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REVIEW ARTICLE

Diagnostic approach to chronic diarrhoea in adult horses

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Summary

Chronic diarrhoea presents a diagnostic challenge for both human physicians and equine veterinarians. There is currently no consensus in the equine veterinary literature on the definition of chronic diarrhoea. The differential list is extensive and identifying diarrhoea by pathophysiologic mechanism can help remove less likely diagnoses. Achieving a definitive antemortem diagnosis is also challenging. Results from non-invasive diagnostics may only lead to the conclusion that inflammation is present. Cellular infiltrate, if present, may not be representative of the underlying disease. Invasive diagnostics resulting in acquisition of full-thickness biopsies may result in a diagnosis when other methods have failed. However, there is currently minimal data correlating these findings with those from full post-mortem examination. This article discusses the various diagnostic options and reviews the available literature on their value in evaluating currently available patients with chronic diarrhoea.

KEYWORDS

horse, absorption test, aetiology, chronic diarrhoea, diagnosis, inflammatory bowel disease

DEFINITION

Chronic diarrhoea in horses has been described as the continuous or intermittent passage of soft or watery faeces for a prolonged period of time (Weese & Munroe, 2011). However, there are inconsistencies with this description. Continuous passage of diarrhoea has never been reported and is unlikely to occur. In humans, chronic diarrhoea is defined as a decrease in stool consistency for more than 4 weeks, however, there is currently no consensus in the equine veterinary literature as to how long diarrhoea must be present to be categorised as chronic (Loscalzo et al., 2022). Chronic diarrhoea has been defined by some authors as diarrhoea present for at least 7–14 days (Emanuela et al., 2013; Oliver-Espinosa, 2018).

Most of the causes of chronic diarrhoea are non-infectious, which contrasts with acute diarrhoea where infectious aetiologies predominate (Loscalzo et al., 2022). Diarrhoea can also be stratified based on pathophysiologic mechanisms. In humans, the basic categories are watery, fatty, and inflammatory (Schiller et al., 2014). In some cases, these categories overlap. These three categories are then subdivided according to aetiopathogenesis. Watery diarrhoea is divided into secretory, osmotic, and functional. Fatty is divided into malabsorption and maldigestion function. Inflammatory is divided into inflammatory bowel disease, infectious diseases (bacterial, viral, and parasitic), neoplastic and radiation colitis (Juckett & Trivedi, 2011).

In horses, diarrhoea is categorised as either acute or chronic, however, there are currently no standard recommendations for further categorisation (Sanchex, 2010). Classification by pathophysiological mechanism and inciting cause have been used. However, classification by either method is inconsistent due to the lack of recognition and definitions for pathophysiologic mechanisms and how infrequently the inciting cause is unknown. For example, a group of horses diagnosed with inflammatory bowel disease were classified as either granulomatous enteritis (GE), multisystemic eosinophilic epitheliotropic disease (MEED), lymphocytic-plasmocytic enterocolitis (LPE), and idiopathic eosinophilic enterocolitis (EC). For each category, a history of chronic diarrhoea was recorded in 30% for GE, 65% for MEED, 35% for LPE, and 0% for EC (Schumacher et al., 2000; Villágran et al., 2021). Diagnosis and classification of chronic diarrhoea presents a significant challenge.

