Cyathostomins: disease, resistance, control and new diagnostics

Nikki Walshe, equine clinician and lecturer in equine clinical studies in University College Dublin, outlines the presentation and management of the equine intestinal parasite, cyathostomins

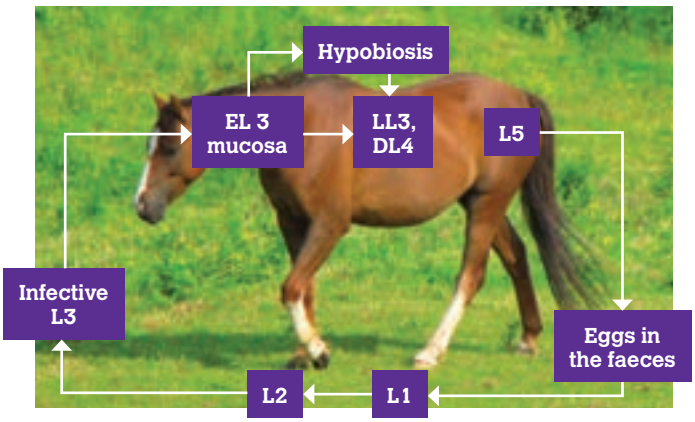

Figure 1: Cyathostomins lifecycle.

Cyathostomins are widely recognised as the most pathogenic of equine intestinal parasites. They are ubiquitous in the environment and it is assumed that all grazing horses have some level of infection (Tolliver, Lyons and Drudge, 1987; Bucknell and Gasser, 1995). There are more than 50 recognised species but the pathogenicity and relevance of each species has yet to be deciphered.

Cyathostomins can cause chronic disease, typically malabsorption and dysmotility, but can also manifest in acute larval cyathostominosis. This year, the Irish Equine Centre had five deaths confirmed due to larval cyathostominosis. With the rise of resistance to anthelmintics among cyathostomin populations, and the perceived increased in clinical disease, the use of diagnostics and an overview of anthelmintic protocols is needed now more than ever.

LIFECYCLE

Cyathostomins have a direct lifecycle. The eggs are released in the faeces and develop into infectious stage 3 larvae (L3) on the pasture. Once ingested these migrate to the colon and caecum where they burrow into the large intestinal mucosa. In the mucosa, they go through a number of encysted stages, early third L3 (EL3), late L3 (LL3) and develop larval stage 4 (DL4). The L4 emerge into the lumen, then develop into the adult stage. However, EL3 can undergo inhibition, and remain encysted within the mucosa of the large intestine for up to two years. While in this arrested development state, they are not susceptible to anthelmintic treatment.

PATHOGENESIS

Cyathostomins are potentially pathogenic in the large intestine at all stages from mucosal infection through to patent infection (see Table 1). A combination of the damage is caused by the invasion, development and emergence of the larvae along with the encysted cyathostomins that occupy the gut wall. The parasite interferes not only with absorption, but also with normal intestinal motility. This can present as a chronic insidious protein losing enteropathy which presents principally as weight loss, but can also cause intermittent colic and diarrhoea (Mair, 1993; Murphy and Love, 1997).

The acute form of the disease is devastating and is referred to as larval cyathostominosis. Encysted cyathostomins emerge as L4 en masse from the intestinal lining into the gut lumen. This synchronised reactivation results in an acute severe colitis. Horses can present with a history of acute severe weight loss with or without diarrhoea (Murphy et al, 1997). Regardless of presentation, the prognosis is poor with a reported mortality rate of 50%-100%, despite intensive treatment (Giles, Urqhart and Longstaffe, 1985; Van Loon et al, 1995; Murphy et al, 1997)progressing in many cases to emaciation and death, associated with the emergence of fourth stage cyathostome (trichoneme.

Key factors of pathogenesis	Clinical relevance
Gut-wall Invasion, inhabitance and emergence	Intestinal mucosal damage in each life stage
Inhibition within the mucosal lining	Build-up of infectious dose within intestinal walls of individuals
Resistance to anthelmintics	Decreased efficacy of treatment

Table 1: Key factors of pathogenesis and their clinical relevance.

RISK FACTORS FOR LARVAL CYATHOSTOMINOSIS

Younger horses have a recognised risk acute larval cyathostominosis in line with the associated higher prevalence of encysted cyathostomins in this age cohort

Figure 2(a) and 2(b): Dramatic weight loss over two weeks in a larval cyathostominosis case.

(Love and Duncan, 1992). Time of year is also receognised as an associated risk with higher incidence in late winter and early spring a time of increased risk (Reid and Hillyers, 1995). There is also a risk associated with treatment of adult cyathostomins with anthelmintics (Reid and Hillyers, 1995). Although this has yet to be re-created experimentally, there is evidence of local intestinal inflammatory reaction post-treatment (Steinbach et al, 2006).

ANTHELMINTIC RESISTANCE

The objective of anthelmintic treatment is to prevent clinical disease and decrease the egg shedding, and therefore pasture contamination, by the horse.

