Daniels, S. P. (2018). Friend or foe? Intestinal parasites of horses and sustainable worm control mechanisms. *Veterinary Nursing Journal*. *In*

Abstract

Intestinal parasites of horses were historically managed solely by anthelmintics. Horse managers have developed a fear of intestinal worms associated with the risk of colic onset. This has driven horse managers to control parasites solely using anthelmintics rather than focussing on diagnostic techniques and pasture management. However anthelmintic resistance is a growing concern and prophylactic anthelmintic use is no longer acceptable. There are four primary intestinal parasites of veterinary importance that should be the focus of parasite management. Practitioners need to encourage horse owners to engage in a holistic and sustainable approach to parasite control to reduce the risk of intestinal disease.

Introduction

Traditional approaches to parasite control in horses were focussed on anthelmintic treatment. Multiple treatments were given throughout the year to target each intestinal parasite. This approach stems from an era when owners would ask veterinary practitioners about worm control and the response would be '*there is a drug for that*' (Sangster, 2003). Fifty years on the approach to parasite control has changed. No longer is a one size fits all approach acceptable, parasite control now needs to be targeted to parasites of veterinary importance (Kaplan and Nielsen, 2010). However horse managers are often still following worm control programmes that are 50 years out of date. There are four key parasites of veterinary importance, large and small strongyles, tapeworms and ascarids, figure 1 (Kaplan and Nielsen, 2010).

The lifecycle of the large strongyles entails ingested larvae migrating from the large intestine through the mesenteric arteries to continue their larval development, before migrating back to the large intestine to reproduce (Proudman and Matthews, 2000). Cyathostomins differ from large strongyles, there are 50 different species and they have an encysted stage in their lifecycle rather than migration. To date we only understand the basic biology of cyathostomins (Matthews, 2011). Once ingested L3 larvae (nematode larvae that have undertaken their third developmental moult in the life cycle and become infective) reside to the caecum and large colon. Here they penetrate the mucosa to complete their encysted stages of development within the gut wall (Matthews, 2011). Under certain conditions, which are not well understood, larvae go into hypobiosis which can last up to three years. During hypobiosis larvae lay dormant within the intestinal mucosa. Once the encysted stages of development are complete cyathostomins re-emerge into the gut lumen to complete their final moult before becoming sexually mature adults. For both large and small strongyles, eggs are excreted in faeces which hatch and mature to the L3 stage on pasture.

Tapeworms, specifically *Anoplocephala perfoilata*, reside around the ileocecal junction (Proudman and Matthews, 2000). Tapeworms require an intermediate host, an oribatid mite, to complete their lifecycle. Sections (proglottids) of the worm break off the end of the tapeworm as they mature. Fertilized eggs inside the proglottid are excreted in the faeces and ingested by the oribatid mite, the horse then ingests the oribatid mite in forage to become re-infected.

Parascaris equorum is of greatest concern in immature animals (Kaplan and Nielsen, 2010). *P. equorum* are ingested from pasture still in the egg. Once ingested the egg hatches and the larvae are already at L3 stage. Larvae reside in the small intestine and then migrate to the liver and then to the lungs before being swallowed and returning back to the small intestine. Most animals, once mature, develop immunity to *P. equorum.* Infection is past between young animals and the eggs of *P. equorum* are particularly hardy and can survive on pasture from year to year (Proudman and Matthews, 2000).

During the 1960's the large strongyles were the most prevalent and most pathogenic parasites of horses. However previous anthelmintic strategies, e.g. interval dosing on a 6-8 week rotation (Drudge and Lyons, 1966), led to a huge reduction of *S. vulgaris* in the horse population. By the 1980s cyathostomins made up to 100% of a horses strongyle egg output (Nielsen *et al*., 2008). Cyathostomins are ubiquitous in grazing horses and are now viewed as the most pathogenic parasite of the horse (Matthews, 2011).

