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Original Research

Intestinal Parasites and Anthelmintic Treatments in a Laboratory Colony of Wild-caught African Pouched Rats (*Cricetomys ansorgei*)

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African giant pouched rats (*Cricetomys* spp.) are large rodents native to subSaharan Africa. Wild-caught pouched rats identified as *Cricetomys ansorgei* (*n* = 49) were imported from Tanzania. A survey of gastrointestinal parasitism by fecal flotation revealed the presence of multiple parasites, including *Nippostrongylus* spp., *Heterakis* spp., *Trichuris* spp., *Hymenolepis* spp., *Raillietina* spp., and *Eimeria* spp. Oral self-administered fenbendazole (150 ppm), topical moxidectin (2 mg/kg), pyrantel pamoate (15 mg/kg), piperazine (100 mg/kg daily), and injectable ivermectin (0.25 mg/kg) were used to determine effective treatment options for the gastrointestinal parasites present in the colony. Pyrantel pamoate in a treat vehicle and piperazine in water bottles were easily administered and significantly reduced the numbers of animals shedding *Nippostrongylus* spp. and *Heterakis* spp. during the study. Moxidectin and ivermectin were clinically ineffective at reducing fecal egg shedding. Fenbendazole was most effective at clearing infection with *Trichuris* spp. Although 10 mg/kg praziquantel was ineffective, a single dose of 30 mg/kg praziquantel significantly reduced the number of African pouched rats that shed cestode embryos. A combination treatment may be necessary to successfully treat all parasites present in any given animal.

Abbreviations: APR, African giant pouched rat; FDR, false-discovery rate; GEE, generalized estimating equation; GSCS, generalized score χ^2

Rodents of the genus *Cricetomys,* collectively known as African giant pouched rats (APR), are large, social rodents native to north and central sub-Saharan Africa. Phenotypically APR resemble large rats, although they have distinct cheek pouches that function similarly to those of hamsters and contribute to their common name.[27] APR weigh as much as 2.8 kg and may reach up to 1 m in total length.[4] In their native range, APR may be kept as pets, used as a food source, or trained in ordnance detection.[4,15,25] In laboratory settings, APR are used primarily for scent detection and parasite transmission studies.[6-8,12,18,24]

The use of wild-caught APR in laboratories is confounded by the fact that they are a reservoir of several zoonotic infectious agents, including monkeypox virus and *Bartonella elizabethae*.[2,10] Transmission studies have shown APR to be a potential host for parasites such as *Giardia lamblia* and *Trypanosoma brucei*, as well as *Hymenolepis nana* (dwarf tapeworm), *Ancylostoma caninum* (canine hookworm), and *Strongyloides stercoralis* (threadworm).[5,8-10,14,16,17,20,22] In addition, *Cricetomys* spp. are known to host a commensal ectoparasitic earwig of the genus *Hemimerus*.[19] Although this earwig may serve as an intermediate host for endoparasites, APR commonly carry fleas, lice, and ticks, which may lead to infection with intestinal parasites.[9,17] However, very few data detailing effective treatments for these organisms are available in nontraditional or exotic animals used in laboratory studies. Instead, recommendations are based on extrapolation of effective treatments in more common species of laboratory rodents.[4]

Broad-spectrum anthelmintics can be used singly or in combination for the treatment of parasites in laboratory rodents. Fenbendazole, a benzimidazole with labeled effectiveness against ascarid roundworms, hookworms, whipworms, and select cestodes (*Taenia* spp.), is most often used in laboratory rodent populations to control pinworms.[23] Moxidectin is a milbemycin compound used most commonly in combination with imidocloprid for dogs and cats; it has labeled effectiveness against ascarids, hookworms, whipworms, and ectoparasites.[23] Ivermectin, a macrocyclic lactone, is used primarily as an ectoparasiticide, although it may be useful in treating roundworms in some livestock species.[23] When administered in drinking water, piperazine is used primarily as a treatment for pinworms in laboratory rodents.[23] Pyrantel pamoate is not often used in rodents but is available in commercial preparations for the treatment of ascarid roundworms in dogs, cats, and horses.[23]

The purpose of the current study was to determine effective protocols for elimination of gastrointestinal parasites present in a population of wild-caught APR from Tanzania identified as *Cricetomys ansorgei*.[21] Gross fecal examination and fecal flotations established that several gastrointestinal parasites, including hookworms (*Nippostrongylus* spp.), roundworms (*Heterakis* sp.), tapeworms (*Hymenolepis* spp., *Raillietina* spp., or *Taenia* spp.), whipworms (*Trichuris* spp.), and coccidia (*Eimeria* spp.) were present in this sample population. The primary hypothesis was that the application of fenbendazole or moxidectin would eliminate fecal egg shedding of hookworms and roundworms

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when used in combination with praziquantel for the treatment of cestodes. Although coccidial organisms weren't targeted in the current study, the number of animals shedding *Eimeria* spp. was monitored throughout treatment. Due to the failure of initial treatments to eliminate patent infections in APR, a second treatment protocol using ivermectin, piperazine, or pyrantel pamoate in combination with praziquantel was developed to identify an appropriate treatment for the remaining infected animals.

Materials and Methods

Wild-caught young-adult APR (n = 49; weight, 0.8 to 1.4 kg) were obtained from a single location in Tanzania and transported to the AAALAC-accredited Animal Resources Unit at Oklahoma State University (Stillwater, Oklahoma). APR were held in CDC-approved international quarantine prior to arrival at the university, and a complete physical exam was performed on all animals on arrival. Buccal swabs and whole-blood samples from all animals tested negative for monkeypox virus. An extended acclimation period (minimum, 90 d) was used prior to starting the treatment protocol.

Due to aggressive conspecific behavior, APR were housed individually in stainless steel commercial rabbit caging (24 in. × 24 in. × 16.75 in., Shor-Line, KS City, KS) with raised, wire-bottom flooring. Shredded newspaper bedding and a commercial rabbit hut (BioServ, Flemington, NJ) were provided for enrichment. Paper tray liners were placed under cages to facilitate removal of feces. Cages, water bottles, and enrichment devices were sanitized during weekly cage changes. APR were fed a diet of 50:50 rodent chow (5001 Laboratory Rodent Diet, LabDiet, St Louis, MO) and dog chow (Canine Maintenance, Hills Pet Nutrition, Topeka, KS) without restriction. All procedures were approved after review by the IACUC and the US Army Animal Care and Use Review Office. The pouched rats were maintained in accordance with current guidelines published in the *Guide for the Care and Use of Laboratory Animals* and AALAS position statements.[11]

Sample collection and analysis. Paper tray liners (Diamond Pads, Envigo, Indianapolis, IN) were changed 1 d prior to sample collection to ensure that fresh fecal samples were examined. After gross examination for tapeworm proglottids and adult worms, the texture and quality of fecal pellets were noted. APR feces were mixed with Sheather sugar solution and centrifuged according to a previously described procedure.[30] Unstained slides were scanned at 100× and 240× for qualitative identification of parasite eggs. Actual fecal egg counts were not performed, given that the purpose of treatment was to completely eliminate fecal egg shedding in all infected animals. Results of fecal flotations were reported as an absolute positive (+) or negative (–) change for the presence of each parasite. APR were considered negative when no parasite ova of any type were present on 2 sequential fecal flotations.