Fenbendazole (FBZ) is a licensed larvicidal for use against cyathostomins. However, research has questioned its efficacy, even at a larvicidal dose – 10mg/kg for five days (Chandler, Collins and Love, 2000).

Moreover, there has been increasing evidence of resistance to FBZ worldwide (Fisher et al, 1992; Chandler, Collins and Love, 2000; Tarigo-Martinie, Wyatt and Kaplan, 2001; Canever et al, 2013). Therefore, post-treatment faecal reduction tests are crucial to ensuring effective treatment.

Moxidectin (MOX) is also a licensed larvicidal drug and is highly effective against LL3 and DL4 (Xiao, Herd and Majewski, 1994; Reinemeyer, Prado and Nielsen, 2015) many strongyle control programs continue to feature regularly scheduled larvicidal treatment with fenbendazole (FBZ). However, there is a worrying trend regarding the reduction of the egg reappearance period (ERP), which can be an indication of resistance development.

When first on the market, the ERP was as long as 22 weeks, but recent studies, in both the UK and the US, show a reduction to six weeks in some cases (Daniels and Proudman, 2016; Tzelos et al, 2017) With no new anthelmintics on the horizon the judicious use of MOX is necessary now more than ever.

CONTROL (CYATHOSTOMINS ONLY)

The prevention of large intestinal burdens without increasing the pressure for resistance development, is the objective of anthelmintic protocols. This is achieved through targeted timely dosing and management strategies that decrease the parasite load on pasture.

STEP ONE: IDENTIFY RISK

Parasitic burden is determined by infectious dose on pasture and the immunity of the animal, thus horses can be divided into low-risk and high-risk groups (see Table 2).

STEP TWO: TARGETED WORMING

Although the reason remains unknown, that L3 encyst over the winter period. Therefore, to decrease the encysted burden of cyathostomins, most horses should be wormed with an effective larvicidal anthelmintic in autumn, particularly after a spring and summer at pasture. As stated, development of L4 to L5 occurs in late winter and early spring, therefore, an appropriate dewormer that will destroy the developed adult worms guided by faecal egg counts (FECs) is sufficient during summer for the high-risk horses. Low-risk horses with an FEC below 200epg do not need to be wormed. There is no associated increase with faecal shedding in adult horses without treatment (Lester et al, 2017).

Low-risk horses:

- mature horses (over three years old);
- no more than two horses per acre;
- new horses are rarely or carefully introduced; and
- faeces picked up regularly.

High-risk horses:

- horses under three years in the group;
- pastures are overstocked;
- new horses introduced to the group regularly; and
- droppings are rarely or never picked.
- NOTE: Horses under three years and foals are always high risk.

Table 2: Low and high-risk groups of horses.

STEP THREE: MANAGEMENT

Poor management controls dramatically increases the risk of resistance and is also associated with the worrying, shortening of ERP of moxidectin (Sallé et al, 2017; Tzelos et al, 2017). Therefore, instituting management protocols (see Table 3) that reduce pasture faecal contamination will be a crucial factor in clinical disease prevention and the preservation of effective anthelmintics (Corbett et al, 2014).

DIAGNOSTICS – THE OLD AND THE NEW

FEC

FECs are the mainstay of diagnostic based targeted protocols. However, it must be remembered that the basic

McMaster technique reflects only the adult strongyle burden. Th larval stages can account for up to 90% of the burden (Eysker, Boersema and Kooyman, 1990). Therefore, in the case of cyathostomins, the FEC will not determine the mucosal burden. There is a need for more specific diagnostics to allow for advised worming protocols based on larval infection intensity.

ENCYSTED CYATHOSTOMIN ELISA

An experimental ELISA to identify encysted cyathostomins has been developed. The Cy-GALA-1 antigen complex is used and is specific for encysted cyathostomins (Mitchell et al, 2016)they can spend a substantial time as encysted larvae in the intestinal wall. The larvae can comprise up to 90% of the total burden, with up to several million worms reported in individuals. These stages can emerge in large numbers to cause life-threatening colitis. Direct methods for detection of encysted larval burdens in live horses do not exist. Previously, two antigen complexes were identified as promising markers for infection.

A component of these, cyathostomin gut associated larval antigen-1 (Cy-GALA-1. The test can potentially indicate the presence of encysted cyathostomins, and is being validated at present. As previously mentioned, cyathostomins encyst in autumn/winter time, making dosing according to FEC redundant. Thus, this test would enable targeted dosing at a crucial time of the life cycle.

In summary, with evidence of increasing anthelmintic resistance in such highly pathogenic parasites, veterinary-led parasite treatment is key to the preservation of effective treatments and prevention of clinical disease.

- **remove faeces from pasture twice weekly (manual or mechanical);**
- **keep stocking density low (two horses per acre); and**
- **quarantine new horses and deworm prior introduction to herd.**

Table 3: Decrease pasture contamination.

REFERENCES ON REQUEST