Cyathostomins (small strongyles) have emerged as the most prevalent and important internal parasites of adult horses following the virtual elimination of large strongyles through widespread use of modern anthelminitics over the past 40 years. Clinical consequences of cyathostomin infections may include reduced performance, weight loss, hypoalbuminemia, diarrhea, and colic. Heavy cyathostomin infections in horses are associated with risk of inflammatory enteropathy of the cecum and colon resulting from damage inflicted by larval emergence of the intestinal mucosa.1 Larval cyathostominosis is the most severe manifestation of clinical disease stemming from the mass emergence of mucosal larvae; although rare, this condition most often affects horses < 5 years of age during late winter or spring, causing sudden-onset diarrhea, pyrexia, and death in 50% of affected horses.1

Horses are exposed to infective cyathostomin larvae while grazing pastures contaminated by infected horses. Cyathostomin eggs passed in feces embryonate, hatch, and molt twice before emerging onto pasture forage as infective third-stage larvae (L3).2 Following ingestion, third-stage larvae move through the intestinal lumen to the large intestine, where they primarily invade the mucosa and submucosa of the cecum and ventral colon to continue maturation. Following penetration of the intestinal wall, early third-stage larvae become encysted in a fibrous capsule. This stage can last for several weeks or may persist in an arrested state of hypobiosis for up to 2 years. Once development re-

Comparison of a single dose of moxidectin and a five-day course of fenbendazole to reduce and suppress cyathostomin fecal egg counts in a herd of embryo transfer–recipient mares

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Objective—To compare larvicidal regimens of fenbendazole and moxidectin for reduction and suppression of cyathostomin fecal egg counts (FEC) in a transient herd of embryo transfer–recipient mares.

Design—Randomized, complete block, clinical trial.

Animals—120 mares from 21 states, residing on 1 farm.

Procedures—An initial fecal sample was collected from each mare; mares with an FEC ≥ 200 eggs/g were assigned to treatment groups. Eighty-two horses received fenbendazole (10.0 mg/kg [4.5 mg/lb], PO, q 24 h for 5 days) or moxidectin (0.4 mg/kg [0.18 mg/lb], PO, once); FEC data were analyzed 14, 45, and 90 days after treatment.

Results—Mean FEC reduction was 99.9% for moxidectin-treated mares and 41.9% for fenbendazole-treated mares 14 days after treatment. By 45 days, mean FEC of fenbendazole-treated mares exceeded pretreatment counts; however, FECs of moxidectin-treated mares remained suppressed below pretreatment values for the duration of the 90-day study. Fecal egg counts were significantly different between groups at 14, 45, and 90 days after treatment.

Conclusions and Clinical Relevance—Failure of the 5-day regimen of fenbendazole to adequately reduce or suppress FEC suggested inadequate adulticidal and larvicidal effects. In contrast, a single dose of moxidectin effectively reduced and suppressed FEC for an extended period. Given the diverse geographic origins of study mares, these results are likely representative of cyathostomin-infected mares in much of the United States, confirming previous findings indicating that fenbendazole resistance in cyathostomins is widespread and that moxidectin remains an effective treatment for control of these important parasites. (J Am Vet Med Assoc 2014;245:944–951)
sumes, cyathostomin larvae develop to late fourth-stage larvae (L4), at which time they emerge from the intestinal wall to continue development into oviparous adults within the lumen of the large intestine.2

Frequent long-term use or misuse of anthelmintics has resulted in emergence of cyathostomin resistance to some of the older classes of these drugs (eg, benzimidazoles and tetrahydropyrimidines) and is a likely factor involved in observations of shortened ERPs in more contemporary compounds (macrocyclic lactones).1,3,5 Anthelmintic resistance is an inherited trait passed from adult parasites to their offspring, and genetic reversion to susceptibility was shown to not occur in a 40-year investigation of drug-resistant strongyles in Kentucky6; therefore, strategies to mitigate the development of resistance should be implemented on all farms. On a given farm, resistant parasites can be selected for over time or can be rapidly introduced into a nematode population through the arrival of an infected horse.7