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DIFFERENTIAL DIAGNOSES

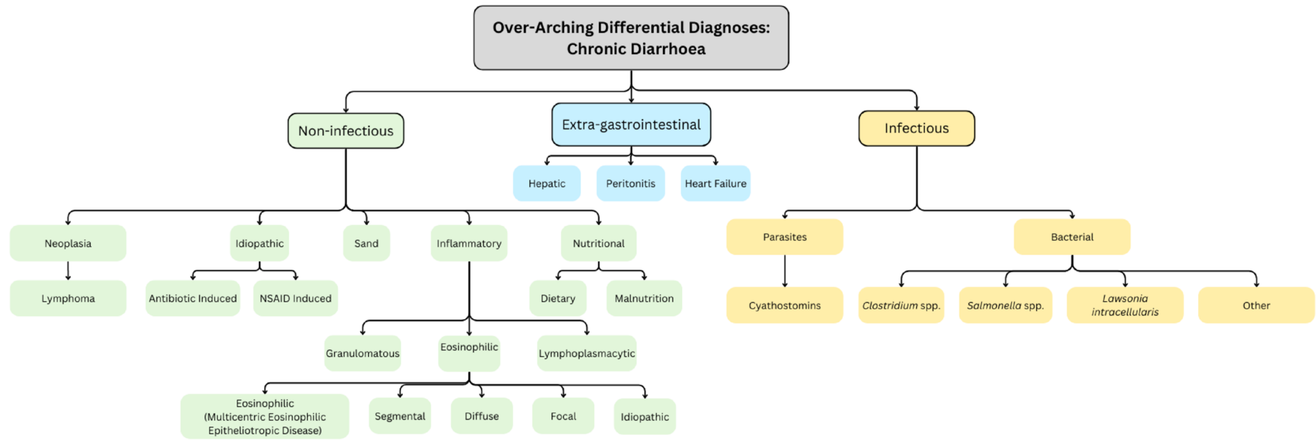

FIGURE 1 A flowchart describing the possible differential diagnoses for a horse with chronic diarrhoea.

CLINICAL HISTORY

A detailed, chronological history including onset, duration, consistency, seasonality, instigating factors, clinical progression, additional clinical signs, diet and dietary changes, supplements, environment, travel, previous medical history and attempted intervention is necessary. Sex and breed have not been identified as specific risk factors, although one study reported that Standardbred horses are more commonly affected (Merritt, 1975). Age is a risk factor for certain conditions that can cause diarrhoea, such as cyathostominosis, as identified in a paper by Lawson et al. (2023). They reported diarrhoea on presentation to the hospital in 33/36 (92%) of horses with larval cyathostominosis, and the median age was 2 years (Lawson et al., 2023).

The duration of diarrhoea can last weeks to months, and an episode of acute diarrhoea may become chronic. The faecal consistency can vary from soft to watery and there may be periods of normal faeces. In humans, the stool form and consistency are classified using the Bristol Stool Scale. In dogs, various scales have been proposed for faecal scoring, however, no scale or scoring system for equine faecal characteristics is currently validated in horses (Allenspach et al., 2007; Meyer et al., 1999; Rolfe et al., 2002; Schiller et al., 2014).

Clinical signs vary according to the inciting cause and involvement of other body systems. Weight loss is commonly reported along with inappetence and dullness (Oliver-Espinosa, 2018). Colic or recurrent colic is a less common clinical sign occurring in 19.6% of horses in a retrospective study by Schumacher et al. (2000). Other signs can include peripheral oedema and skin lesions.

PHYSICAL EXAMINATION

Vital parameters are frequently normal, even with longstanding disease. Fever may be transient or persistent and is more common in diseases of inflammatory aetiology; however, it may also occur as a paraneoplastic syndrome (Oliver-Espinosa, 2018). Low or decreased body condition and muscle mass are a frequent finding and subcutaneous oedema of the limbs, ventrum, mandible and throatlatch may be present. Increased gastrointestinal (GI) sounds may be auscultated. Performing an examination per rectum is recommended in all cases. Findings may include masses, enlarged lymph nodes, increased thickness of the intestinal wall, and adult or larval cyathostomins (Oliver-Espinosa, 2018).

The presence of dermatitis, ulcerative coronitis, and oral ulceration should increase the clinical suspicion for MEED, as approximately 77% of the cases documented in the literature have dermatitis at presentation (Bosseler et al., 2013). The dermatitis is typically located on the face, limbs, and ventrum, and is characterised by alopecia, exudate, hyperkeratosis and lichenification (Schumacher et al., 2000).

Ancillary testing

Clinical pathology

Complete blood count and serum biochemistry should be performed in all cases of chronic diarrhoea. Clinicopathological findings are likely affected by the cause of the chronic diarrhoea and the stage of the disease when the samples are collected. Anaemia may be present due to malabsorption of essential nutrients, iron sequestration, whole blood loss, or immune-mediated disease. Horses with GE have the highest incidence of anaemia at 87% (Schumacher et al., 2000). Abnormalities in the white blood cell count or differential may present. Neutropenia and neutrophilia have been reported with GE, and eosinophilia has been reported in approximately 14% of the documented cases of MEED (Villágran et al., 2021). Neutrophilia and basophilia, with no eosinophilia, have also been reported in some cases of MEED

(Bosseler et al., 2013; Villágran et al., 2021). Horses with other types of eosinophilic intestinal disease uncommonly have changes to the white blood cell count and distribution (Brosnahan, 2020).

