# Article

# Comparative long-term efficacy of ivermectin and moxidectin over winter in Canadian horses treated at removal from pastures for winter housing

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**Abstract** – The impact of a late fall treatment on the spring rise of fecal egg counts was evaluated in a controlled study with Canadian horses treated with 2 different dewormers immediately after removal from pasture for winter housing. The horses were stabled until the end of the trial period. Seventeen weanlings, 20 yearlings, and 15 2-year-old horses located in Ontario, which were presumed to be naturally infected with cyathostomins after pasture grazing, were randomly allocated to either a group treated with 0.4 mg/kg of moxidectin and 2.5 mg/kg of praziquantel or a group treated with 0.2 mg/kg of ivermectin and 1.5 mg/kg of praziquantel. Three weeks after treatment, all strongyle fecal egg counts were reduced to zero for both treatment groups. However, at 5 months post-treatment, mean geometric fecal egg counts were statistically higher for the yearlings and 2-year-old horses treated with ivermectin than for the yearlings and 2-year-old horses treated with moxidectin (P < 0.0001).

**Résumé – Efficacité comparative de l'ivermectine et de la moxidectine 5 mois après le traitement automnal de chevaux retirés du pâturage pour la durée de l'hiver canadien.** L'impact sur l'augmentation printanière du comptage d'œufs fécaux d'un traitement automnal à la sortie du pâturage pour hivernement a été évalué dans une étude contrôlée avec des chevaux canadiens ayant reçu soit un gel oral contenant 2,0 % de moxidectine ou soit une pâte orale contenant 1,87 % d'ivermectine. Dix-sept poulains sevrés, 20 poulains d'un an et 15 poulains de 2 ans résidant dans une écurie localisée en Ontario, et présumés être infectés naturellement par des cyathostomes après une saison de pâture, furent répartis de façon aléatoire entre un groupe traité avec 0,4 mg/kg de moxidectine et 2,5 mg/kg de praziquantel et un groupe traité avec 0,2 mg/kg d'ivermectine et 1,5 mg/kg de praziquantel. Trois semaines après le traitement automnal, tous les comptages d'œufs fécaux furent réduits à zéro pour les deux groupes traités. Cependant, à 5 mois après le traitement, les comptages géométriques moyens des poulains âgés de un et deux ans furent statistiquement plus élevés pour ceux traités avec l'ivermectine que pour ceux traités avec la moxidectine (P < 0,0001).

(Traduit par les auteurs)

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#### Introduction

**C** yathostomins (small strongyles) are the most prevalent nematodes found in horses around the world, including Europe and North America (1). A clinical syndrome, characterized by diarrhea, weight loss, dehydration, and, sometimes, death, has been associated with larval cyathostominosis in several countries, including Canada (1–4). In 2 Canadian studies, cyathostomin eggs represented 100% of the total strongyle fecal egg counts (5–6).

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The infection by small strongyles is direct and occurs when the horse is on pasture (7). After ingestion by horses, the infective larvae migrate to the mucosa of the large intestine, where inhibition can occur at the early 3rd larval (EL3) stage (1). Although the causes for larval inhibition are not well understood, it has been hypothesized that the harsh winter climate conditions in northern countries are responsible for the inhibition of fall-ingested larvae (7). This could represent a strategy for the larvae to survive through harsh winter conditions. It has been hypothesized that the immunity acquired by the horse through exposure promotes cyathostomin inhibition (8).

A spring rise in excreted fecal eggs has been reported in horses in several countries in Europe and North America, including Canada (9–16). A possible explanation for this spring rise would be the re-emergence of inhibited cyathostomin larvae in early spring and their development into mature stages. The synchronous massive emergence of encysted larvae is responsible for causing clinical larval cyathostominosis (1).

In the macrocyclic lactone family, ivermectin has little or no efficacy against encysted larvae (EL3) and developing larvae

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(DL) at the label dose and at up to 5 times the label dose (17–20). In contrast, several studies have shown the efficacy of moxidectin against encysted larvae at the label dose (1,19–25). Moreover, among macrocyclic lactones, pyrimidines, and benzimidazoles, moxidectin has the longest period of fecal egg suppression (26–33). This finding could be partially explained by the efficacy of moxidectin against encysted cyathostomins.

The objective of this study was to compare the impact the spring rise of fecal egg counts in horses treated with ivermectin or moxidectin in the fall, after being removed from pasture for winter housing.