An FEC is the most common method for identification of parasite infection and quantification of the egg shedding by individual horses. In herds where anthelmintics are frequently used, nearly 100% of the strongyle eggs observed may be produced by cyathostomins.1,3-4,6,8,9 This phenomenon is attributable to the high efficacy of all currently licensed equine anthelmintics against large strongyles. Additionally, large strongyles have long prepatent periods (minimum, 6 months), which allows for their virtual elimination in herds where effective anthelmintics are frequently used.1,3,8 An FEC reduction test performed 14 days after anthelmintic treatment is considered the practical gold-standard in vivo diagnostic test for detecting anthelmintic resistance in horses.9 Anthelmintic resistance and treatment failure are recognized if mean FEC reduction fails to reach the commonly accepted cutoff of > 95% reduction with macrocyclic lactone treatment (ivermectin and moxidectin), > 90% reduction with benzimidazole administration (fenbendazole and oxibendazole), and > 85% reduction with tetrahydropyrimidine treatment (pyrantel pamoate).9

Effective control of cyathostomins in horses presents unique challenges owing to the pervasive nature of exposure, prevalence of anthelmintic resistance, and encysted stages of cyathostomin larvae, which are susceptible to only 2 anthelmintic agents. Macrocyclic lactones, tetrahydropyrimidines, and benzimidazoles each have licensed efficacy against some luminal stages of the cyathostomin life cycle; however, only 2 anthelmintic protocols are approved by the FDA and licensed for use in controlling encysted cyathostomins in horses in the United States: moxidectin (0.4 mg/kg [0.18 mg/lb], PO) as a single dose and fenbendazole (10 mg/kg [4.5 mg/lb], PO) for 5 consecutive days.3,9

Because mucosal stages of the cyathostomin life cycle present a threat to equine health and serve as a reservoir for transfer of anthelmintic-resistant parasites to new locations with horse movement, anthelmintic therapy targeting mucosal larvae is widely considered one of the foundations of contemporary equine parasite control.2,9 Strategic use of larvicidal anthelmintic regimens, targeting encysted cyathostomins when the mucosal burden is at its peak, will biologically extend suppression of fecal egg shedding by eliminating cyathostomins prior to sexual maturity as well as mature worms, thus reducing the number of annual treatments needed to provide adequate parasite control.9 Likewise, use of larvicidal doses of appropriate anthelmintics for reducing fecal egg counts, particularly in horses that shed high numbers of eggs, helps to minimize pasture contamination, limit exposure to infective parasites, curtail the risk of parasitic infection and disease, and improve facility biosecurity against nematodes.8

Results of a 2001 study2 revealed that resistance of cyathostomins to benzimidazole anthelmintics was highly prevalent on horse farms throughout the southern United States and suggested resistance was likely prevalent throughout the country. To our knowledge, no other multfarm studies investigating this issue have been performed in the United States since that report, although several prevalence studies10-13 performed in other countries suggest the problem of benzimidazole resistance in cyathostomins is a worldwide issue. Although evidence for widespread resistance to a single dose of fenbendazole is strong, there is a common belief among some horse owners and equine veterinarians that a 2-day larvicidal regimen of fenbendazole can overwhelm the resistance and remain effective. However, limited data suggest otherwise; the larvicidal regimen of fenbendazole was poorly effective in reducing FEC in horses of several reports.3,8,10,14-16 Unfortunately, it remains unknown how effective this regimen is on most horse farms.