A consistent clinicopathologic finding of horses with chronic diarrhoea is the presence of hypoproteinaemia, characterised by hypoalbuminaemia. The globulin concentrations are variable and may be reduced, normal or elevated.

Mair et al. (1993) examined the usefulness of serum protein electrophoresis as a diagnostic and prognostic aid for horses with chronic diarrhoea. Significantly lower albumin levels and significantly higher alpha-2-globulin levels were observed in non-survivors compared to survivors. The hypoalbuminaemia was suspected to occur due to leakage of albumin from the intestinal mucosa into the lumen, whereas the high alpha-2-globulin levels were most likely a reflection of the degree of inflammation. Although the study concluded that serum protein electrophoresis can be helpful in chronic diarrheic cases, the individual variations mean that these measurements cannot be used to predict accurately the diagnosis or outcome in individual horses and can only be used as a guide (Mair et al., 1993). Nevertheless, hypoalbuminaemia is a frequent finding in horses with chronic diarrhoea. Kemper et al. (2000) reported hypoproteinaemia in 6/13 (46%) and hypoalbuminaemia in 9/12 (75%) cases of lymphocytic plasmacytic enteritis. Similarly, Lawson et al. (2023), reported hypoalbuminaemia as a consistent finding in horses with cyathostominosis.

Acute phase proteins, including fibrinogen and serum amyloid A protein (SAA) concentrations, can be normal or elevated (Oliver-Espinosa, 2018). Serum electrolyte concentrations are usually within normal limits, however, hyponatraemia, hypokalaemia, hypochloraemia, and hypocalcaemia have been reported (Jones, 2020). Acid–base abnormalities are present in severe cases, secondary to electrolyte derangements and increased lactate concentration.

Elevations in hepatocellular and hepatobiliary enzymes may occur. Taylor and colleagues reported evidence of liver disease characterised by elevations in sorbitol dehydrogenase (SDH), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and γ-glutamyl transferase (GGT) in 41% of horses with intestinal neoplasia (Taylor et al., 2006). Increased ALP and GGT are often present in horses with MEED. Elevated GGT was present in 73% of MEED cases versus 0% of GE cases; therefore, increased GGT has been considered a potential way to differentiate between MEED and GE (Schumacher et al., 2000).

Although uncommon, prerenal azotaemia may occur in dehydrated horses.

Abdominocentesis

Abdominocentesis is another diagnostic tool that can be used for investigating cases of chronic diarrhoea. Peritoneal fluid analysis should include total protein concentration, total nucleated cell count, red blood cell count, and cytology. Additionally, lactate, fibrinogen, glucose, serum amyloid A, total bilirubin, amylase, and lipase may be measured (Radcliffe et al., 2022).

Horses with GE typically have normal peritoneal fluid (Schumacher et al., 2000). Eosinophilic gastrointestinal disease occasionally results in increased eosinophils in the abdominal fluid (Schumacher et al., 2000). In cases with abdominal neoplasia, the total nucleated cell count and protein may be elevated, and depending upon the underlying neoplasm, exfoliated neoplastic cells may be detected (Spanton et al., 2020; Taylor et al., 2006; Zicker et al., 1990). In a study conducted by Zicker et al. (1990), 44% of neoplasms (11/25) were definitively diagnosed by cytologic examination of peritoneal fluid; however, in two of the horses, multiple samples were required. However, in a second study by Taylor et al. (2006), only 21% of neoplasms were diagnosed with peritoneal fluid, all of them were diagnosed with lymphoma. In horses with lymphoma, neoplastic cells were detected on cytology in 38% of lymphoma cases; however, in horses with adenocarcinoma, neoplastic cells were never detected on cytology (Taylor et al., 2006; Zicker et al., 1990).

Faecal examination, microbiological, and molecular biological investigations

Visual inspection of the faeces may provide information regarding abnormalities in digestion or transit time of the gastrointestinal tract. Dental or masticatory disorders, colonic microbial dysbiosis, or abnormal colonic transit times may result in increased faecal water content or poorly digested feed particles.