# Materials and methods

#### Animals and treatments

Fifteen 2-year-old, 20 yearlings, and 17 weanling warmblood horses of both sexes, which were presumed to be naturally infected with cyathostomins after pasture grazing, were blocked by age and randomly allocated by the use of a random number table to 1 of the following 2 groups: Group 1 treated PO with 0.4 mg/kg bodyweight (BW) of moxidectin and 2.5 mg/kg BW of praziquantel (MP) (Quest Plus Gel; Wyeth Animal Health, Guelph, Ontario), or Group 2 treated PO with 0.2 mg/kg BW of ivermectin and 1.5 mg/kg BW of praziquantel (IP) (Equimax; Pfizer Animal Health, Montreal, Quebec). All the horses were located on the same farm in the Ottawa valley, Ontario. Praziquantel was included in the treatments at the request of the owner's local veterinarian in order to treat for tapeworms.

The horses were treated on December 13, 2006, (weanlings) or on December 19, 2006, (2-year-olds and yearlings) after removal from pasture by the farm manager. On the day of treatment, all the horses were put into stalls without feed to ensure that no feed was present in their mouth at the time of treatment. Each horse was individually weighed on a digital scale (Instaweight Digital animal Scale model LCD-U2100U, indicator model 83-10; Norac System International, Saskatoon, Saskatchewan). The farm manager was instructed by his local veterinarian on how to administer oral dewormers. The products were administered in the back of the mouth, at the base of the tongue, with prefilled syringes set at the upper nearest 25 kg mark (MP) or 100 kg mark (IP). The products were kept at room temperature until treatment. The horses were then housed for the winter and fed dry hay and commercial grain feed until the end of the trial. They were kept in individual stanchions and were exercised daily in an outdoor paddock. There was no natural re-exposure to strongyle infective larvae between the late fall treatment and the spring fecal sampling.

#### **Fecal examination**

Fecal samples were taken from all horses by the farm manager on the day of treatment, 16–21 d after treatment (January 3, 2007, for weanlings and January 4, 2007, for 2-year-olds and yearlings), and approximately 5 mo later [before turn-out to pasture (May 7, 2007, for weanlings and May 24, 2004, for 2-year-olds and yearlings)]. The fecal samples were sent by the farm manager to the Parasitology Laboratory of the Université de Montréal. The technician, who was blinded to treatment protocols, counted the strongyle fecal eggs per 5 g by performing a modified Wisconsin sugar centrifugation technique (34). Since the horses were treated with praziquantel at the request of the owner's local veterinarian, tapeworm fecal eggs were also counted to estimate the tapeworm prevalence rate and to compare 2 different testing methods; these results will be reported elsewhere.

#### Statistical analysis

Logarithmic transformations  $[\log 10(x + 1)]$  were done on strongyle fecal egg counts to obtain a normal distribution of values. A linear repeated-measure model, with age (3 levels) and treatment (2 levels) as between-subject factors and time (3 levels) as a within-subject factor, was used to analyze the data (SAS version 9.1; SAS Institute, Cary, North Carolina, USA). A priori contrasts were used to examine differences between means for each categorical variable. To examine the effect of treatment as a function of time for each age subgroup, a separate model for each age subgroup was used to handle the triple interaction term. Geometric means for both treatment groups in each age subgroup were calculated, using the log-transformed values. A linear repeated-measure model, including month as a withinsubject factor, treatment as a between-subject factor, and the interaction between month and treatment, was used for each age subgroup separately. A priori contrasts were used to examine differences between pairs of means for each categorical variable. Differences were regarded as significant at a level of P < 0.05.

## Results

Two horses from the 2-year-old subgroup of Group 2 were excluded because they were moved to another farm before the fecal sampling in May 2007.

The statistical model revealed a significant effect of treatment for all ages and all times considered (P = 0.0008), and of time for all ages and treatments considered (P < 0.0001), but there was no effect of age for all times and treatments considered (P = 0.16). However, age interacted with time (P = 0.02) and treatment (P = 0.01), indicating that some of the effects of time and treatment probably varied with age.