Successful parasitic control relies on the use of anthelmintics that are effective for their intended use.9 Given the importance of larvicidal treatment in the management of cyathostomins, the high prevalence of resistance to benzimidazole anthelmintics reported in the southeast United States and other areas of the world, and the dearth of recent efficacy data for the 2 FDA-licensed larvicidal treatments, there is an urgent need for additional data addressing this issue. Because of the logistical challenge involved with conducting anthelmintic efficacy studies across wide geographic regions, a large commercial herd of embryo transfer-recipient mares from diverse geographic locations across the United States with no exposure to either fenbendazole or moxidectin since arrival was identified. Given the mixed geographic origin of mares residing on this farm and the farm’s history of frequent herd turnover (attributable to the nature of its commercial operations), the cyathostomin population on this farm was expected to represent a broad heterogeneity of cyathostomin genetics from across the United States. Furthermore, given that the horses had not received treatment with either fenbendazole or moxidectin since their arrival on the farm, no further selection pressure for resistance would have occurred. Thus, the mean drug efficacy across all horses tested was expected to be representative of the cyathostomin populations carried to this farm by these horses. The objective of the study reported here was to use this geographically diverse group of mares to compare the efficacy of the 2 FDA-approved larvicidal regimens currently available (a single dose of moxidectin [0.4 mg/kg, PO] and a 5-day course of fenbendazole [10 mg/kg, PO, q 24 h]) for reduction and suppression of cyathostomin FEC.
Materials and Methods

Animals and farm—A comingled herd of embryo transfer–recipient mares from diverse geographic backgrounds was selected for participation in the study, which took place between June 28 and October 10, 2013. The herd resided in central Missouri and consisted of a mixed population of 120 light-breed and draft mares ranging in age from 2 to 14 years (mean, 6.15 years). The horses originated from 21 states, most of which were outside the southern United States (Figure 1). Mares on the farm at study initiation had arrived individually over a period spanning the preceding 16 months. The mare in residence for the longest period had arrived 16 months prior, and the most recently arrived mare was received the week before study initiation. The mean time of arrival within the herd was 6 months prior to the start of the study.

The mares had an unknown anthelmintic treatment history prior to arrival. Review of medical records from the date of arrival forward revealed no history of moxidectin or fenbendazole administration; the operation’s anthelmintic protocol exclusively used ivermectin (200 µg/kg [91 µg/lb], PO) every 2 to 3 months. The last dose of ivermectin was administered 12 weeks prior to study initiation.

The study farm had hosted transient populations of embryo transfer–recipient mares since 2004. Prior to its establishment as a recipient mare farm, the property had been used as an alfalfa hay field and cattle feedlot. The farm comprised 55 acres of pasture divided into 3 paddocks by the herd owner to facilitate efficient husbanding between 35 and 45 recipient mares. Paddocks of approximately 15 to 20 acres, each housing between 35 and 45 recipient mares.

The mares had been grouped and assigned to paddocks by the herd owner to facilitate efficient husbandry for the commercial operations of the farm. In addition to forage available from pasture access, mares had free-choice access to hay and water, supplemented with 2.7 kg (6 lb) of a locally mixed sweet feed grain ration (14% crude protein) once daily.

Consent was obtained from the herd owner for inclusion of mares in the study, and the study treatment protocols were consistent with FDA-approved labeled use of fenbendazole and moxidectin.

Sample collection and processing—Mares were restrained in stocks for fecal sample collection. Personnel performing the study (a technician [AAG], technician’s assistant, and licensed veterinarian [NDV]) had been previously trained in humane animal handling techniques. All mares had previously been trained to enter the stocks, and all had previously undergone rectal examination. Samples were manually collected per rectum from all 120 mares at study initiation (day 1). Each fecal sample was placed in a sealable plastic bag labeled with the freeze brand identification number located over the mare’s left shoulder joint. Air was manually removed from each bag, and the sample was immediately cooled by refrigeration to 4°C (39°F). Samples were shipped in a polystyrene foam cooler lined with ice packs to maintain temperature during shipment. Samples were transported by commercial courier to the University of Georgia College of Veterinary Medicine Department of Infectious Diseases for FEC. A modified McMasters technique with a minimum sensitivity of 25 eggs/g was used to determine strongyle FEC. All samples were continuously stored at refrigerated temperatures and processed ≤ 5 days after collection from the mares.

Additional fecal samples were collected from the study mares 14, 45, and 90 days after anthelmintic treatment (study days 29, 60, and 105, respectively). All posttreatment samples were collected, packaged, shipped, and processed in the same manner as pretreatment samples.