Larval cyathostomiasis is among the most common causes of chronic diarrhoea (Love et al., 1992). Infective third-stage larvae are acquired while on pasture, then after ingestion, the larvae reach the large intestine and invade the mucosa and submucosa, forming a cyst. Arrested development may occur at this stage of development and can last for up to 2 years. As the 4th stage larvae grow in the intestinal wall, the cyst eventually ruptures, and the larvae enter the intestinal lumen. Larval excystment is the main pathologic event and incites significant inflammation. This can result in protein-losing enteropathy, alterations in intestinal motility, and diarrhoea (Peregrine et al., 2006).

Adult cyathostomins and/or 4th-stage larvae may be observed in the faeces, but microscopic examination of wet faecal smears may be more helpful in identifying the larvae. The absence of larvae does not rule out cyathostomins as a cause of clinical disease, but antemortem identification of cyathostomin larvae in the faeces supports the diagnosis of these cases. Faecal flotation for parasites should be performed in any horse with hypoalbuminaemia, weight loss, and/or chronic diarrhoea. Nevertheless, faecal egg counts (FEC) tests do not correlate with the intra-host burden of cyathostomins, and there are currently no specific diagnostic tests that provide information on cyathostomin burden. A commercial serological test based on specific antibody level measured, which also considers the grazing management and historic parasitological (FEC) parameters of the individual or group being tested, has been available in the United Kingdom since 2019 (Lightbody et al., 2024; Tzelos et al., 2020). The "serum score" given to a particular sample, when interpreted along with the grazing management and historic parasitological (FEC) parameters of the individual or group being tested, can aid in selecting thresholds for anthelmintic treatment.

The detection of sand or gravel in the faeces can be easily performed with a simple sedimentation test and is highly suggestive if significant quantities are present in the manure. Geographic variation has been reported with sand enteropathy and is more common in geographic areas with loose sandy soil, or in horses grazing on sand or gravel lots (Ragle et al., 1989). Hart et al. (2013) reported the presence of sand or gravel in the faeces during transrectal examination in 10/27 (24%) horses, and faecal sedimentation for sand was positive in 12/25 (48%) horses. Another study in Finland reported a sensitivity, specificity, positive predictive value, and negative predictive value of 83%, 71%, 90% and 56%, respectively for the faecal glove sedimentation test when it was compared with radiography (Hukkinen, 2015). Of note, 29% of horses in the study had received treatment prior to the faecal sample collection which may have affected the sensitivity of the test.

In horses, the detection of a single causative agent in each case is often negative, however, the submission of faecal samples for microbiological testing of common enteropathogens is still recommended. Faecal culture and, more recently, molecular test panels are used to screen for multiple enteropathogens associated with horse diarrhoea. Positive results should be carefully interpreted and used to build large databases for further analyses. For example, *Salmonella* spp. infection is commonly associated with chronic diarrhoea in horses; however, evidence of causation remains to be proven.

There are reports of intestinal trichomoniasis and equine protozoal diarrhoea as aetiological agents for chronic diarrhoea. *Trichomonas faecalis* has been observed in large numbers in the faeces of horses with chronic diarrhoea, but causality has not been established (Manahan, 1970; Tzelos et al., 2020). *Campylobacter fetus* subsp. *fetus* was also isolated from a two-year-old Quarter Horse with chronic diarrhoea (Hart et al., 2013; Hurcombe et al., 2009).

Mycobacterium branderi was isolated from a horse with granulomatous enteritis and lymphadenitis (Silva et al., 2019). The horse had a 3-month history of chronic diarrhoea, cachexia, and ventral and cervical oedema. Some non-tuberculous mycobacteria are known to affect horses and should be considered in horses with chronic diarrhoea (Silva et al., 2019).

Lawsonia intracellularis is a well-characterised cause of chronic diarrhoea in young horses, and faecal PCR is the current method of choice for a confirmatory diagnosis. Serological testing is also commercially available. Immunoperoxidase monolayer assay (IPMA) confirms the presence of circulating antibodies to *L. intracellularis* and is indicative of active or recent infection. The sensitivity of serology and PCR are 90–91% and 39–67%, respectively, with a specificity of 100% for both techniques, which was reported in pigs experimentally challenged with *L. intracellularis* (Guedes et al., 2002).