The geometric mean eggs per gram (EPG) count was larger in Group 2 than in Group 1 in both 2-year-old (P = 0.0005) and yearling (P = 0.007) horses, but not in weanling (P = 0.66) horses, for all times considered. There was no significant effect of treatment in December (P = 0.44) and in January (P = 0.92), but the geometric mean EPG count was significantly lower in Group 1 than in Group 2 in May (P < 0.0001) when all age subgroups within the same treatment group were pooled together. For Group 2, the geometric mean EPG count was significantly lower in January than in December (P < 0.0001), significantly higher in May than in January (P < 0.0001), but similar in May and December (P = 0.49) when all age subgroups were pooled together. For Group 1, the geometric mean EPG count was significantly lower in January than in December (P < 0.0001), significantly larger in May than in January (P < 0.0001), and significantly lower in May than in December (P < 0.0001) when all age subgroups were pooled together.

In December 2006, pretreatment strongyle fecal egg counts were quite high for all subgroups, with individual EPG counts

			Strongyle fecal eggs per gram		
	Number of horses	Before fall [Dec] treatment (mean log-transformed egg counts)	Three weeks after fall [Jan] treatment (mean log-transformed egg counts)	Five months after fall [May] treatment (mean log-transformed egg counts)	
Group 1	9	$429^{a}$ (3.33, $s = 0.20$ )	$0^{a} (0.00, s = 0.00)$	$28^{a}$ (2.15, $s = 0.56$ )	
Group 2	8	$182^{a}$ (2.96, $s = 1.22$ )	$0^{a} (0.00, s = 0.00)$	45ª (2.35, <i>s</i> = 0.23)	

<sup>a,b</sup> Values with different superscripts within columns differ significantly (P < 0.0001).

s — standard deviation.

Table 2. Mean	geometric stro	ngyle fecal	egg counts c	over time for	r the yea	rling horses

			Strongyle fecal eggs per gram			
	Number of horses	Before fall [Dec] treatment (mean log-transformed egg counts)	Three weeks after fall [Jan] treatment (mean log-transformed egg counts)	Five months after fall [May] treatment (mean log-transformed egg counts)		
Group 1	10	$199^{a}$ (3.00, $s = 0.30$ )	$0^{a} (0.00, s = 0.00)$	$35^{a}$ (2.25, $s = 0.43$ )		
Group 2	10	$198^{a}$ (3.00, $s = 0.25$ )	$0^{a} (0.00, s = 0.00)$	$363^{\rm b}$ (3.26, $s = 0.36$ )		

<sup>a,b</sup> Values with different superscripts within columns differ significantly (P < 0.0001).

s — standard deviation.

Table 3.	Mean geometric	strongyle feca	l egg counts over t	time for the	2-year-old horses
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			Strongyle fecal eggs per gram			
	Number of horses	Before fall [Dec] treatment (mean log-transformed egg counts)	Three weeks after fall [Jan] treatment (mean log-transformed egg counts)	Five months after fall [May] treatment (mean log-transformed egg counts)		
Group 1	8	$165^{a}$ (2.92, $s = 0.39$ )	$0^{a} (0.00, s = 0.00)$	$6^{a}$ (1.47, $s = 0.91$ )		
Group 2	5	194ª (2.99, <i>s</i> = 0.34)	$0^{a} (0.00, s = 0.00)$	222 <sup>b</sup> (3.05, <i>s</i> = 0.98)		

<sup>a,b</sup> Values with different superscripts within columns differ significantly (P < 0.0001).

s — standard deviation.

ranging from 0 to 1234 for weanling, 63 to 624 for yearling, and 49 to 496 for 2-year-old horses. The geometric mean EPG counts for pretreatment samples did not differ significantly between treatment groups for any age subgroup (P > 0.05) (Tables 1–3).

Three weeks after treatment, all strongyle fecal egg counts were reduced to zero. At this time, the geometric mean EPG counts did not differ significantly between treatment groups for any age subgroup (P > 0.05) (Tables 1–3).

Approximately 5 mo after winter housing, spring strongyle fecal egg counts had increased, with individual EPG counts ranging from 4 to 224 for weanling, 11 to 1132 for yearling, and 0 to 908 for 2-year-old horses. For the weanling horses, the spring geometric mean EPG counts did not differ significantly between Groups 1 and 2 (P > 0.05), while for the yearling and the 2-year-old horses, the spring geometric mean EPG counts of Group 2 were significantly higher than the spring geometric mean EPG counts of Group 1 (P < 0.0001) (Tables 1–3).

#### Discussion

Although no larval cultures were done on fecal samples in this study, previous studies conducted in Canada found only small strongyle larvae after larval culture (5–6). Therefore, it is highly

probable that all, or close to 100%, of the eggs found in the horses collected during this trial were small strongyle eggs.