Environmental data—Ambient temperature information was collected from the Missouri Agricultural Weather Database, which records hourly weather data from an automated weather station at the Bradford Research and Extension Center located 8 miles south of the study farm.

Treatment groups—Mares with FEC ≥ 200 eggs/g were included in the treatment phase of the study. Mares were examined for overall health, and body weight was determined by girth tape for dose calculations. Sorting for treatment group assignment was accomplished by ranking mares on the basis of FEC in the initial sample obtained on day 1. Starting with the highest counts, each consecutive sequence of 2 mares was grouped together to form a block. The 2 mares in each block were then randomly allocated to 1 of 2 treatment groups. Mares in treatment group 1 received a single dose of moxidectin® (0.4 mg/kg, PO) on day 15, and mares in treatment group 2 received fenbendazole® (10 mg/kg, PO, q 24 h) on 3 consecutive days (study days 11 through 13).

Mares were maintained in their commercially assigned paddock groups throughout the study. As a result, each of...
the 3 paddocks contained a mix of study mares from both treatment groups and herdmates that were excluded from the study after the first sample collection. Each paddock group was moved daily to a common pen for the farm’s commercial activities, examination, anthelmintic treatment when applicable, and periodic fecal sample collection. As horses were removed from the farm as part of its commercial operations, the number of mares in the study decreased over time.

Facilities used were the herd’s regular pasture, feeding, and holding pens. Mare age and anthelmintic history were obtained from the medical record. All weight determinations, dose calculations, and anthelmintic administrations were performed by a licensed veterinarian (NDV). All horses were observed twice daily throughout the study period.

Data analysis—For each group, mean FEC reduction was calculated 14 days after treatment and mean FEC suppression was calculated 45 and 90 days after treatment. Treatment failure attributed to anthelmintic resistance was determined if mean FEC reduction was ≤ 95% 14 days after treatment with moxidectin or ≤ 90% 14 days after treatment with fenbendazole.9

Statistical analyses were performed separately to investigate differences in the age of mares and FEC at each time point between treatment groups. Counts were transformed by log10(count + 1) transformation prior to analysis to stabilize the variance and normalize the data.

Age, pretreatment FEC, and each posttreatment FEC were analyzed with a linear mixed model approach by use of statistical software. Age, in addition to log-transformed pretreatment and posttreatment FEC, was analyzed with a model that considered the fixed effect of treatment and the random effects of block and residual error. Pretreatment FEC was included as a covariate in the analysis of posttreatment FEC. The overall treatment effect and the comparison of least squares mean were performed by means of a 2-sided Student t test at the 5% level of significance.

Moxidectin percentage FEC reduction, relative to fenbendazole and based on arithmetic and geometric means, was calculated as follows:

\[
\text{((Fenbendazole mean – moxidectin mean)/fenbendazole mean) \times 100}\%
\]

Geometric means were calculated as \(10^{\text{LSM/10}} - 1\), where LSM is the least squares mean determined via ANOVA.

Results

Mean daily ambient temperature during the study was 22.0°C (71.6°F), with temperature extremes ranging from 4.9°C to 36.8°C (40.9°F to 98.2°F) during the 105-day period.4 Ambient temperatures were constantly above the minimum required for cyathostomin egg development (4°C [39°F]) and within the range for larval development on pasture (6°C to 40°C [43°F to 104°F]),14 with the brief exception of a few hours the morning of October 6, when temperatures were < 6°C (< 43°F).