Any clinically ill APR that were euthanized during the study (n = 4) underwent full necropsy, after which gastrointestinal contents were submitted to the National Center for Veterinary Parasitology (Stillwater, OK) for collection and morphologic identification of any adult helminths and cestodes.

Anthelmintic treatment. ***Treatment phase 1.*** For the first treatment protocol, APR were assigned to 1 of 2 groups to receive either oral fenbendazole or topical moxidectin, according to the animal's sex and the presence of parasite ova identified on initial fecal flotation (Figure 1). Groups were balanced to prevent significant differences between the number of APR shedding different classes of gastrointestinal parasites. These agents were selected due to their labeled effectiveness against *Trichuris* spp. in dogs and against hookworms and roundworms in other species, such as rodents and domestic pets.[3,9,28] Nontreated control groups were not used for this study because of the need to treat animals for any parasites that may have compromised the health of the APR or university rodent colony or presented a health risk to human handlers. The study design is summarized in Figure 1, phase 1.

The oral fenbendazole treatment group consisted of 25 APR (10 female, 15 male), which received oral fenbendazole at a concentration of 150 ppm in water replacement gel packs (4 oz Napa Nectar, Systems Engineering Lab Group, Napa, CA) provided for 1 wk on, 1 wk off per application period. Water bottles were removed during this time to ensure accurate dosing and were replaced on cages after 1 wk. APR consumed multiple entire gel packs during each 1-wk period during which they were provided, and the number of fenbendazole-impregnated gel packs that were consumed was recorded throughout the treatment period.

The topical moxidectin treatment group consisted of 22 APR (12 female, 11 male), which received topical moxidectin (Cydectin, Bayer, Shawnee Mission, KS) between the shoulder blades at a dose of 0.2 mg/kg once per application period. APR were transferred from the home cage by using a transport box and restrained with a huck towel for safe medication application.

Medications were administered every 2 wk for 3 application periods. Applications were administered even when APR had negative fecal flotations during the treatment phase. APR with evidence of tapeworm proglottids on gross fecal examination or hexacanth embryos on fecal flotation (n = 18)—regardless of treatment group—were treated with 10 mg/kg praziquantel (Droncit, Bayer, Shawnee Mission, KS) subcutaneously at the time of observation. Because the effective dose and side effects of this medication have not been established in APR, the 10-mg/kg dose was chosen initially as a conservative dose effective against cestodes in dogs and cats.[23] Animals were monitored throughout the treatment period for adverse reactions to either medication. Qualitative fecal flotations were performed immediately after each treatment period; fecal flotations were performed twice on sequential fecal samples to confirm negative results. Applications of fenbendazole or moxidectin occurred every 2 wk for 3 application periods.

Treatment phase 2. After the initial protocol, 37 APR continued to shed parasite ova. Of these, 4 animals were shedding tapeworm proglottids only and were excluded from the following treatment groups. For the second treatment protocol, animals that continued to shed parasite ova (n = 33) were redistributed among 3 secondary treatment groups, which received subcutaneous injectable ivermectin, oral piperazine, or oral pyrantel pamoate (Figure 1, phase 2). Groups were balanced for the presence of hookworm and roundworm infections, with no significant difference between sexes or prior treatment groups. APR received medications every 2 wk for 2 treatment periods. APR remaining positive for tapeworms after the first treatment protocol, regardless of second treatment group, were given praziquantel (30 mg/kg SC).

The injectable ivermectin group consisted of 11 pouched rats (5 female, 6 male), of which 6 originated from the oral fenbendazole group and 5 from the topical moxidectin group. These animals received ivermectin (0.25 mg/kg SC; 1% injectable solution, Ivomec, Merial, Duluth, GA) once per treatment period.

The oral piperazine treatment group consisted of 11 pouched rats (4 female, 7 male), of which 6 were previously treated with topical moxidectin and 5 with oral fenbendazole. These animals

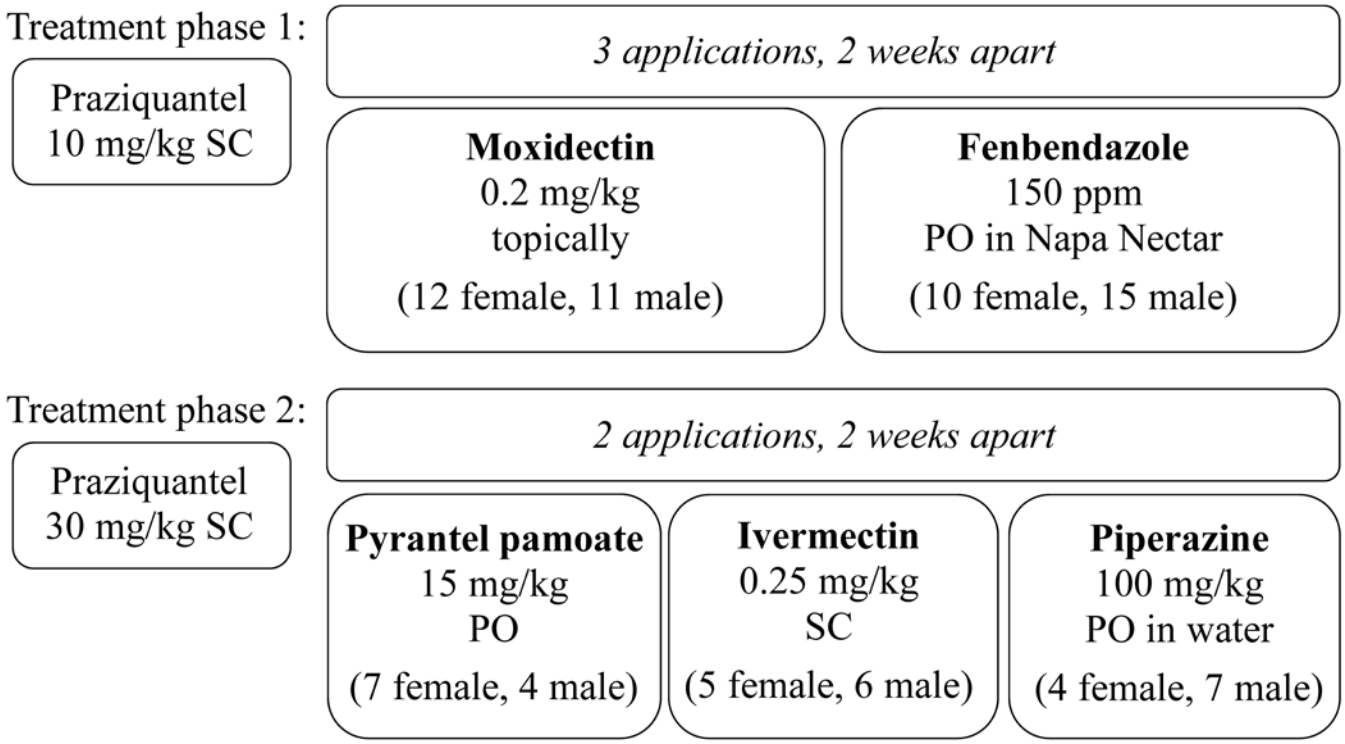

Figure 1. Study design for treatment of APR parasitic infection consisted of 2 treatment phases. In phase 1, animals received 3 applications of the treatment over a 6-wk period. In phase 2, animals received 2 applications of the treatment over a 4-wk period. All animals with patent cestode infections received praziquantel regardless of treatment group.

received oral piperazine (Wazine, Fleming Laboratories, Charlotte, NC) at a dose of 100 mg/kg daily in water bottles for 1 wk on, 1 wk off during each treatment period. Piperazine was added to a small volume of water and hung on APR cages. After consumption of the daily 100-mg/kg dose, the bottles were removed, and regular water bottles were replaced.