According to Uhlinger (35), several parasitologists and equine clinicians identified 100–300 EPG as the threshold for initiation of anthelmintic treatment for a group of horses. Based on a threshold of 100 EPG, all the age subgroups in this study would have required a treatment in the fall, while the yearling and 2-year-old horses treated with IP would have required a treatment in the subgroups treated with MP in the fall were well below the threshold for treatment in the spring.

Selective therapy, or the treatment of individual horses with EPG counts exceeding a pre-established cut-off value, is recommended by some authors (36–39). However, selective therapy is intended for adult horses only, where there is a large variation in fecal egg counts within a herd and several animals have negative egg counts. Selective treatment is not recommended for young horses, as they excrete a larger numbers of eggs, show a higher prevalence of positive fecal egg counts, are reinfected much faster following treatment, and are more susceptible to clinical disease associated with helminth parasites (36). Studies reporting success with selective therapy were done in adult horses (36–39).

The higher spring EPG counts in the IP group could be explained by the difference in efficacy for destroying encysted cyathostomins between ivermectin and moxidectin. Because ivermectin does not kill EL3 and developing small strongyle larvae, inhibited larvae that survived treatment may have emerged in the spring, molted into adults, and started laying eggs (17–20). In contrast, studies done in horses necropsied 14 d after treatment with moxidectin showed a partial efficacy of 60% to 80% against encysted cyathostomin larvae (19–20). Later studies discovered that delaying necropsy up to 8 wk after treatment allowed dead larvae to be eliminated from tissues. In the 2 most recent studies done with moxidectin, the horses were necropsied at 8 wk post-treatment and a > 90% reduction in early L3 and a > 99% reduction in tissue developing stage larvae were observed (1,24).

The development of resistance to ivermectin, expressed by a shortened egg reappearance period (ERP), cannot be completely ruled out as an explanation for the difference in spring EPG counts between Groups 1 and 2 for the yearling and 2-year-old horses, since no fecal samples were taken between 3 and 8 wk post-treatment in this study. However, shortened ERPs with ivermectin have been observed mainly in herds with fecal worm egg count reductions below 100% at 2–3 wk after treatment (40–41). Since 100% of the young horses treated with ivermectin in our study had negative strongyle fecal egg counts at 3 wk after treatment, a shortened ERP for ivermectin is unlikely.

It is interesting to note the relatively high EPG counts in the weanlings, in the fall, for both treatment groups (very similar to the yearling and 2-year-old horse counts), and the absence of a significant difference in EPG counts in the spring between weanling subgroups (which differs from the finding in the yearling and 2-year-old subgroups). One explanation would be that the weanlings treated with moxidectin were more infected than the weanlings treated with ivermectin at the initiation of the study, although there was no statistical difference. One other possible explanation would be that in the weanling subgroup, most of the ingested larvae did not get into an inhibited stage, as in the older subgroups. This may be due to a shorter life exposure and therefore a lower immune response in this younger age group (8). Finally, because the weanlings were sampled approximately 17 d earlier in May than were the 2 other age subgroups, it may have been too early to detect the maximum spring rise occurring on this farm.

In conclusion, yearling and 2-year-old horses treated in late fall with MP had lower fecal egg counts at the end of the winter housing period as compared with yearling and 2-year-old horses treated with IP at the same time. This difference between treatment groups might be explained by the efficacy of moxidectin against encysted cyathostomins and the inefficacy of ivermectin against this larval stage. Because the mean EPG counts of the horses treated with MP were all below threshold for treatment in the spring, this study shows that there is little or no point in deworming horses in the spring before turn-out to pasture, as is common practice in Canada, if they have been treated with moxidectin in the fall after removal from pasture and kept in a stable, unexposed to strongyle infective larvae, over the entire winter season. If horses treated in the fall with moxidectin do not require a treatment against cyathostomins in the spring before turn-out to pasture, equine practitioners should postpone the spring treatment for these horses until after turn-out. This practice would prevent dewormer overuse by reducing the total number of treatments required during a pasture season and, therefore, should decrease the risk of cyathostomin resistance development.

#### Authors' contributions

Both authors were involved in the design of the trial protocol and approved the version of the manuscript submitted for publication. Dr. Elsener monitored the trial and wrote the manuscript. Dr. Villeneuve conducted the laboratory tests and was involved in revising the manuscript.

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