Faecal water syndrome has been reported in several European countries and North America (Ertelt & Gehlen, 2015; Kienzle et al., 2016; Laustsen et al., 2021; Schoster et al., 2020). Although faecal water syndrome is likely a multifactorial disease in origin, dysbiosis has been suggested to play a role in the development of this condition. A faecal microbiome study found only minor differences in the microbiota composition between horses with free water syndrome and healthy controls (Schoster et al., 2020). Nevertheless, the authors suggested that these changes may be an indication that the microbiota is a potential factor in the development of clinical signs. A similar study investigated differences in faecal microbial composition between horses with and without free faecal liquid and no general differences in the faecal bacterial composition between groups were found (Lindroth et al., 2021). Similarly, Laustsen et al. (2021), also reported that the hindgut microbiota of horses suffering from free faecal water was no different than that of healthy horses. Nevertheless, faecal microbiota transplantation treatment of horses with free faecal water from a healthy donor animal resulted in a decrease in the severity of clinical signs attributed to this syndrome (Laustsen et al., 2021). Despite that research has shown no significant differences in hindgut microbiota of horses with faecal water syndrome and healthy horses, it is still considered a form of chronic diarrhoea.

Assessment of the equine faecal microbiome is predominantly used in a research setting. Given the diversity of the microbiota and range of factors that affect the intestinal bacterial population, developing a standard method that can be used to assess the faecal microbiome is difficult. 16S gene sequencing is currently the most widely used method to investigate the faecal microbiome in horses (Costa et al., 2012; Long et al., 2024; Stewart et al., 2017). A study by Costa et al. (2012) found significant differences in the microbiome between healthy horses and horses with colitis. Clinical interpretation of these differences is difficult as there are differences in the normal equine microbiome depending on geographic location, housing, and diet (Stewart et al., 2017). In the future, assessment of the faecal microbiome is likely to be of use in diagnosis and treatment of chronic colitis, however, the clinical application is currently limited.

Biomarkers

In human medicine, numerous biomarkers have been developed for use in research and clinical cases. In equine medicine, only a limited number of biomarkers have been investigated and not all of these have sufficient data to support their utility or are commercially available.

The clinical utility of thymidine kinase (TK1) activity, a tumour marker used as a prognostic indicator for lymphoma (i.e. humans, dogs and cats), was investigated by Larsdotter et al. (2015) in horses. A significantly higher TK1 activity was observed in horses with lymphoma, therefore, the measurement of TK1 activity was considered a potentially useful biomarker for equine lymphoma. There is currently no data on the potential usefulness of this marker for the investigation of intestinal lymphoma in horses with chronic diarrhoea. Furthermore, a recent study found that serum TK1 values were not predictive of antemortem definitive diagnosis of lymphoma in horses (Moore et al., 2021).

As mentioned above, serum IgG(T)-based ELISA (CT3) that exhibits utility for the detection of mucosal/luminal cyathostomins has been optimised/validated for commercial use horses. The test claims to provide evidence of low cyathostomin burdens that do not require anthelmintic treatment and to support diagnosis of infection in clinical practice (Lightbody et al., 2024).

Diagnostic imaging

Ultrasonography

Transcutaneous ultrasound is one of the most widely used imaging modalities both in the field and at referral centres to assess internal organs. Ultrasound evaluation can be very useful for choosing a site for peritoneal fluid sampling, assessing parenchymal organ appearance, detecting abnormal structures (masses and abscesses), and measuring intestinal lumen distension, motility, and thickness.

Horses with infiltrative bowel disorders, including lymphoma and various forms of inflammatory or infiltrative bowel disease (IBD), can present with increased small or large intestinal wall thickness. For example, Kemper et al. (2000) reported diffuse thickening of the small intestine was apparent grossly in 10/13 (77%) horses examined.

Equine proliferative enteropathy caused by *Lawsonia intracellularis* in young horses causes enterocyte proliferation resulting in markedly thickened small intestinal mucosa and occasionally large intestinal mucosa. Increased small intestinal wall thickness is a common finding on abdominal ultrasound examinations of affected foals, but the frequency of abnormal intestinal wall thickness has not been investigated.