After initial sample collection, 82 of the 120 herd mares were retained in the study on the basis of meeting the minimum FEC inclusion criterion of ≥ 200 eggs/g. Each treatment group contained 41 mares. Mean ± SD age of all mares in the fenbendazole treatment group was 5.6 ± 2.6 years (range, 2 to 13 years), and that of the moxidectin treatment group was 5.7 ± 2.6 years (range, 2 to 13 years). Fecal samples were collected from 76 mares 14 days after treatment (study day 29), 64 mares 45 days after treatment (study day 60), and 44 mares 90 days after treatment (study day 105). As a result of commercial operations on the farm, 6 study mares had left the farm by day 14 (2 in the moxidectin treatment group and 4 in the fenbendazole treatment group), 18 had left by day 45 (5 in the moxidectin treatment group and 13 in the fenbendazole treatment group), and 38 had left by day 90 (14 in the moxidectin treatment group and 24 in the fenbendazole treatment group). All study mares that left the farm had either been relocated to another farm after receiving a transferred embryo and being confirmed pregnant or were sold after uterine biopsy results revealed they were not candidates as embryo transfer recipients; these mares were not followed up further. No adverse events were observed during the study. Pretreatment and posttreatment FEC as well as 14-day posttreatment FEC reduction and 45- and 90-day posttreatment FEC suppression results were summarized (Table 1).

Comparison of least squares mean indicated no significant difference in age or pretreatment FEC between treatment groups (Table 2). Analysis of posttreatment FEC indicated that moxidectin treatment resulted in significantly lower FEC at 14 days (\(P < 0.001\)), 45 days (\(P < 0.001\)), and 90 days (\(P = 0.004\)), compared with fenbendazole treatment. On the basis of comparison of arithmetic and geometric means, the single dose of moxidectin was 99.8% and 99.9%, respectively; more effective than the 5-day regimen of fenbendazole in reducing FECs at 14 days after treatment; 90.6% and 98.1%, respectively, more effective in suppressing FECs 45 days after treatment; and 75.0% and 95.4%, respectively, more effective in suppressing FECs 90 days after treatment.

Treatment failure attributed to anthelmintic resistance was observed in the fenbendazole treatment group 14 days after treatment with an arithmetic mean FEC reduction of 41.9%. At 45 days after treatment, mean FEC of fenbendazole-treated horses was higher than the pretreatment value for the same group and > 10 times that of moxidectin-treated horses. Anthelmintic success was observed in the moxidectin treatment group with an arithmetic mean FEC reduction of 99.9% 14 days after treatment, and mean FEC for this group remained below pretreatment levels for the remainder of the study.

Pretreatment FEC data revealed similar proportions of horses in each treatment group that shed high, moderate, or low numbers of parasite eggs in feces prior to anthelmintic administration (Table 3). Most (100%, 86.1%, and 51.9%) moxidectin-treated mares shed ≤ 200 eggs/g in a given sample at each posttreatment FEC (14, 45, and 90 days after treatment, respectively). There was no posttreatment sample collection point at which most fenbendazole-treated mares were found to shed ≤ 200 eggs/g (with only 40.3%, 14.3%, and 0% meeting this cutoff at 14, 45, and 90 days after treatment, respectively).
In this unique population of horses, in which parasites were expected to represent a heterogenous population of cyathostomins from various regions across the United States, moxidectin (0.4 mg/kg, PO) was significantly more efficacious in reducing and suppressing FEC than was fenbendazole (10.0 mg/kg [4.5 mg/lb], PO, q 24 h for 5 days). In the fenbendazole treatment group, mean

### Table 1—Summary of FEC, 14-day FEC reduction, and 45- and 90-day FEC suppression in 82 embryo transfer–recipient mares (age range, 2 to 13 years) treated with moxidectin (0.4 mg/kg [0.18 mg/lb], PO, once) on study day 15 or fenbendazole (10.0 mg/kg [4.5 mg/lb], PO, q 24 h) for 5 days (study days 11 through 15).