Parasitism and intestinal disease

There is a clear link between parasitism and colic (Proudman, 1999). Colic has been associated with large and small strongyles, *Anoplocephala perfoilata* and *Parascaris equorum* (Uhlinger, 1990; Archer and Proudman, 2006; Reinemeyer and Nielsen, 2009). The relationship between parasites and colic links to both infection intensity and the parasites lifecycle. Large strongyles when migrating through the mesenteric arteries cause thrombosis and arteritis which can lead to thromboembolism. The resulting colic, caused by the clot, leads to necrosis and infarction of the intestinal wall. It was once proposed that 90% of colic cases in domesticated horses were due to *Stongylus vulgaris* (White, 1997). However this figure has never been scientifically validated, nor has there been a notable reduction in colic since *S. vulgaris* has been in low prevalence.

Cyathostomins pose greatest threat of colic to young horses. This is most common in the early spring if there is a large larval emergence of dormant encysted larvae back into the intestinal lumen (Murphy *et al*., 1997; Matthews, 2011). Larval cyathostominosis has a 50% mortality rate, however its occurrence is rare. It is associated with reactivation of dormant larvae which can be brought on by the use of adulticidal anthelmintics in early spring (Proudman and Matthews, 2000).

Tapeworm associated colic is linked to infection intensity, leading to ileal impaction and/or spasmodic colic (Proudman and Matthews, 2000). *P. equorum* associated colic occurs due to the size of the worms within the small intestine leading to an impaction, however this is not common in managed animals.

Large strongyles pose the greatest threat of colic and this parasite is now in low prevalence in the horse population. Effective parasite management has been linked to a reduction in parasite associated colic (Uhlinger, 1990; Proudman, 1999). However it is important to remember that managing parasites does not need to be solely chemically. The use of anthelmintics should be evidenced by diagnostic tools.

One of the most effective forms of parasite control is faeces removal from pasture (Herd, 1986; Coles, 2002; Lloyd *et al*., 2000; Nielsen *et al.,* 2010). Removal at least once per week, preferably twice, ensures nematode larvae and eggs are removed from the pasture. Cross grazing with ruminants is also an effective form of nematode control (Coles, 2002). The practice of chain harrowing pastures to break up dung should be avoided as this spreads parasite larvae and leads to pasture fouling (Herd, 1990). Ideally pastures should not be over stocked with animals as this encourages horses to graze close to dung piles which increases the risk of infection. Effective pasture management breaks the parasite lifecycle, thus animals exposure to re-infection is reduced.

Why is the reliance on anthelmintics such a problem?

Unfortunately the worms have out smarted us, through overuse of anthelmintics, nematodes have developed resistance to the anthelmintics. The concept of anthelmintic resistance is not new, the first report of benzimidazole (BZ) resistance in the UK was in 1965 (Herd, 1990). This was only five years after benzimidazole anthelmintics were introduced for equine nematode treatment. Resistance to benzimidazoles in cyathostomins is now widespread worldwide (Matthews, 2008). Once resistance occurs there appears to be no reversion to susceptibility. Even when premises had not used benzimidazole anthelmintics for 10+ years cyathostomins harboured by horses on those premises still demonstrated BZ resistance (Daniels and Proudman, 2016a). More concerning is the development of resistance within the macrocyclic lactone group of anthelmintics. To date in the UK there are no confirmed reports of resistance to ivermectin or moxidectin within cyathostomins. However there have been several reports of early egg reappearance following treatment. The first step towards resistance is a reduction in the egg reappearance period (ERP) after treatment (Sangster, 1999), which should be 8-10 weeks for ivermectin (Borgsteede *et al.,* 1993) and 13 weeks or greater for moxidectin (Jacobs *et al.,* 1995; DiPetro *et al.,* 1997). Over the past 10 years in the UK there has been a reduction in the ERP of both ivermectin and moxidectin in both leisure horses and performance animals. It is now not uncommon for strongyle eggs to reappear in faecal samples from five weeks after treatment for both macrocyclic lactones (Dudney *et al*., 2008; Lester *et al*., 2013; Relf *et al*., 2014; Daniels and Proudman, 2016b; Tzelos *et al*., 2017). Recently the data sheets for ivermectin products have stopped stating an expected ERP. As of October 2018 praziquantel (Equitape, Zoetis), a tapeworm specific anthelmintic for horses, is being withdrawn from the market (BEVA, 2018). This limits the treatment options for tapeworm to a broad spectrum only approach, praziquantel will still be available combined with ivermectin and moxidectin. Alternatively a double dose of a pyrantel can be used if tapeworm treatment is necessary. However these broad spectrum approaches mean when treating tapeworm cyathostomins will also be exposed to that anthelmintic at the same time. This poses further threats to the development of anthelmintic resistance.

