

# Investigation of the relationship between helminths, the host immune system and intestinal dysbiosis in horses

In association with



Researchers at University College Dublin are currently investigating ways to provide better diagnostics and treatment of horses at risk from acute larval cyathostominosis

## Nikki Walshe

Nikki Walshe worked in clinical practice both in the southern hemisphere and here in Ireland before taking a role in the UCD equine field service. In this role she provides a clinical service and facilitates the teaching of the equine clinical studies rotation. From her experience in the field Nikki developed a particular interest in the area of equine parasitology, which is the basis of her PhD. Under the guidance of her supervisors, Professor Grace Mulcahy and Associate Professor Vivienne Duggan, Nikki will pursue the investigation of mechanisms behind parasite associated disease in the horse.



mucosa can occur, allowing for accumulation of large burdens. Clinical disease can manifest as chronic weight loss, but in some individuals, it presents as an acute severe local and systemic inflammatory syndrome – acute larval cyathostominosis (ALC), which can be fatal.



**Figure 1. Different encysted larval stages in colonic mucosa of a heavily infested horses who died of ALC.**

The human gut microbiome is grabbing headlines regarding its influence on health and disease, with connections shown to major societal issues such as obesity and depression. Now that we have access to more sophisticated affordable analysis of the microbiome, there are countless studies adding to the ever-growing library of human microbiome-related conditions. Similar studies in veterinary species, including horses, have lagged behind but it is becoming clear that the equine gut microbiome also plays a part in disease processes.

In addition to a complex bacterial gut microbiome, all horses with access to grazing have a resident population of parasitic helminths, comprising mostly mixed infections with the cyathostomins (small strongyles), of which over 50 species have been documented. We call this the helminthome. Cyathostomins are the most common and pathogenic endoparasites in horses. Within the cyathostomin life cycle, hypobiosis of encysted larvae in the large intestinal

ALC became of particular interest to our group due to a number of cases that had different signalments, different anthelmintic treatment histories and presented at unusual times of the year. It made us realise that the risk factors and pathophysiology of ALC are incompletely understood, and that although it may be triggered by anthelmintic treatment removing adult worms, other, as yet unknown, elements may be involved in determining individual susceptibility to ALC. We hypothesise that the pathogenesis of ALC may involve interference with the host's intestinal ecological balance that arises from interplay between gut bacterial microbiota, resident helminths, and the host immune system. Anthelmintics could disrupt the microbiome through removal of the helminths from their ecological niche. We propose that dysbiosis of the gut microbiota, accompanied by systemic inflammation, may occur in ALC, and we have recently completed a study providing substantial evidence in support of

this (Walshe *et al* IJP, In press).

This study documented the effects of anthelmintic treatment on both the faecal microbiome and inflammatory responses in 32 horses, using faecal and serum inflammatory markers and 16s rRNA sequencing of faecal samples. Treatment was associated with dysbiosis occurring seven days post-treatment, along with an inflammatory response, both of which were largely resolved by day 14.

We conclude that bacterial gut microbiome changes are associated with systemic and local inflammation following anthelmintic treatment. We propose that similar, but more severe, changes in these parameters would be seen in horses that develop ALC. Fortunately, we have now had the opportunity to document the clinico-pathological and faecal microbiota changes during an ALC outbreak of 14 horses from a herd of 24 horses (Walshe *et al* [publication in preparation]). Clinical signs included sudden weight loss, diarrhoea, dull demeanour, pyrexia, colic and vasculitis. Clinico-pathological parameters showed evidence of marked systemic inflammatory response. The post-mortem findings were characterised by a marked ulcerative typhlocolitis consistent with the mass emergence of cyathostomin larvae. We are excited to continue this line of research in order to provide better diagnostics and treatment of horses at risk from ALC.



**Figure 2. A two-year-old filly with acute severe weight loss, muscle wastage and diarrhoea associated with ALC.**