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Review

Anthelmintic resistance in important parasites of horses: Does it really matter?

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ABSTRACT

Parascaris equorum and cyathostomins are currently considered the most important parasites of horses and have traditionally been controlled with anthelmintics belonging to three drug classes: benzimidazoles, the tetrahydropyrimidine pyrantel, and macrocyclic lactones. Unfortunately, resistance to benzimidazoles, and to a lesser extent pyrantel, is widespread in cyathostomins around the world. Furthermore, resistance to macrocyclic lactones appears to be in the early stages of development in cyathostomins in multiple locations. In contrast, *P. equorum* populations have remained susceptible to the three anthelmintic drug classes for a considerably longer period of time. However, over the last 10 years, resistance to macrocyclic lactones has been described in multiple countries. In contrast, resistance to pyrantel has only been described in the USA; resistance to benzimidazoles has yet to be reported. Despite the large number of reports of anthelmintic resistance in both cyathostomins and *P. equorum*, there are presently no reports that definitively link anthelmintic resistance with clinical problems in horses. However, that generally appears to be due to a publication bias toward well managed horse farms and the lack of appropriate diagnostic methods for rapidly quantifying anthelmintic resistance in these parasites. Management-based, and other, reasons likely responsible for this apparent anomaly are also discussed. Finally, future research priorities in this area, identified from a discussion at the *9th International Conference on Equine Infectious Diseases*, are summarized.

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1. Introduction

In October 2012, a discussion took place at the *9th International Conference on Equine Infectious Diseases (ICEID IX)*, Lexington, Kentucky, USA, on anthelmintic resistance in parasites of horses and the clinical impact of anthelmintic-resistant infections. The following is a summary of the presentations made at the beginning of the session, a review of the relevant scientific literature, and a summary of future research needs in this area that were identified during the lively discussion that followed. A transcript of the entire discussion session can be found under supplementary files.

2. Background

For at least the last two decades, *Parascaris equorum* and cyathostomins have been considered the two most important parasites of horses (Love et al., 1999; Kaplan and Vidyashankar, 2012). However, while *P. equorum* typically only occurs in animals less than 2 years of age (Clayton, 1986), and is more common in animals maintained indoors, cyathostomins infect most grazing horses and, overall, are considered the most important parasitic pathogens of horses (Love et al., 1999; Lichtenfels et al., 2001; Kaplan, 2002). As such, it should be recognized that cyathostomins are considered responsible for approximately 95–100% of all strongyle eggs shed in the feces of horses (Kaplan, 2002; Bello and Allen, 2009).

2.1. P. equorum

With respect to the pathogenic effect of *P. equorum* infections, the clinical impact is typically dependent upon the parasite burden. Thus, when large burdens are present, one or more of the following clinical signs may be observed: coughing, nasal discharge, lethargy, inappetence, ill thrift, rough hair coat, decreased weight gain, diarrhea, and colic (Clayton and Duncan, 1978; Austin et al., 1990; Ryu et al., 2004; Cribb et al., 2006). In addition, substantive burdens may be associated with spontaneous non-strangulating obstruction, and occasionally perforation or intussusception, of the small intestine (Ryu et al., 2004; Cribb et al., 2006; Laugier et al., 2012); treatment with anthelmintics within the previous 24 h, particularly macrocyclic lactones or pyrantel, appears to be a risk factor for these clinical problems (Ryu et al., 2004; Cribb et al., 2006). However, while all these clinical presentations are commonly reported in the literature, the reality is that most horses infected with *P. equorum*, when maintained under optimal husbandry and nutritional conditions, have subclinical infections, i.e. morbidity appears to be minimal, even when burdens are typically at their maximum.

2.2. Cyathostomins

In contrast to the intestinal development of *P. equorum*, which is restricted to the lumen of the small intestine, intestinal development of cyathostomins occurs both within the lumen and wall of the large intestine. Furthermore, in contrast to *P. equorum*, horses often do not develop strong levels of protective immunity. As a result, substantive burdens of cyathostomins may occur in all ages of animals (Chapman et al., 2003). Clinical signs associated with cyathostominosis are variable, but most commonly include decreased levels of performance, reduced growth rates, weight loss, rough hair coat, debilitation, diarrhea and various types of colic (Uhlinger, 1991; Murphy and Love, 1997; Love et al., 1999; Mair et al., 2000). Cyathostomin infections may also cause larval cyathostominosis, a disease that is potentially life threatening, associated with development of large numbers of immature stages in the wall of the large intestine. Larval cyathostominosis is typically diagnosed in horses of 1–3 years of age and is most commonly associated with one or more of the following clinical signs: severe weight loss, weakness, acute or chronic diarrhea, subcutaneous edema, pyrexia, colic (Lyons et al., 2000; Peregrine et al., 2006). Surprisingly, these cases sometimes have a normal appetite and water intake (Love, 1992; Paul, 1998). Identification of epidemiological risk factors for the occurrence of cyathostominosis has received little attention in the literature. However, in work carried out in the United Kingdom, age (<5 years), season (winter) and the time since last deworming (<2 weeks) were all identified as risk factors for the occurrence of this disease (Reid et al., 1995). Finally, although few studies have reported clinical pathology changes associated with larval cyathostominosis, the following four abnormalities were consistently observed in six cases: hypoalbuminemia, hypoproteinemia, microcytosis and elevated serum fibrinogen (Peregrine et al., 2006). The former two changes are consistent with earlier observations (Mair et al., 1993).

Almost all the aforementioned clinical signs associated with cyathostomin infections are highly non-specific. As a result, the true prevalence of clinical and subclinical disease associated with cyathostomin infections is unclear. The current debate about appropriate strongyle fecal egg counts for determining whether horses require treatment with an anthelmintic (i.e. different thresholds are being used in different parts of the world, with little justification for the selected thresholds) confounds this issue. However, field experience indicates that while cyathostomin infections are ubiquitous in horses kept on pasture, most infections are subclinical and of little detriment to the animal (Klei and Chapman, 1999; Love et al., 1999; Fritzen et al., 2010). Furthermore, substantive cyathostomin burdens (i.e. >10,000) may be tolerated without any significant morbidity impact (Love et al., 1999; Nielsen et al., 2010).