Encouraging clients to engage with sustainable parasite control

Sustainable parasite control has been in the public eye for the last 10 years, yet there still appear to be barriers to uptake. Duncan and Love (1991) identified that the use of faecal egg counting was more economically viable than interval dosing. Yet even today some horse managers would still prefer to buy anthelmintics rather than use a diagnostic tool to see if anthelmintic treatment is necessary. It appears that over time horse owners have developed an irrational fear of parasites (Kaplan and Nielsen, 2010). This fear appears to stem from the association between parasitism and colic. However with good parasite management, built around pasture management and diagnostics the risk of colic is greatly reduced in the same way that it would have been historically through prophylactic anthelmintic use.

There may be other barriers to horse managers moving to diagnostic monitoring techniques for worm control. Previous findings of owner attitudes towards parasite control identified that many horse owners were unhappy with using anthelmintics routinely but were bound by livery yard rules on worm control, meaning they could not employ monitoring led worm control practices (Allison *et al*., 2010).

It is apparent that a focus on emphasising anthelmintic resistance alone is not enough to change horse owner behaviour (Viner *et al*., 2017). However owners who seek worm control advice from veterinary practices are also more likely to employ both routine faecal egg counts and drug efficacy testing (Easton *et al*., 2016). It is therefore essential that owners are engaged in effective knowledge transfer and training through veterinary practitioners to support behavioural change.

Diagnostic testing

Faecal egg counts (FEC) are seen currently as the cornerstone of equine parasite control diagnostics. There are many techniques but fundamentally they all do the same thing, float eggs within a grid that allows quantification (Nielsen *et al.,* 2010). The McMaster method and modifications of this is employed by most commercial laboratories. Attempts have been made to create farm side diagnostic tools. Most recently in the USA a mechanised FEC system that connects to a smart phone has been developed (Scare *et al*., 2017) and marketed as Poop2Proof. If commercialised this technique could be employed in practices to standardize and speed up the process of FECs while providing photographic evidence of nematode eggs to show clients.

Coprological measures are not a reliable identifier of tapeworm in horses, however it is possible to identify infection using an ELISA assay (Proudman and Trees, 1996). The original method developed by Proudman and Trees (1996) required clinicians to submit serum samples to the University of Liverpool for analysis. More recently Lightbody *et al*. (2018) validated a tapeworm ELISA available as a commercial kit that uses saliva to detect tapeworm presence which is more accessible to horse owners.

An ELISA assay has been developed for the detection of pre-patent cyathostomins in horses (Mitchell *et al.,* 2016), however this test is not yet commercially available. Until such a time when immunology led diagnostics are readily available, faecal egg counts remain the gold standard for monitoring strongyle and ascarid burdens and for anthelmintic efficacy testing.