Ultrasonographic measurement of mural thickness and the appearance of the right dorsal colon can be supportive of the diagnosis of right dorsal colitis. The right dorsal colon can be imaged at the right 11th, 12th, and 13th intercostal spaces, below the margin of the lung and axial to the liver. Mural colonic thickness and a prominent hypoechoic layer has been described as a result of the submucosal oedema and inflammatory infiltrate (Jones et al., 2003). A recent retrospective multicentre study reported right dorsal colon wall thickening in 77% (24/31) of cases using ultrasonography (Flood et al., 2023).

Horses with encysted cyathostomins can develop marked caecal and colonic oedema, and therefore marked intestinal wall thickness, which can be seen with transabdominal ultrasonography. Since there is currently no confirmatory antemortem diagnosis of larval cyathostomins, ultrasonography can be used in combination with the signalment, and deworming history to aid in the diagnosis.

Ultrasound can be useful in diagnosing sand impactions, with a reported sensitivity and specificity of 87.5% when compared with radiography (Korolainen & Ruohoniemi, 2002; Manahan, 1970). Korolainen and Ruohoniemi (2002) reported that findings including slow or absent movement of the intestine, location of the intestine lying against the abdominal wall, and hyperechoic material within the intestine were considered to be suggestive of sand accumulation.

Abdominal radiology

Abdominal radiographs have limited diagnostic value due to the size and mass of the average adult horse's abdomen. Chronic diarrhoea is commonly reported in horses diagnosed with sand enteropathy, and radiography is considered the reference standard for diagnosis of sand accumulation (Niinistö & Sykes, 2022). An owners-reported survey in Finland described diarrhoea and “faeces with water” in 53% of horses confirmed with sand impaction (Niinisto et al., 2019). A grading system has been used to categorise sand accumulations based on height and length of the accumulation visible in the radiographs. However, sand accumulation in the intestine can be found in horses with no apparent clinical significance, and therefore, the clinical applicability of the grading system is questionable (Kendall et al., 2008).

Endoscopic examination and biopsy

With the advent of endoscopic equipment designed for horses, adequate assessment of the pylorus and proximal segment of the duodenum can be performed. In suspected IBD cases, duodenal and/or rectal biopsies should be taken to assess for infiltration of the intestinal mucosa by different cell types. Gastric ulcers have been observed in horses with chronic diarrhoea, however, it is unknown if these lesions are associated with the underlying cause of the diarrhoea or due to the inappetence that is commonly reported with it (Sykes et al., 2015).

Pinch biopsies can be obtained from the stomach and duodenum. These may be obtained in cases where there are macroscopic mucosal abnormalities, ultrasonographic abnormalities, or when infiltrative disease is suspected based on other diagnostics (Boshuizen et al., 2018; Divers et al., 2006). This procedure is performed via endoscopy and is non-invasive, however, biopsy samples obtained by this method contain the mucosa and occasionally the superficial submucosa. This method does not allow for the acquisition of samples containing the deep submucosa or muscularis layers. Superficial biopsy segments may only consist of villi or small segments of crypts which limits the ability to interpret the sample (Boshuizen et al., 2018; Hostetter & Uzal, 2022). Detection of one or more infiltrating cell types provides may provide supportive evidence for the diagnosis of IBD, however, there are resident mucosal cells including lymphocytes, plasma cells, eosinophils, and macrophages that reside in the GI tract of normal horses (Rocchigiani et al., 2022). Differentiating resident mucosal cells from pathologic infiltration is difficult and can result in unreliable interpretations. Diseases that do not impact the mucosa or are sporadic in their distribution are unlikely to be detected by these biopsies (Evans et al., 2006). Boshuizen et al. (2018) compared rectal and duodenal biopsies and found that 56.8% of the duodenal biopsies were of moderate quality and the other 43.2% were of poor quality or were of insufficient quality to be assessed.

Rectal mucosal biopsies are commonly recommended for investigating cases of chronic diarrhoea, with reported accuracy ranging from 50 to 82% (Boshuizen et al., 2018; Lindberg et al., 1996). They can be performed using the same endoscopic guided pinch biopsy technique or without direct visualisation with the use of a uterine biopsy instrument (Lindberg et al., 1996; Mair et al., 2011). The same study by Boshuizen et al. (2018) that compared the pinch biopsy technique for duodenal and rectal biopsies found that 93.3% of the rectal biopsies were of moderate quality and only 6.7% were of insufficient quality to be assessed. Nevertheless, Kemper et al. (2000) reported that rectal mucosal biopsies showed abnormal histopathological findings in 3/7 (43%) horses with lymphocytic-plasmacytic enteritis.

