliminated 91 per cent to 99 per cent of early L3 to late L4 larvae – figures that exceed those for moxidectin. However, in more recent studies this regimen has not been effective[27].

Benzimidazole resistance is now common, even ubiquitous, in the UK[2],[3] and it has been

established that where adult cyathostomins are resistant, larval stages will also be refractory to benzimidazoles[28-30].

It is a common misconception that fenbendazole is a “gentler” means of eliminating cyathostomin larvae and it is often used prior to moxidectin. As resistance to fenbendazole is so common in the UK it may be gentler in the majority of cases by virtue of having little or no effect; however, where it is effective its use is actually likely to result in a greater intestinal inflammatory response than moxidectin[31]. The use of fenbendazole in the treatment of cyathostominosis is therefore difficult to justify over moxidectin, even if faecal egg count reduction tests have demonstrated efficacy against the relevant population of cyathostomins.

In mild cases of larval disease, treatment with anthelmintics may be all that is required; however, repeated doses of anthelmintics may be necessary to bring about sufficient reduction in larval numbers.

In more severe cases where there is evidence of moderate to marked intestinal inflammation (hypoalbuminaemia, thickening of the caecum and ventral colons on ultrasonographic examination, increases in plasma acute phase proteins and so on) further adjunctive treatments may be required. Glucocorticoids are often used to reduce inflammation in cases of larval cyathostominosis[32] and may be administered to acute cases 24 hours before administration of an anthelmintic.

NSAIDs are probably of limited benefit in reducing intestinal inflammation, but can be useful for analgesia. The potentially deleterious effects of both glucocorticoids and NSAIDs on mucosal healing have to be considered. The author will use glucocorticoids for their apparent (all be it anecdotal) effects on intestinal inflammation and patient demeanour, but will avoid NSAIDs where possible and instead use opioids or other forms of analgesia. Opioids such as morphine, butorphanol and codeine may also help to reduce fluid losses by virtue of their inhibitory effects on intestinal motility.

Support of colloidal oncotic pressure is critical in cases with marked hypoalbuminaemia and colloids such as hetastarch, pentastarch or plasma are indicated when albumin levels drop much below 20g/L. In horses with marked protein-losing enteropathy, the use of large quantities of crystalloids without prior administration of colloids may worsen intestinal oedema and may be deleterious.

Other treatments that may be beneficial in the treatment of cyathostominosis include intestinal adsorbents and nutritional support. Recovery may take many months – presumably as a result of the amount of time it takes for intestinal inflammation to resolve and for the intestine to repair.

The author will typically taper treatment, but will continue it until albumin and other acute phase proteins return to within normal limits.

Where clinical cases of cyathostominosis are identified, investigation and treatment of cohorts should also be considered. A thorough review of anthelmintic use on the property should be performed, anthelmintic resistance should be investigated using faecal egg count reduction tests, and targeted or strategic deworming programmes should be implemented.