The oral pyrantel group consisted of 11 pouched rats (7 female, 4 male), of which 7 originated from the oral fenbendazole treatment group and 4 from the topical moxidectin group. These animals received pyrantel pamoate (Strongid T, Zoetis, Parsippany, NJ) administered at a dose of 15 mg/kg PO once per treatment period by using a peanut-butter treat vehicle given inside the home cage.

All animals were monitored throughout each treatment period for adverse reactions to the anthelmintic agents. Qualitative fecal flotations were performed immediately after each treatment period. Fecal flotations were performed on 2 sequential fecal samples to confirm negative results. During the study, applications were administered even when APR had negative fecal flotations during the treatment phase.

Statistical analysis. Confidence intervals for initial parasite surveys were generated by using Quantitative Parasitology 3.0.[26] Efficacy of each anthelmintic treatment for each gastrointestinal parasite was determined by using generalized linear models. Specifically, generalized estimating equations (GEE) were used to compare animal parasite burdens after treatment with those before treatment in each instance. In these models, the rat's microchip identification number was used as a repeated-subjects measure, and presence of infection was used as the dependent variable. We looked for main effects of sex, treatment (for example, oral fenbendazole or topical moxidectin during phase 1; injectable ivermectin, oral piperazine, or oral pyrantel in phase 2), and application (for example, baseline, first, second, or third treatment of the drug in phase 1; baseline, first, or second treatment in phase 2). Generalized score chi-square (GSCS) analysis was used for categorical analysis in conjunction with GEE models. Where specific comparisons between continuous variables were made, Wilcoxon rank-sum testing was used.

To be statistically conservative, we adjusted the α criteria by using the false-discovery rate (FDR) for multiple comparisons within each anthelmintic treatment regimen,[1] and adjusted *P* values are provided. A treatment was considered clinically effective when more than 90% of the APR in the treatment group ceased to shed ova.

Results

Initial parasite identification. Although external parasites, including lice, mites, and fleas, are commonly found on APR, these were not noted in animals upon arrival to the university. Prior to arrival, *Hemimerus* spp. were noted on wild-caught APR at the colony location in Tanzania but were not present on arrival at the university. Trichostrongyles were identified by the diagnostic lab as morphologically similar to *Nippostrongylus brasiliensis*, with eggs measuring 70 to 80 µm by 40.0 to 42.5 µm (Figure 2 A). Ascarids were morphologically similar to *Heterakis spumosa*, with eggs measuring 65 to 70µm by 45.0 to 47.5 µm (Figure 2 B). Whipworms were consistent with *Trichuris muris*, with eggs measuring 62.5 to 67.5 µm by 32.5 µm (Figure 2 C). Coccidial organisms measuring approximately 20 µm by 16 µm and containing a single operculum were preliminarily identified as *Eimeria* spp. (Figure 2 D). Adult tapeworms with ovoid hexacanth embryos measuring 52.7 to 65.0 µm by 37.5 to 55.0 µm were consistent with *Hymenolepis nana* (Figure 2 E). Proglottids noted in the feces of 8 pouched rats were microscopically identified as egg sacs containing hexacanth embryos most consistent with *Raillietina* tapeworms. At necropsy, one rat was identified with intrapericardial, retroperitoneal, and subcutaneous parasitic cysts preliminarily identified as *Taenia* spp. coenuri; a

Figure 2. Parasite ova recovered from Sheather sugar fecal flotation of *Cricetomys* spp. rats. (A) *Nippostrongylus brasiliensis*, (B) *Heterakis gallinarum,* (C) *Trichuris muris*, (D) *Eimeria* sp., (E) *Hymenolepis nana.* Magnification, 400×.

second APR had an unidentified adult tapeworm encysted in the liver.

Fecal flotation prior to treatment revealed that 48 of the 49 (98.0%) APR in the colony were infected with an enteric parasite. Furthermore, 45 of the 49 (91.8%) animals were coinfected with at least 2 types of gastrointestinal parasite, most commonly hookworms and roundworms (n = 13) or hookworms, roundworms, and coccidia (n = 9). In addition, 39 (79.6%) APR had ova consistent with *N. brasiliensis*, 38 (77.6%) had ova consistent with *Heterakis spumosa*, 13 (26.5%) had ova consistent with *T. muris*, and 15 (30.6%) had ova consistent with *Eimeria* spp. (Table 1). Although 6 APR (11.5%) had ova consistent with *H. nana* prior to the start of anthelmintic treatment, 35 (71.4%) were identified as intermittently shedding cestode embryos or proglottids during the treatment protocol.

Anthelmintic treatments. *Treatment phase 1.* Two animals were euthanized due to health concerns unrelated to the treatment protocol prior to the completion of the treatment phase. Of these, one APR received 2 applications of moxidectin prior to euthanasia and was excluded from further analysis.

APR in the oral fenbendazole treatment group were self-dosed by using gel packs impregnated with fenbendazole. On average, pouched rats consumed a total of 40.0 mg (range, 17.0 to 67.8 mg) of fenbendazole during the first treatment period, 46.8 mg (17.0 to 76.3 mg) during the second, and 58.8 (50.9 to 84.8 mg) during the third. No significant difference existed between the amount of fenbendazole ingested and whether an animal became completely free of parasites after 1, 2, or 3 treatment applications (Wilcoxon rank-sum test, $P > 0.13$ in all cases). Of the 25 animals in the oral fenbendazole treatment group, 8 were negative at the end of application period 3 (32% reduction). However, only *Trichuris* spp. were eliminated completely from this group.

Of the 22 APR that were assigned to the topical moxidectin group and received the full course of treatment, 2 were negative after the final application (8.7% reduction). The reduction in the number of APR with *Nippostrongylus*, *Heterakis*, and *Trichuris* infections was not clinically significant. In a majority of APR, application of topical moxidectin appeared to leave visible spots of alopecia, with some animals showing evidence of partial-thickness skin ulceration and scabbing at the application site after treatment.

The data (Table 2) show no main effects of sex or treatment for helminths and coccidia, but a main effect of application was seen for all intestinal parasites identified (Figure 3). Given the significant main effect, we investigated the overall effect of each drug over the course of treatment application. The drug itself (fenbendazole or moxidectin) is referred to as 'treatment' and the course of treatment (baseline or first, second, or third exposure to the drug) as 'application'.