<table>
<thead>
<tr>
<th>Time and treatment</th>
<th>FEC (eggs/g)</th>
<th>FEC reduction or suppression (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arithmetic mean ± SD</td>
<td>Geometric mean</td>
</tr>
<tr>
<td>Before treatment (day 1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 41)</td>
<td>857.3 ± 808.6</td>
<td>632.9</td>
</tr>
<tr>
<td>Moxidectin (n = 41)</td>
<td>807.3 ± 632.6</td>
<td>630.0</td>
</tr>
<tr>
<td>14 days after treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 37)</td>
<td>346.6 ± 347.3</td>
<td>207.4</td>
</tr>
<tr>
<td>Moxidectin (n = 39)</td>
<td>0.6 ± 4.0</td>
<td>0.10</td>
</tr>
<tr>
<td>45 days after treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 28)</td>
<td>1,033.9 ± 883.3</td>
<td>579.0</td>
</tr>
<tr>
<td>Moxidectin (n = 36)</td>
<td>97.2 ± 178.8</td>
<td>10.8</td>
</tr>
<tr>
<td>90 days after treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 17)</td>
<td>1,413.2 ± 594.3</td>
<td>1,394.0</td>
</tr>
<tr>
<td>Moxidectin (n = 27)</td>
<td>352.8 ± 437.3</td>
<td>64.0</td>
</tr>
</tbody>
</table>

Study-qualifying mares were maintained on a single farm and had been received from 19 states at various times during the 16 months prior to the study. Number of horses in each group changed over time as horses left the farm as part of its commercial activities.

*The 14-day values represent arithmetic mean percentage reduction; 45- and 90-day values indicate arithmetic mean percentage suppression.

NA = Not applicable.

### Table 3—Number (%) of mares categorized as shedding a low, moderate, or high number of parasite eggs before and after treatment with fenbendazole or moxidectin.

<table>
<thead>
<tr>
<th>Fecal egg shedding</th>
<th>Low (&lt; 200 eggs/g)</th>
<th>Moderate (201–500 eggs/g)</th>
<th>High (&gt; 500 eggs/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire herd (n = 120)*</td>
<td>39 (32.5)</td>
<td>37 (30.8)</td>
<td>44 (36.7)</td>
</tr>
<tr>
<td>Fenbendazole (n = 41)</td>
<td>1 (2.4)</td>
<td>18 (43.9)</td>
<td>22 (53.7)</td>
</tr>
<tr>
<td>Moxidectin (n = 41)</td>
<td>0 (0)</td>
<td>19 (46.3)</td>
<td>22 (53.7)</td>
</tr>
<tr>
<td>14 days after treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 37)</td>
<td>15 (40.5)</td>
<td>16 (43.2)</td>
<td>6 (16.2)</td>
</tr>
<tr>
<td>Moxidectin (n = 39)</td>
<td>39 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>45 days after treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 28)</td>
<td>4 (14.3)</td>
<td>5 (17.9)</td>
<td>19 (67.8)</td>
</tr>
<tr>
<td>Moxidectin (n = 36)</td>
<td>31 (88.1)</td>
<td>4 (11.1)</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>90 days after treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenbendazole (n = 17)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>17 (100)</td>
</tr>
<tr>
<td>Moxidectin (n = 27)</td>
<td>14 (51.9)</td>
<td>5 (18.5)</td>
<td>8 (29.6)</td>
</tr>
</tbody>
</table>

*An initial sample was obtained from 120 mares in the herd from 21 states; 38 mares that did not have an FEC of ≥ 200 eggs/g were excluded from further study participation. The number of mares in each treatment group was reduced over time because of mares leaving the farm as part of its normal commercial operations.

### Discussion

In this unique population of horses, in which parasites were expected to represent a heterogenous population of cyathostomins from various regions across the United States, moxidectin (0.4 mg/kg, PO) was significantly more efficacious in reducing and suppressing FEC than was fenbendazole (10.0 mg/kg, PO, q 24 h for 5 days). In the fenbendazole treatment group, mean...
FEC rose rapidly after an initial 41.9% decline 2 weeks following treatment and exceeded pretreatment counts by day 45. However, FEC of the mean moxidectin treatment group remained below the pretreatment values throughout the 90-day study.