Evaluation of cytokine gene expression and number of T regulatory cells in rectal biopsies from horses affected with inflammatory bowel disease were compared to healthy controls in a prospective study by Olofsson et al. (2015). In this study, horses with IBD had increased expression of IL-17A, IL-12p40, and TLR4. T regulatory cells were increased in horses classified as having chronic active simple proctitis; however, this was not statistically significant. In human medicine, increased IL-17A expression and increased number of mucosal T regulatory cells are associated with the pathogenesis of IBD (Olofsson et al., 2015). Increased TLR4 and TLR3 expression is thought to play a role in gastrointestinal immune hyperresponsiveness (Olofsson et al., 2015). Specific TLR4 polymorphisms are associated with an increased risk of IBD, giving some support for a genetic predisposition (Olofsson et al., 2015).

In both duodenal and rectal mucosal biopsies, the findings may not represent the entire GI tract since only a small section of the mucosa is examined, and this section may be remote from the site of pathology. Pathological findings in such samples are likely clinically relevant, and a diagnosis is reached. For example, the presence of neoplastic cells and neutrophils within the surface epithelium or crypts on biopsy histopathology is always considered abnormal (Lindberg et al., 1996).

Intestinal absorption tests

Absorption tests are used to assess the absorptive capacity of the small intestine specifically the efficiency of sugar absorption from the intestinal lumen. Oral D-xylose or glucose absorption (OGAT) tests are indicated in chronic diarrhoea and/or weight loss with hypoproteinaemia.

The OGAT can be performed stall side with minimal equipment. The results are immediate, and it is inexpensive. Factors such as dietary history, gastric emptying rate, intestinal transit, age, and hormonal effects can influence the glucose peak and curve shape (Jacobs & Bolton, 1982).

The OGAT is arbitrarily divided into 3 categories according to the results obtained (Mair et al., 1991). A blood glucose curve is considered normal when the peak glucose value is greater than an 85% increase over the resting values within 90–120 min of glucose administration, and a return to baseline within 6 h. If the peak glucose levels reach between a 15–85% increase over baseline it is classified as partial malabsorption and total malabsorption if glucose levels only reach a ≤15% increase over baseline (Mair et al., 1991).

The D-xylose absorption is not affected by hormonal or metabolic factors and, therefore, may be a better test option. Other factors like gastric emptying, intestinal motility, intraluminal bacterial overgrowth, and renal clearance can affect the curve shape (Guedes et al., 2002; Mair et al., 2006). The length of fasting was shown to markedly affect the D-xylose absorption and abnormal xylose absorption curves had been detected even in horses with no small intestinal histopathological abnormalities (Freeman et al., 1989; Roberts, 1985). In addition, one of the major drawbacks of D-xylose testing includes the biochemical analysis and turnaround time (Bolton et al., 1976).

Kemper et al. (2000) reported that the OGAT or D-xylose absorption test was abnormal in 9/12 (75%) horses with lymphocytic-plasmacytic enteritis.

Bracher et al. (1995) used the breath hydrogen (H_2) excretion test combined with the xylose absorption test in horses with chronic diarrhoea ($n=3$) or chronic weight loss without diarrhoea ($n=6$) and healthy controls ($n=4$). Only slight alterations in either peak concentrations or times to reach peak levels of plasma xylose occurred in diseased horses, except for horses with granulomatous enteritis. Some diseased animals ($n=5$) showed increased breath hydrogen (H_2) of variable heights and higher fasting levels than normal horses.

Abdominal exploratory laparotomy/laparoscopy

These diagnostic evaluations are usually recommended as a last resort due to the expense and invasive nature of the procedures. The most common reason for exploratory surgery is to collect full-thickness intestinal biopsies in cases of suspected infiltrative bowel disease. Other reasons include further investigation of suspected or confirmed intra-abdominal masses, abscesses, and neoplasia for diagnostic and/or treatment purposes. The advantages of surgical biopsies are that the sample obtained is full thickness and often includes multiple crypts and villi, and the tissue architecture and orientation are better preserved and often easier to interpret (Hostetter & Uzal, 2022).