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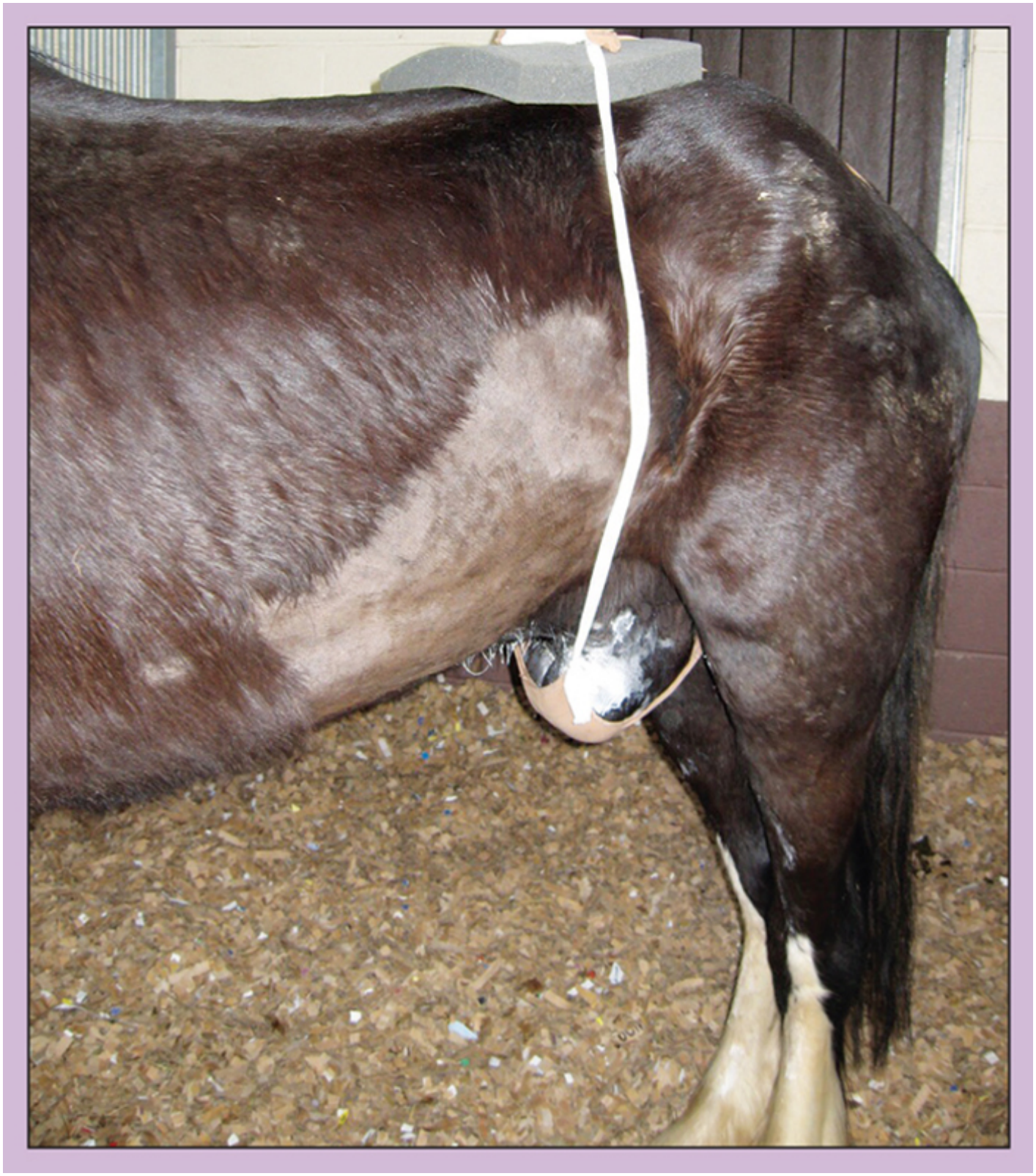
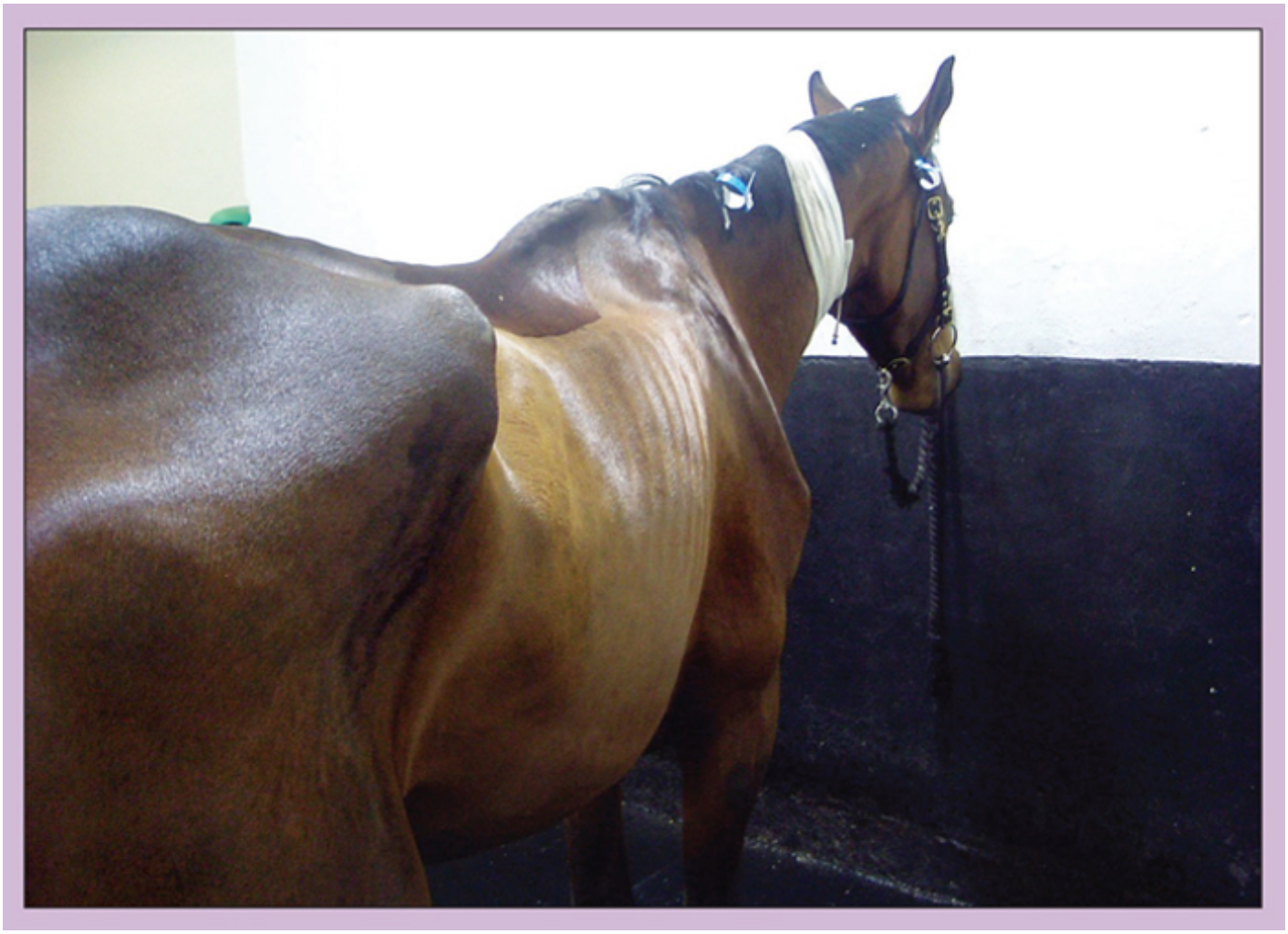