Both oral fenbendazole and topical moxidectin significantly reduced the number of APR infected with hookworms (Wald χ^2: $39.543_{(3)}$, $P < 0.001$ for oral fenbendazole; and $31.750_{(3)}$, $P < 0.001$ for topical moxidectin). Pairwise comparisons indicated that the number of APR shedding parasites differed significantly between baseline and each application period for both oral fenbendazole (FDR-adjusted $\alpha = 0.03$; all $P < 0.001$) and topical moxidectin (all $P \leq 0.001$). However, there was no further significant reduction with increasing numbers of applications. In addition, intermittent shedding of hookworm ova, in which an animal had 2 or more negative fecal flotations but was positive in subsequent application periods, occurred in both treatment groups.

Furthermore, application of fenbendazole or moxidectin significantly reduced the number of APR shedding roundworm ova (Wald χ^2; oral fenbendazole: $16.245_{(3)}$, $P = 0.001$; topical moxidectin: $11.396_{(3)}$, $P = 0.01$). Pairwise comparisons indicated that the number of infected APR was significantly reduced by 2 or 3 applications of oral fenbendazole (FDR-adjusted $\alpha = 0.0375$; $P = 0.011$ and $P < 0.001$, respectively). In addition, the number of animals continuing to shed roundworm ova was significantly lower after the third application compared with the first and second applications ($P = 0.005$ and $P = 0.03$, respectively). Pairwise comparisons for topical moxidectin treatment of roundworms indicated that the number of APR with patent infections was significantly lower after 2 or 3 applications ($P = 0.02$ and $P = 0.001$, respectively). The number of APR shedding roundworm ova did not differ significantly between baseline and the first application ($P = 0.24$) or between the first and second application of topical moxidectin ($P = 0.12$). A third application of topical moxidectin was required to significantly reduce the number of APR shedding roundworm ova compared with either 1 or 2 applications ($P = 0.004$ and $P = 0.03$, respectively).

Both treatments significantly reduced the number of APR shedding whipworm eggs (Wald χ^2; oral fenbendazole: $8.228_{(3)}$, $P = 0.04$; topical moxidectin: $11.396_{(3)}$, $P = 0.01$). Pairwise comparisons among fenbendazole applications showed that 2 treatments were required to significantly ($P = 0.008$) reduce the number of animals shedding whipworm ova; all other pairwise comparisons for oral fenbendazole were not significant (all $P \geq 0.017$; FDR-adjusted $\alpha = 0.017$). The number of APR shedding whipworm ova was significantly reduced by application of moxidectin for 2 ($P = 0.002$) or 3 ($P = 0.006$) applications; no other comparisons were significantly different (all $P > 0.04$).

Unlike the treatments for the other parasites previously discussed, only oral fenbendazole significantly reduced the number of APR that shed coccidia (Wald χ^2; oral fenbendazole: $10.719_{(3)}$, $P = 0.01$; topical moxidectin: $7.177_{(3)}$, $P = 0.07$). Pairwise comparisons indicated that the number of animals shedding coccidia decreased significantly after 1, 2, or 3 applications of fenbendazole (FDR-adjusted $\alpha = 0.029$; $P \leq 0.002$); or 1, 2, or 3 applications of moxidectin ($P \leq 0.01$). No other pairwise comparisons for oral fenbendazole or topical moxidectin were significantly different (all $P = 1.0$).

Table 1. Summary of initial gastrointestinal parasite prevalence in *Cricetomys ansorgei* of Tanzanian origin by sex

	Male (n = 26)		Female (n = 23)		Total (n = 49)	
Parasites	Prevalence (no. [%])	95% confidence interval (%)	Prevalence (no. [%])	95% confidence interval (%)	Prevalence (no. [%])	95% confidence interval (%)
Nippostrongylus brasiliensis (a, o)	22 (84.62)	65.64–94.56	16 (69.57)	47.79–85.48	38 (77.55)	63.39–87.37
Heterakis spumosa (a, o)	21 (80.77)	61.70–92.10	18 (78.26)	56.66–91.01	39 (79.60)	66.27–89.13
Trichuris muris (o)	7 (26.92)	12.86–46.50	6 (26.09)	12.03–47.78	13 (26.53)	15.90–40.74
Eimeria spp. (o)	10 (38.46)	21.17–57.78	5 (21.74)	8.99–43.34	15 (30.61)	19.19–44.86
Hymenolepis nana (a, o)	3 (11.54)	3.22–30.37	3 (13.04)	3.66–32.35	6 (11.50)	3.22–30.37

a, adult; o, ova
Adult specimens collected at necropsy.

Table 2. Summary of phase 1 treatment results regarding prevalence of selected intestinal parasites in African giant pouched rats

	Hookworm (*Nippostrongylus* spp.)		Roundworm (*Heterakis* spp.)		Whipworm (*Trichuris* spp.)		Coccidia (*Eimeria* spp.)		Tapeworm[a] (*Hymenolepis* spp.)	
GEE model	GSCS (df)	*P*	GSCS (df)	*P*	GSCS (df)	*P*	GSCS (df)	*P*	GSCS (df)	*P*
Sex	0.326 (1)	0.568	0.052 (1)	0.819	0.010 (1)	0.920	0.466 (1)	0.495	0.001(1)	0.981
Treatment	1.049 (1)	0.306	3.565 (1)	0.059	0.003 (1)	0.959	1.360 (1)	0.244	10.484 (1)	0.001
Application	21.488 (3)	<0.001	11.282 (3)	0.010	11.750 (3)	0.008	9.600 (3)	0.022	16.759 (3)	0.001
Treatment across applications										
	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*
Fenbendazole	39.543 (3)	<0.001	16.245 (3)	0.001	8.228 (3)	0.042	10.719 (3)	0.013	6.650 (3)	0.084
Moxidectin	31.750 (3)	<0.001	11.369 (3)	0.010	11.047 (3)	0.011	7.7177 (3)	0.066	33.739 (3)	<0.001
Treatment within applications										
	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*
Baseline	1.094 (1)	0.296	3.552 (1)	0.059	0.004 (1)	0.949	1.300 (1)	0.254	6.112 (1)	0.013
Application 1	1.087 (1)	0.297	4.446 (1)	0.035	0.004 (1)	0.950	0.804 (1)	0.370	1.871 (1)	0.171
Application 2	1.052 (1)	0.305	3.801 (1)	0.051	0.004 (1)	0.950	1.070 (1)	0.301	9.632 (1)	0.002
Application 3	1.109 (1)	0.292	3.524 (1)	0.060	0.004 (1)	0.950	1.119 (1)	0.290	13.593 (1)	<0.001

Generalized linear model results by using a generalized estimated equation (GEE) are presented. Main effects for sex (female or male), treatment (fenbendazole or moxidectin), and application period (baseline and applications 1 through 3) are reported by using generalized score χ^2 (GSCS), degrees of freedom (df), and the corresponding *P* value. Wald χ^2, df, and *P* are reported for overall test results comparing treatment across applications (that is, the efficacy of each drug over the course of treatment) and the treatment within application (that is, the difference for each drug between baseline and applications 1 through 3).
[a]Note that significant differences over treatment represent increases in tapeworm prevalence.