Exploratory laparoscopy is a minimally invasive technique that may be considered as an alternative to midline celiotomy. However, there are several limitations when laparoscopically exploring the abdomen, including potentially poor visualisation of targeted organs/structures, limited access, and inability to collect adequate samples. Both left and right flank laparotomies have been reported as a method for full thickness intestinal biopsies (Coomer et al., 2016; Schambourg & Marcoux, 2006). Additional limitations include access to laparotomy equipment and comfort with the laparoscopic equipment and suturing (Schambourg & Marcoux, 2006).

Incisional healing has been a concern in horses that are systemically compromised (hypoproteinaemia), but no definitive information supports this concern.

CONCLUSION

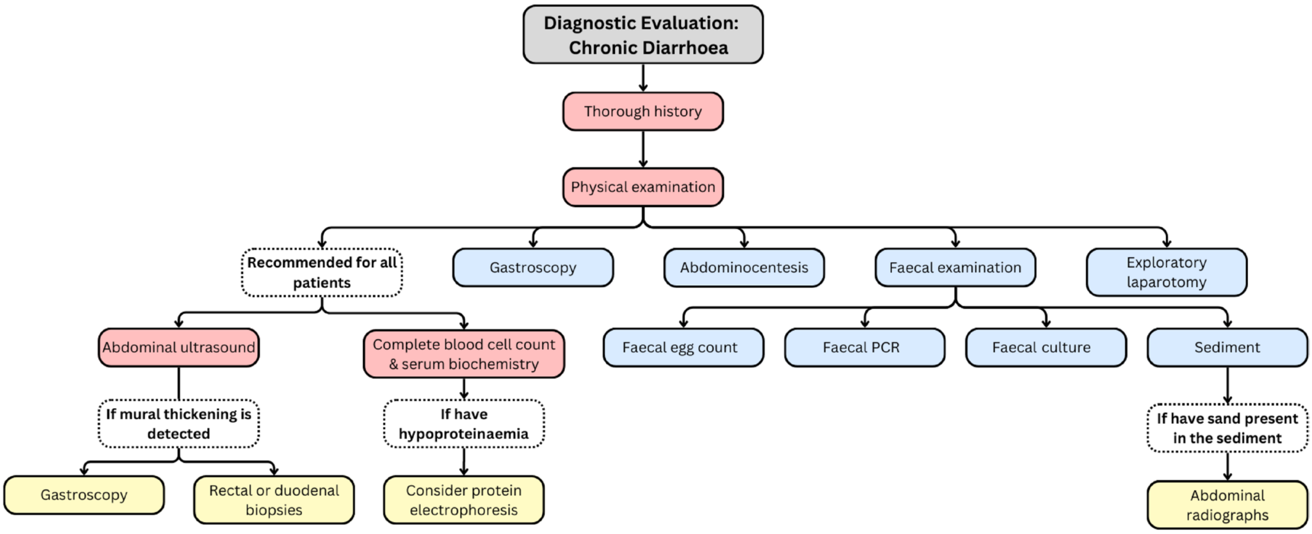

FIGURE 2 A flowchart for diagnostic decision-making.

In summary, a diagnostic investigation of chronic diarrhoea may require a great deal of economical and time investment and commitment by the owner and veterinary clinician. There are many different diagnostic approaches, and the selection of diagnostic tests can be difficult. It is recommended to begin the investigation with a thorough history, physical examination, abdominal ultrasound, complete blood cell count, and serum biochemistry profile; and the selection of additional diagnostic tests depends on the initial results, and owner commitment and finances. The inciting cause is commonly non-infectious, and an aetiological diagnosis is often not determined. Establishing a diagnosis is imperative to directing treatment and providing information on prognosis.

AUTHOR CONTRIBUTIONS

E. Sjolin: Writing – review and editing; conceptualization; writing – original draft. **A. Lack:** Conceptualization; writing – review and editing; writing – original draft. **L. G. Arroyo:** Conceptualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest have been declared.

ETHICS STATEMENT

The authors have adhered to the Principles of Veterinary Medical Ethics of the AVMA.

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