A mean FEC reduction rate of 99.9% was observed at 14 days for the moxidectin treatment group, indicating a high degree of efficacy against adult worms. By day 45, the mean FEC suppression was 77.5%. This rate would usually be considered egg reappearance; however, in comparison, fenbendazole-treated horses had a large increase (57.7%) in mean FEC, rather than suppression, on day 45. Thus, it would seem that FECs were naturally increasing within the herd overall because of epidemiological factors. When relative efficacy was calculated, moxidectin was 90.6% and 98.1% more effective than fenbendazole (on the basis of arithmetic and geometric means, respectively) for FEC suppression 45 days after treatment.

When moxidectin was first introduced for use in horses, ERPs > 12 weeks and intervals as long as 16 to 20 weeks were reported. More recently, ERPs for moxidectin were reported to be as short as 5 weeks in yearlings on farms in Kentucky. The ERP is defined as the interval between the last effective anthelmintic treatment and the resumption of substantial strongyle egg shedding. Although the acceptable limits of cyathostomin fecal egg shedding are a subject of debate, several leading equine parasitologists in the United States have suggested that the ERP be defined as the week after treatment when the FEC reduction decreases below a cutoff of 80% for benzimidazoles and pyrantel pamoate and < 90% reduction for ivermectin and moxidectin.

Reduction in ERP has been suggested as a possible first sign of anthelmintic resistance; however, confounding epidemiological factors having little to do with the presence of resistance can heavily impact anthelmintic efficacy when measured by FEC reduction. Age, immune status of the host, initial degree of parasitic infection, previous anthelmintic treatment history, and husbandry practices for animals as well as variation in egg shedding among cyathostomin species and local climate conditions can contribute to observed anthelmintic performance. Furthermore, studies of anthelmintic efficacy over the past 20 years have used a variety of study designs, statistical methods, and ERP definitions, making direct comparison of study results difficult.

Although FEC of moxidectin-treated mares remained suppressed below pretreatment counts for the duration of the present study, the return to fecal egg shedding observed in these heavily parasitized mares from diverse geographic regions of the United States occurred earlier than was reported for horses in studies performed when the product was first introduced. These data serve as a reminder that although moxidectin remains highly effective in reducing and suppressing FEC, this drug should be used strategically to help preserve its larvicidal efficacy in the future.

The FEC reduction of only 41.9% at 14 days in fenbendazole-treated mares indicated considerable survival rates of adult cyathostomins following anthelmintic treatment. Additionally, rapid return to high rates of fecal egg shedding after treatment was likely reflective of considerable survival rates of larval stage cyathostomins in these horses. When adult and mucosal larvae are efficiently eliminated, the return to fecal egg shedding should closely mirror the 6- to 12-week cyathostomin prepatent period.

The significant reduction (at 14 days after treatment) and suppression (at 45 and 90 days) of FECs in the moxidectin treatment group, compared with treatment failure and increased FEC, respectively, in the fenbendazole treatment group indicated a much greater elimination of the total cyathostomin burden for moxidectin-treated mares. Although there is no direct linear correlation between FEC and actual cyathostomin worm burdens in horses, in a multiyear study in Kentucky, horses with strongyle FECs < 500 eggs/g harbored significantly smaller worm burdens than did horses with FECs > 500 eggs/g. These data support the use of cutoffs in the range of 0 to 300 eggs/g for treatment.

Results of the present study illustrated the biological impact of treatment choice through the large disparity in pasture contamination potential between the 2 treatment groups. Failure of the 5-day fenbendazole treatment regimen suggests that the cyathostomin population infecting these horses was resistant to that treatment. Because the study herd was composed of horses recently acquired from throughout the United States and no additional fenbendazole treatment selection was applied after they arrived, the impact of these data can be extended far beyond the confines of this commercial operation in central Missouri.

Prior to 2004, the property hosting the study population had been used for hay and cattle production. Since that time, the farm has consistently hosted between 90 and 130 recipient mares originating from a number of geographic locations. At study initiation, 120 mares from 21 states were residing on the farm, with the mare in residence longest having arrived 16 months prior. Because no cyathostomins would be expected to be present on the farm prior to 2004, the cyathostomin population in horses of the study herd would reflect the parasitic diversity of all mares that had been members of the transient herd at any time but should primarily comprise the mixture of the cyathostomin populations brought by the current group of mares from their farms of origin.