Finally, although there was no main effect of sex (GSCS = $0.001_{(1)}$, $P = 0.98$) for tapeworms, this was the only phase 1 treatment where a main effect was identified for both treatment (GSCS = $10.484_{(1)}$, $P = 0.001$) and application (GSCS = $16.759_{(3)}$, $P = 0.001$). Treatment for tapeworms differed from other phase 1 treatments in that efficacy differed between the 2 drugs. Specifically, at baseline (Wald $\chi^2 = 6.112_{(1)}$, $P = 0.01$), application 2 (Wald $\chi^2 = 9.632_{(1)}$, $P = 0.002$), and application 3 (Wald $\chi^2 = 13.593_{(1)}$, $P < 0.001$), the number of APR shedding tapeworm embryos was higher for topical moxidectin than oral fenbendazole even though APR in both groups received praziquantel. However, topical moxidectin and oral fenbendazole did not differ in their efficacy for treating tapeworms at application 1 (Wald $\chi^2 = 1.871_{(1)}$, $P = 0.17$), indicating that, as expected, neither drug was more efficacious in treating cestodes than the other. In contrast to the other parasites seen on fecal flotation, the number of tapeworm-infected APR actually increased over the course of treatment. Specifically, infections significantly increased for topical moxidectin (Wald $\chi^2 = 33.739_{(3)}$, $P < 0.001$) and tended to increase for oral fenbendazole (Wald $\chi^2 = 6.650_{(3)}$, $P = 0.08$).

Treatment phase 2. Two APR were euthanized due to health concerns unrelated to the treatment protocol prior to the start of the treatment phase. These animals were excluded from further analysis.

One of the 11 animals treated with injectable ivermectin was negative at the end of treatment period 2 (9.1% reduction). Reductions in parasite burden were not clinically significant throughout this treatment. Of the 11 animals treated with oral piperazine, 9 were negative at the end of the second treatment period (81.8% reduction). Of the 11 animals treated with oral pyrantel pamoate, 10 had negative fecal flotations at the end of the second treatment period (90.9% reduction).

As earlier, the effects of each drug are referred to as 'treatment' (ivermectin, piperazine, or pyrantel pamoate) and the course of treatment (baseline and first and second exposures to drug) as 'application.'

No significant difference was identified between sexes or treatments for any of the phase 2 treatments for hookworms (GSCS = $0.347_{(1)}$, $P = 0.56$; $0.661_{(2)}$, $P = 0.72$, respectively; Table 3), but a main effect of application (GSCS = $10.723_{(2)}$, $P = 0.005$) was identified. Examining how each drug affected infection over the course of application showed that, although oral piperazine and oral pyrantel significantly reduced the number of APR that shed hookworm ova (Wald $\chi^2 = 16.610_{(2)}$, $P < 0.001$ for oral piperazine; Wald $\chi^2 = 14.471_{(2)}$, $P = 0.001$ for oral pyrantel), the number of APR with fecal egg shedding actually increased significantly from baseline during injectable ivermectin treatment ($17.120_{(2)}$, $P < 0.001$). Pairwise comparisons indicated that the

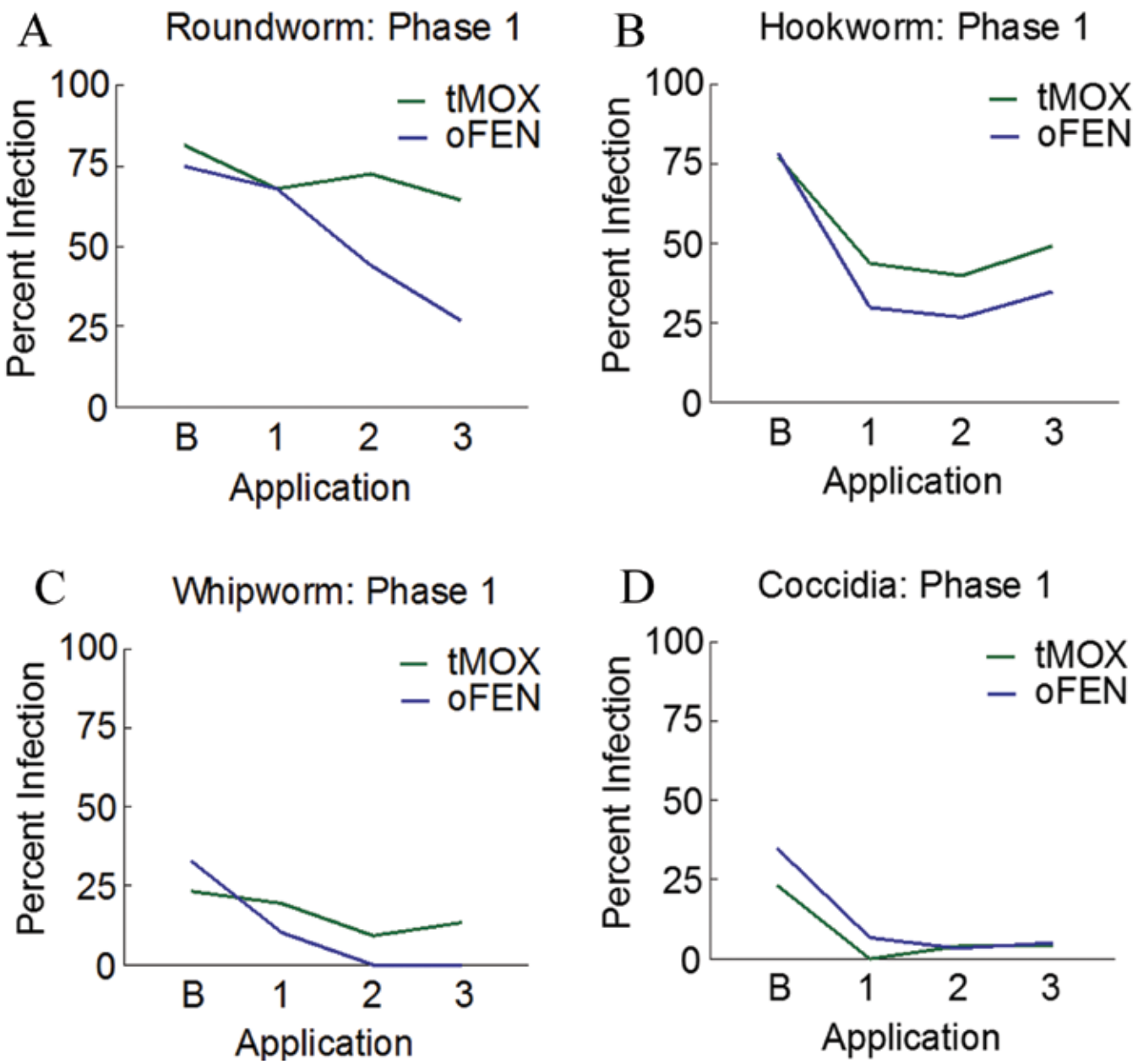

Figure 3. The percentage of APR with patent infections of selected gastrointestinal parasites from baseline (B) through 3 applications of either topical moxidectin (tMOX, green) or oral fenbendazole (oFEN, blue).

baseline number of APR shedding ova was lower than that after 1 or 2 applications of injectable ivermectin (FDR-adjusted $\alpha = 0.0389$; $P = 0.001$ and $P < 0.001$, respectively), but the number of APR shedding ova did not differ between 1 and 2 applications of injectable ivermectin ($P = 0.06$). In contrast, oral piperazine applications 1 and 2 both significantly reduced shedding of hookworm ova compared with baseline ($P = 0.001$ and $P < 0.001$, respectively), but multiple treatments did not significantly decrease ($P = 0.08$) the number of APR that continued to shed ova compared with that after a single treatment.