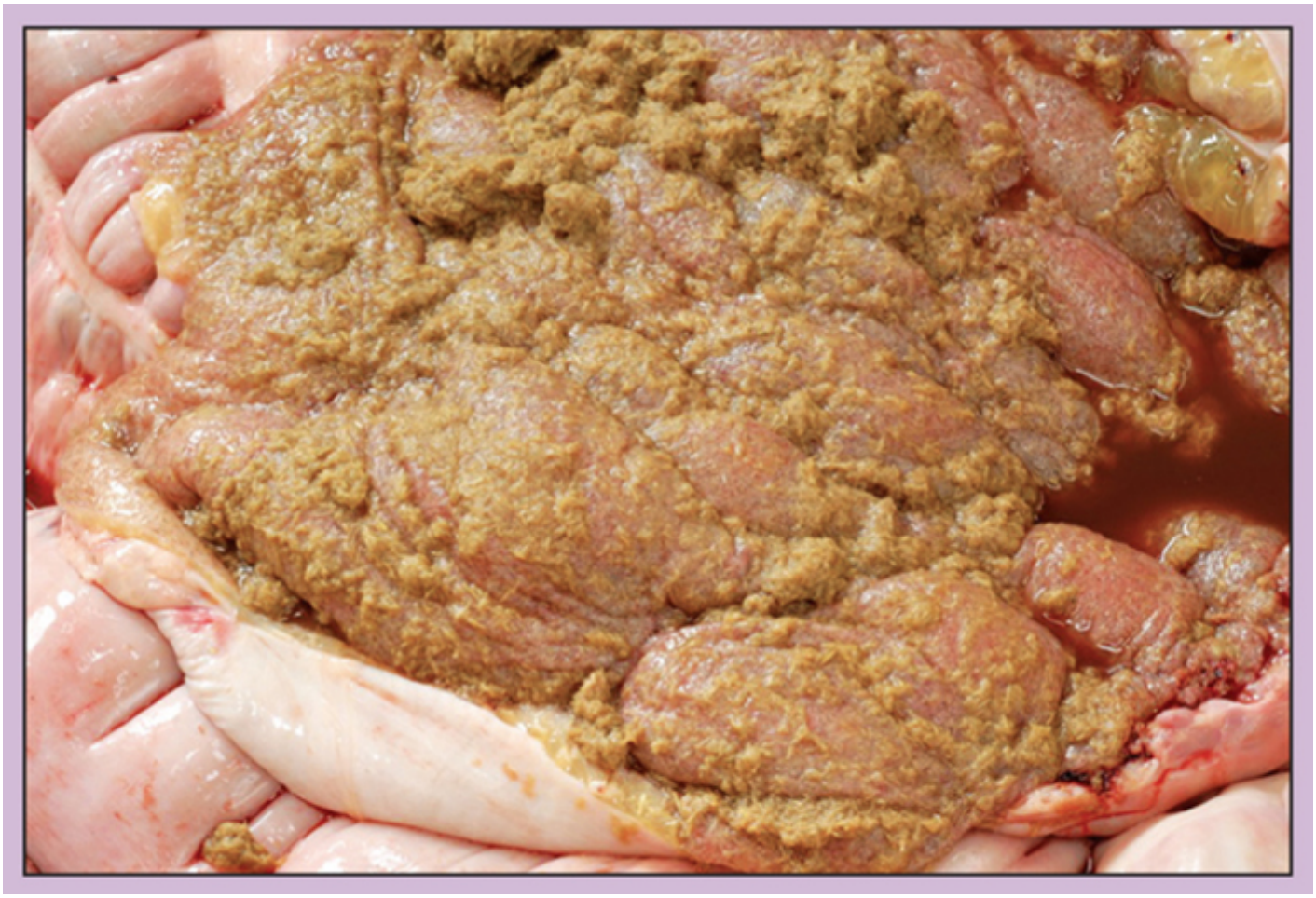