Medical records revealed that ivermectin had been the exclusive anthelmintic treatment used for parasite control in the embryo transfer–recipient mares of the study herd. Ivermectin efficacy against cyathostomins is limited to luminal L4 and adult stages. Mucosal stages (encysted early L3, late L3, and developing L4), which may represent > 90% of a horse's total cyathostomin worm burden, are unaffected by ivermectin. Use of effective adulticidal compounds depopulates luminal parasites, signaling encysted larvae to resume maturation and rapidly repopulate the large intestine with egg-producing adult cyathostomins. Because encysted-stage larvae had not been specifically targeted in this operation's parasite control program, pasture contamination by cyathostomins with the genetic makeup of populations from previous grazing locations was a biological certainty, further supporting the assertion that parasite
population in this study was representative of worms from a wide geographic range.

Because there was no previous history of benzimidazole use on the study farm, the resistance to fenbendazole observed could not have been selected for locally but must have been present in the parasite burdens of incoming mares. Because the herd population originated from a broad geographic range throughout much of the United States, the presumption that fenbendazole resistance is widely prevalent was supported by the results of this study. Cyathostomin resistance to fenbendazole in horses has been extensively reported. Studies that evaluated a single dose (5.0 mg/kg [2.3 mg/lb], PO) in the southeast United States, northwestern Arkansas, and Southern England and a higher dose (7.5 mg/kg [3.4 mg/lb], PO) in France and Scotland found fenbendazole to be ineffectively for control of these parasites on nearly all farms investigated.

In 1985, the FDA granted supplemental approval for the administration of fenbendazole to horses in the United States at a dosage of 10 mg/kg/d for 5 days. The supplemental approval expanded the spectrum of fenbendazole to include treatment against encysted small strongyles, which would be expected to lengthen the ERP after treatment owing to efficacy against additional cyathostomin life stages. Furthermore, administration of the increased dose for 5 consecutive days should be expected to overcome some degree of drug resistance in cyathostomin; however, evidence suggests this effect is lost as drug resistance increases in parasite populations. Results of 1 study indicate that administration of the larvicidal regimen of fenbendazole to horses infected with populations of cyathostomins with preexisting resistance creates intense selection pressure for a higher degree of resistance. In studies evaluating the 5-day fenbendazole regimen in yearlings in the United Kingdom and Kentucky, the multiday dose regimen failed to achieve acceptable FEC reduction.

Although most contemporary reports cite widespread fenbendazole resistance, there are still sporadic reports of acceptable efficacy against cyathostomins in horses. It is unknown whether the property in this study had ever hosted a population of fenbendazole-susceptible cyathostomins; however, the farm clearly accumulated a predominantly fenbendazole-resistant population of cyathostomins within a short period of time after hosting a transient population of mares. Although every mare coming to the farm since 2004 may not have harbored fenbendazole-resistant parasites, the fact that this resistance was observed in our study suggests there has been little dilution of the worm population with susceptible genotypes and supports the contention that most properties from which these mares originated harbored fenbendazole-resistant cyathostomins.

Larvicidal control of encysted small strongyles is one of the foundations of contemporary parasite control because of the health risks posed by heavy infections and the biosecurity risk of transferring anthelmintic-resistant worms, which appear to be prevalent in the United States. Successful reduction and suppression of fecal egg shedding attenuate the intensity of cyathostomin exposure in grazing horses, thus relieving the necessity of frequent anthelmintic administration. Reduction in the use of anthelmintics through highly effective anthelmintics used in a selective targeted manner should reduce parasite transmission and selection pressure for the development of anthelmintic resistance, thus improving the sustainability of nematode control programs reliant on anthelmintic drugs.

References

15. Chandler KJ, Love S. Patterns of equine faecal egg counts following spring dosing with either fenbendazole or moxidectin. 