Lastly, the number of infected APR significantly decreased between baseline and applications 1 ($P = 0.001$) and 2 ($P < 0.001$) after treatment with oral pyrantel (Figure 4). However, as seen with piperazine, there was no significant decrease in the number of positive APR after multiple treatments. As with treatment phase 1, APR shed hookworm ova intermittently during treatment phase 2.

GEE modeling of treatments for roundworms revealed no main effect of sex (GSCS = $1.368_{(1)}$, $P = 0.24$) but did identify a main effect for both treatment (GSCS = $10.263_{(2)}$, $P = 0.006$) and application (GSCS = $14.629_{(2)}$, $P = 0.001$). The overall results for treatment indicated that injectable ivermectin, oral piperazine, and oral pyrantel significantly differed in their efficacy in treating roundworms over the course of phase 2 (that is, baseline through application 2; injectable ivermectin: Wald $\chi^2 = 19.435_{(2)}$, $P < 0.001$; oral piperazine: $17.029_{(2)}$, $P < 0.001$; oral pyrantel: $14.711_{(2)}$, $P = 0.001$). Among these pairwise differences, after adjusting for multiple comparisons (FDR-adjusted $\alpha = 0.039$), significant differences were found between injectable ivermectin and oral piperazine ($P = 0.01$, $P < 0.001$, $P = 0.002$), and injectable ivermectin and oral pyrantel ($P < 0.001$, $P < 0.001$, $P < 0.001$) at baseline, application one, and application 2, respectively. No pairwise differences between oral piperazine and oral pyrantel were found at any application. In addition to detecting a

Table 3. Summary of Phase 2 treatment results on prevalence of selected intestinal parasites in African giant pouched rats

	Hookworms (*Nippostrongylus* spp.)		Roundworms (*Heterakis* spp.)		Whipworms[a] (*Trichuris* spp.)		Coccidia (*Eimeria* spp.)		Tapeworms (*Hymenolepis* spp.)	
GEE model	GSCS (df)	*P*	GSCS (df)	*P*	GSCS (df)	*P*	GSCS (df)	*P*	GSCS (df)	*P*
Sex	0.347 (1)	0.556	1.368 (1)	0.242	0.387 (1)	0.534	0.411 (1)	0.521	0.064 (1)	0.801
Treatment	0.661 (2)	0.719	10.263 (2)	0.006	0.387 (1)	0.534	0.871 (2)	0.647	0.070 (2)	0.966
Application	10.723 (2)	0.005	14.629 (2)	0.001	2.185 (2)	0.335	4.333 (2)	0.115	7.361 (2)	0.025
Treatment across applications										
	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*
Ivermectin	17.120 (2)	<0.001	13.578 (2)	0.001	0.873 (1)	0.350	2.559 (2)	0.278	11.901 (2)	0.003
Piperazine	16.610 (2)	<0.001	17.014 (2)	<0.001	na	na	3.013 (2)	0.222	6.371 (2)	0.041
Pyrantel pamoate	14.471 (2)	0.001	13.119 (2)	0.001	1.766 (1)	0.184	2.582 (2)	0.275	6.082 (2)	0.048
Treatment within applications										
	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*	Wald χ^2 (df)	*P*
Baseline	0.923 (2)	0.630	19.435 (2)	<0.001	0.552 (1)	0.457	0.537 (2)	0.765	0.072 (2)	0.965
Application 1	0.831 (2)	0.660	17.029 (2)	<0.001	0.344 (1)	0.558	0.779 (2)	0.677	0.072 (2)	0.964
Application 2	0.767 (2)	0.681	14.711 (2)	0.001	0.344 (1)	0.558	1.005 (2)	0.605	0.071 (2)	0.965

na, not applicable

Generalized linear model results by using a generalized estimated equation (GEE) are presented. Main effects for sex (female or male), treatment (ivermectin, piperazine, or pyrantel pamoate), and application (baseline and applications 1 and 2) are reported by using generalized score χ^2 (GSCS), degrees of freedom (df), and the corresponding *P* value. Wald χ^2, df, and *P* are reported for overall test results comparing treatment across applications (that is, the efficacy of each drug over the course of treatment), and treatment within application (that is, the difference for each drug between baseline and applications 1 and 2).

[a]Whipworm results do not include piperazine in the analysis because no rats receiving this treatment were infected with this parasite.

difference among the drugs, a significant application effect was seen over different application periods for all 3 drugs (Wald $\chi^2 = 13.578_{(2)}$, $P = 0.001$; Wald $\chi^2 = 17.014_{(2)}$, $P < 0.001$; and Wald $\chi^2 = 13.119_{(2)}$, $P = 0.001$). Among these pairwise differences, after adjusting for multiple comparisons (FDR-adjusted $\alpha = 0.039$), significant differences were found between baseline and application 1 ($P = 0.01$, $P < 0.001$, $P = 0.001$) and application 2 ($P = 0.001$, $P < 0.001$, $P < 0.001$), but not between application 1 and 2 ($P = 0.70$, $P = 0.72$, $P = 0.71$) for injectable ivermectin, oral piperazine, and oral pyrantel, respectively.

Unfortunately, none of the APR that received oral piperazine had patent whipworm infections at the time of treatment, due to an inability to counterbalance all animals across all treatments and infection rate for all parasites a priori. As a result, oral piperazine was not analyzed in the GEE model for whipworm treatment. In contrast to the other parasites, whipworm infection showed no main effects for sex (GSCS = $0.387_{(1)}$, $P = 0.53$), treatment (GSCS = $0.387_{(1)}$, $P = 0.53$), or application (GSCS = $2.185_{(1)}$, $P = 0.33$). Consequently there were no overall effects for drug at each treatment (Wald $\chi^2 = 0.552_{(1)}$, $P = 0.46$; Wald $\chi^2 = 0.344_{(1)}$, $P = 0.57$; Wald $\chi^2 = 0.34_{(1)}$, $P = 0.56$) or across each treatment (Wald $\chi^2 = 0.873_{(1)}$, $P = 0.35$; Wald $\chi^2 = 1.766_{(1)}$, $P = 0.18$).

The GEE model for *Eimeria* spp. showed no main effects of sex (GSCS = $0.411_{(1)}$, $P = 0.52$), treatment (GSCS = $0.871_{(2)}$, $P = 0.65$), or application (GSCS = $4.333_{(2)}$, $P = 0.12$). As seen with whipworms, there were no overall effects for drug at each treatment (Wald $\chi^2 = 0.537_{(2)}$, $P = 0.77$; Wald $\chi^2 = 0.779_{(2)}$, $P = 0.68$; Wald $\chi^2 = 1.005_{(2)}$, $P = 0.61$) or across each treatment (Wald $\chi^2 = 2.559_{(2)}$, $P = 0.28$; Wald $\chi^2 = 3.013_{(2)}$, $P = 0.22$; Wald $\chi^2 = 2.582_{(1)}$, $P = 0.28$).