An important aspect of diagnostic use is interpretation of the results and the application of any treatments. It is important for clients to remember that a zero faecal egg count does not mean that the horse is parasite free. It is more likely that the parasite burden is very low and therefore unable to be detected and not accounting for pre-patent cyathostomin burden. The concept of *refugia* (allowing some parasitic worms to remain untreated by anthelmintics within a horse population) is also extremely important for sustainable worm control. In its simplest form a *refugium* is created in a population when some animals are left untreated. For example, if there were four horses grazing one pasture, one has a FEC of 500epg and the other three a FEC >200epg. By only treating the horse with 500epg any resistant parasites harboured by that animal that remain following treatment, of which the eggs will be excreted on to the pasture. The untreated horses will harbour a mixture of resistant and susceptible parasites and therefore will be excreting eggs of susceptible and resistant parasites. On the whole the parasites on the pasture the horses are grazing remain drug susceptible, if all horses were treated then it is more likely that the parasite population would be skewed to predominantly resistant parasites that survived treatment, this can be seen in figure 2. At a more complex level in cyathostomins, *refugia* can also be considered to occur when treating parasites with a drug that is not efficacious against the encysted stages e.g. ivermectin, pyrantel or a single dose of fenbendazole which leave the encysted larval stages in *refugia* (Kaplan and Nielsen, 2010). It is therefore important that all diagnostic results and follow up treatments are advised by someone that is suitably qualified to ensure appropriate treatments are delivered while maintaining a *refugium* to ensure parasites remain anthelmintic sensitive for as far into the future as possible.

Helping clients on worm control

When advising clients on worm control it is important to gain as much information as possible on the animals involved. Effectively a risk assessment of the animal and premises are required to ascertain stocking densities, pasture management, animal ages, past treatment history, use of diagnostics and past results to build a picture of the risk of parasitic infection. The key message is to ensure that sustainable diagnostic techniques are employed to monitor and manage parasite loads before the use of anthelmintic intervention, Figure 3. It is important to ensure clients understand that when using anthelmintics there are limited drug classes for treating equine parasites.

Until it is possible to diagnose encysted cyathostomins an annual treatment with moxidectin (Equest, Zoetis) in the late autumn/ early winter should be employed to target encysted pre-patent larvae (BEVA, 2018). If tapeworm treatment is required then moxidectin and praziquantel can be used (Equest Pramox, Zoetis). This annual treatment should also be enough to supress other parasites outside of the four of veterinary importance (Kaplan and Nielsen, 2010). Where anthelmintics are used to reduce strongyle and ascarid burdens efficacy tests should be routinely employed to check for anthelmintic effectiveness.

The future of equine parasite control

Alongside the awaited cyathostomin ELISA there have been other developments in the world of parasitology that may change the way we detect parasitism and anthelmintic resistance in the future. In cattle parasites, next generation sequencing has been used to profile the nemabiome, this has allowed the detection of resistant parasites through nematode genetics (Avarmenko *et al.,* 2017). It is therefore a possibility that in future parasite detection and resistance monitoring in horses may be conducted though 'omics technologies, however for now this remains a research tool rather than a diagnostic aid.

Conclusions

Parasite control strategies should be sustainable to ensure that nematode burdens are controlled but not eradicated. Worm control is important to reduce the risk of intestinal disease, however it is important to reduce the reliance on anthelmintics to reduce the speed of development of anthelmintic resistance. Horse owners need to be led away from the historical fear of parasites and worm control needs to considered more holistically. Faecal egg counts and tapeworm ELISA tests should form the basis of a worm control programmes, alongside good pasture management with programmes tailored to the individual horse. It is also important to check efficacy of anthelmintics to ensure worm control practices are effective.

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Figures legends

Figure 1. A: *Strongylus vulgaris* in a section of intestinal infarction, B: encysted cyathostomins in the large colon, C: heavy tapeworm burden at the ileocecal junction, D: *Parascaris equorum* impaction in the small intestine.

Figure 2. Schematic representation of *refugia,* horses with <200epg remain untreated and continue to excrete eggs of anthelmintic sensitive and anthelmintic resistant worms onto the pasture. The horse with >200epg is treated and excretes mainly resistant worm eggs onto the pasture. Due to the three untreated horses there is a mix of resistant and sensitive worm larvae on the pasture which are ingested by all horses. Thus the *refugium* created by the untreated horses means this population of horses harbours worms that remains treatable by anthelmintics. If all horses in this example were treated then the population would be skewed to predominantly resistant parasites increasing the speed of resistance developing in this population.

Figure 3. When helping clients with worm control, consider the cycle in the figure above to ensure that worm control is evidence based and sustainable.