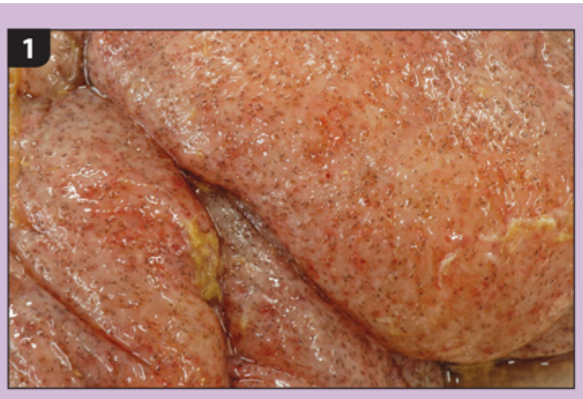
Preputial oedema as a result of low colloidal oncotic pressure due to protein losing enteropathy caused by the inflammatory response to cyathostomin larvae.



Acute weight loss as a result of larval cyathostominosis.



Marked intestinal oedema in a horse euthanised as a result of cyathostominosis.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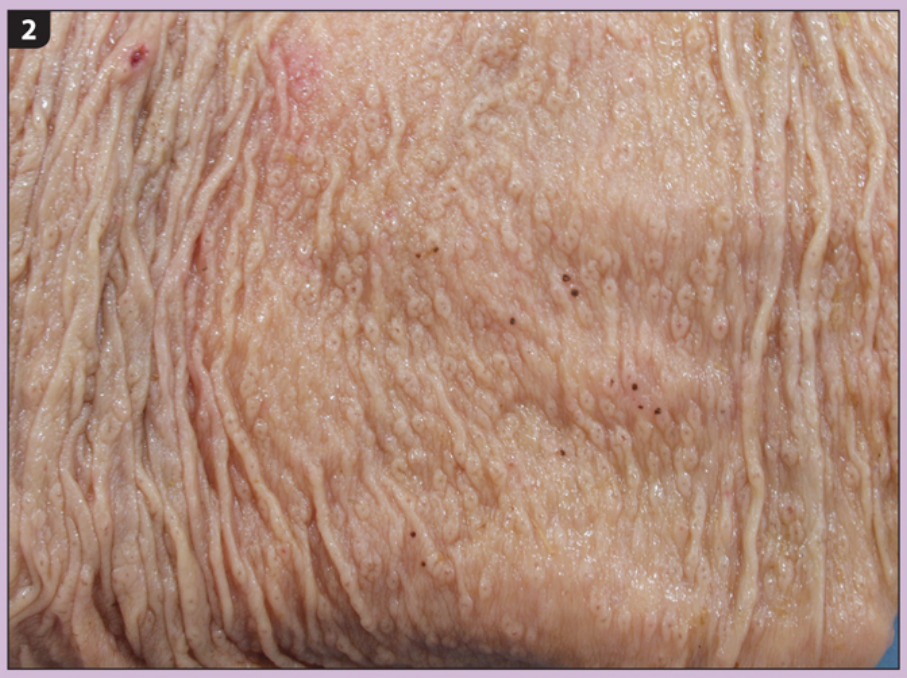