As expected, GEE modeling of phase 2 treatments showed no main effects of sex (GSCS = $0.064_{(1)}$, $P = 0.80$) or treatment (GSCS = $0.070_{(2)}$, $P = 0.97$) for tapeworms, but our model did show a main effect of application (GSCS = $7.361_{(2)}$, $P = 0.025$), which likely is confounded due to concurrent application of high-dose praziquantel. Although the number of patent tapeworm infections changed over the course of treatment (injectable ivermectin: Wald $\chi^2 = 11.901_{(2)}$, $P = 0.003$; oral piperazine: Wald $\chi^2 = 6.371_{(2)}$, $P = 0.04$; oral pyrantel: Wald $\chi^2 = 6.082_{(2)}$, $P = 0.05$), the pattern of tapeworm infection in phase 2 differed from previous cases. Specifically, pairwise comparisons indicated only one difference was found for drug efficacy over application. In this instance, the baseline infection rate was significantly lower than the second application for injectable ivermectin (FDR-adjusted $\alpha = 0.011$; $P = 0.004$). All other pairwise comparisons were non-significant (all $P \geq 0.016$).

Praziquantel treatment. Any APR identified as having patent tapeworm infection by gross fecal examination for proglottids or identification of hexacanth embryos on fecal flotation was treated with praziquantel concurrent with other treatment applications. Fecal flotations performed throughout the first treatment protocol identified 23 APR as shedding cestode embryos consistent with *Hymenolepis* spp. A low-dose treatment of praziquantel (10 mg/kg) was used in these animals, which did not reduce shedding of proglottids in the feces after multiple doses.

Concurrent with the second treatment phase, all APR with continuing patent *Hymenolepis* spp. ($n = 23$) or *Raillietina* spp. ($n = 7$) infections were treated with 30 mg/kg injectable praziquantel. Because APR were treated at the time of identification of patent cestode infection, treatment periods were not coincident in all animals. Only those APR ($n = 16$) that were identified at baseline and received 2 consecutive applications of praziquantel were included for analysis. After one application period, 3 of the 16 APR continued to shed tapeworm embryos (81.2% reduction). A significant association existed between treatment with praziquantel and reduction in the amount of animals with continued patent infections (adjusted α after Bonferroni correction for multiple comparisons, 0.002; Pearson χ^2 test, $\chi^2 = 18.656$, df = 1, $P < 0.001$). A second application period did not significantly reduce the number of animals shedding embryos in the feces ($P = 1.0$).

Discussion

APR from the Tanzanian colony had a variety of gastrointestinal parasites with a much higher prevalence of infection

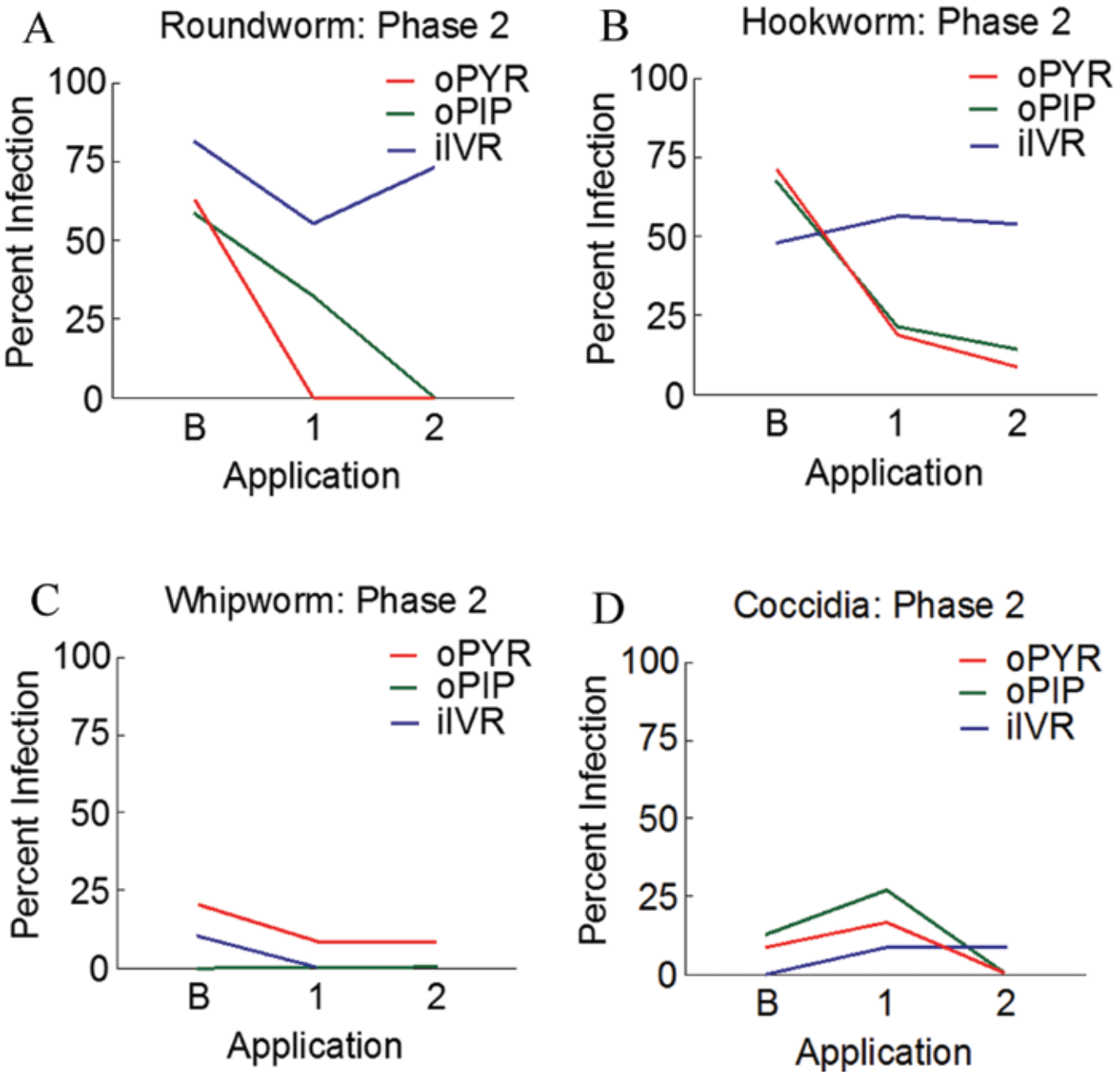

Figure 4. The percentage of APR with patent infections of selected gastrointestinal parasites from baseline (B) through 2 applications of oral pyrantel (oPYR, red), oral piperazine (oPIP, green), or injectable ivermectin (iIVR, blue).