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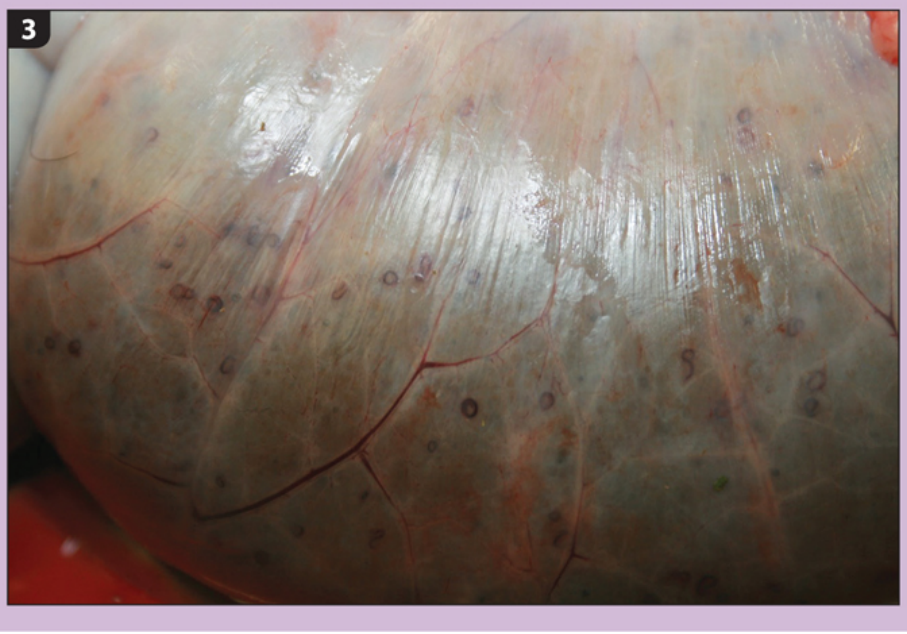
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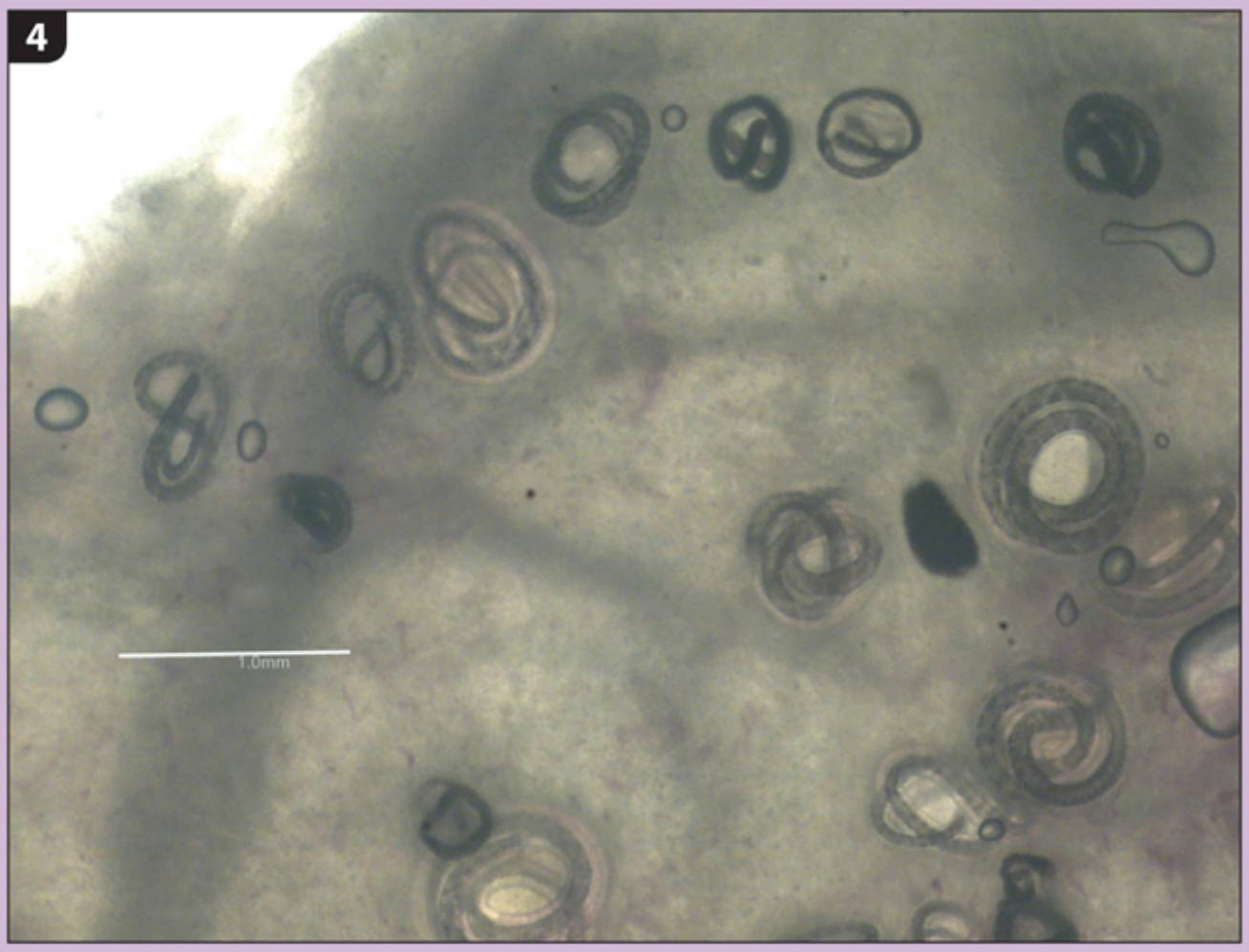
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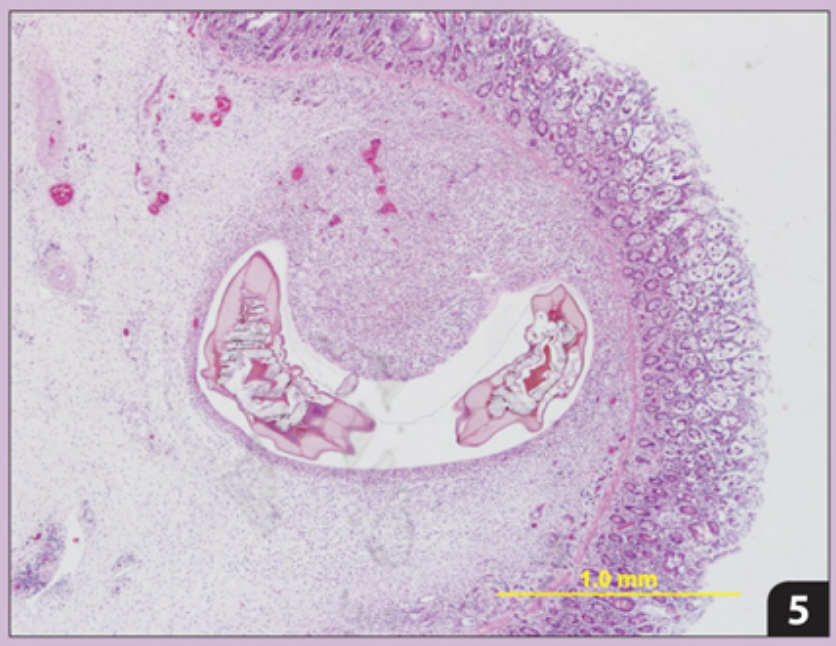
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Images 1 to 5. Cyathostomin larvae within the walls of the large intestine.

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