(98%) than that found in previous surveys of *Cricetomys* spp.[9,17,20] However, APR in the current colony were a different species, *C. ansorgei*, and from a different geographic range than those in previous studies. In addition, according to previous surveys,[17] higher parasite burdens can be expected with adult animals, such as those in the current study. *N. brasiliensis* and *H. spumosa* were the most common eggs found on fecal flotation, with more than 75% of all APR exhibiting fecal egg shedding of these parasites. *N. brasiliensis* is a common parasite of pouched rats and embeds itself in the proximal small intestine of host animals.[9] Although ectoparasites such as fleas and ticks may serve as vectors for some parasites in APR, no external parasites were identified after the animals' arrival to the university, making it unlikely that these could contribute to reinfection during the current study.

Although small *Eimeria* spp. have been identified previously in APR,[29] no prevalence data have been reported to date. These organisms had a relatively high prevalence in the study colony (30.6%), but they did not appear to cause any associated symptoms prior to treatment. *Eimeria* spp. were not targeted for treatment because of their host specificity. However, initial treatment with fenbendazole and moxidectin appeared to significantly decrease the number of APR shedding coccidia.

Intermittent shedding of *Heterakis* spp. hookworm ova was noted during both phases 1 and 2 of treatment, indicating that APR may have increased reinfection rates with these species, possibly due to coprophagy, or that 2-wk intervals of treatment were too short to ensure that larval forms of this parasite were sufficiently mature to be affected by the selected treatments.

Treatments in phase 1 were chosen based on their likely efficacy against both hookworms and roundworms (*Nippostrongylus* and *Heterakis* spp.), whereas fenbendazole has known action against whipworms (*Trichuris* spp.).[23] We chose conservative doses due to the lack of information regarding efficacy and side effects of treatment in this species. GEE modeling indicated that phase 1 treatment significantly reduced the number of APR with patent gastrointestinal helminths and coccidial infection, whereas the number of animals with patent tapeworm infections actually increased. A single dose of moxidectin or fenbendazole was just as effective as multiple doses in reducing the number of APR shedding hookworm or roundworm ova. Both oral fenbendazole and topical moxidectin significantly reduced the number of APR shedding hookworms, roundworms, or whipworms when each parasite class was considered individually. However, as expected, fenbendazole was the only treatment that significantly reduced the number of APR shedding whipworm eggs. Furthermore, given the local skin reaction present in APR that received moxidectin, care should be taken when using this agent topically in this species. Although moxidectin is often used at a much higher dose in cats and rodents (2.5 mg/kg),[23] increased doses of moxidectin were not pursued because of the presence of lesions in APR at the dose of 0.2 mg/kg.

When self-administered in gel packs, fenbendazole was statistically effective in reducing infection with most of the parasites prevalent in APR. However, when treating wild-caught pouched rats, fenbendazole may be useful only as an adjunct to other therapies because it does not appear to clinically eliminate other gastrointestinal parasites even when given in multiple applications. Although statistical differences in parasite burden were achieved with only 1 or 2 applications for most parasites, only 8 of 25 pouched rats in this treatment group were completely cleared of all targeted parasites after 3 treatment periods. Differences in self-administration of the gel pack and low overall ingestion may have contributed to the lack of efficacy of this medication. However, no significant difference existed between the amount of fenbendazole ingested and an animal being positive or negative for parasites at the end of any application period. Fenbendazole dosage in rodents is typically 20 to 50 mg/kg daily for the treatment of pinworms;[23] in the current study, APR consumed only 1.89 to 12.11 mg/kg daily during all application periods, which may be a significant barrier to the efficacy of this treatment. It is possible that fenbendazole may show increased efficacy with a larger sample size or with higher average self-dosing or bolus dosing.

In phase 2, animals that previously were exposed to fenbendazole or moxidectin and that had continued patency of gastrointestinal parasite infection were treated with injectable ivermectin, oral piperazine, or oral pyrantel pamoate. Treatments in phase 2 were chosen both to ensure APR received a more controlled amount of drug and that handling was minimized where possible during drug application. GEE modeling indicated that all 3 drugs were effective at further reducing the number of APR shedding hookworm and roundworm ova. In combination with praziquantel, these 3 drugs also had a significant effect on the number of patent tapeworm infections in the colony.

Oral pyrantel pamoate at 15 mg/kg and oral piperazine at 100 mg/kg were effective in the current study, significantly decreasing the number of APR with fecal egg shedding after only 2 treatments. In addition, the ease of administration of pyrantel and piperazine confers an advantage above avermectins, in that APR are spared the stress associated with handling while receiving these treatments. Although doses in the range of 200 to 600 mg/kg daily are commonly used in laboratory rodents to treat pinworms,[23] a dose of 100 mg/kg daily was effective at reducing the number of APR shedding hookworm and roundworm eggs in the current study. In addition, despite the common use of avermectins to treat multiple parasites in conventional rats,[4] whipworm and coccidia in APR appeared to be completely resistant to treatment with these medications, and ivermectin appeared to be the least effective among the medications evaluated. Although piperazine was not analyzed for the treatment of whipworms, neither ivermectin nor pyrantel pamoate was effective in treating this class of parasites in APR.

Initially, *H. nana* was the least common parasite identified. Whether APR may serve as a reservoir for human infection is unknown.[13] Nevertheless, the high prevalence of this parasite in human and rodent populations throughout the APR's range, the use of this species as a source of meat, and the ability of rodent *H. nana* strains to infect other species make it likely that APR could serve as a host in the transmission of these parasites to humans.[15,17,20,22] Decreased recovery from initial fecal flotations may have been due to the high specific gravity of the flotation solution used and the fact that tapeworm embryos are passed in proglottids rather than distributed throughout the feces, as is typical for helminths and coccidial ova. Increasing sensitivity in proglottid detection led to increased numbers of APR identified as having patent tapeworm infections. No significant side effects were noted during administration of either 10 or 30 mg/kg praziquantel. The 10-mg/kg dose of praziquantel was ineffective in eliminating egg shedding. However, a 30-mg/kg dose of praziquantel was sufficient to decrease fecal egg shedding in a significant number of APR. Despite the apparently common shedding of *Hymenolepis* spp. in the feces, few *Raillietina* spp. proglottids or embryos were recovered on fecal flotation from the Tanzanian APR. The significant difference between treatment applications during phases 1 and 2 was confounded by concurrent application of praziquantel during both phases. Interestingly, unlike with moxidectin, tapeworm incidence did not significantly increase under fenbendazole treatment, suggesting perhaps that fenbendazole may play a role in preventing increased patency of cestode infection when animals are receiving concurrent praziquantel treatment (Table 2).

Although statistical significance indicates whether treatments are effective in reducing the number of animals shedding a given parasite, the clinical significance of whether the animals were completely free of parasites was the ultimate goal of this study. None of the treatments, during the time of study, were clinically effective in completely eliminating all parasites from any single treatment group. As demonstrated here, wild-caught APR host several classes of intestinal parasites which may present a risk to established rodent colonies or animal care staff. Combination treatments and environmental management may be necessary to completely eliminate parasites present in wild-caught APR, depending on the parasite present. Coprophagy by rodents, including pouched rats, may be a continuing source of reinfection with single-host gastrointestinal parasites, making repeated treatments based on the life cycle of the targeted parasite necessary. Reducing the transmission of parasite vectors and decreasing fomites by separating animals during treatment and thoroughly sanitizing caging and enrichment devices may help to reduce reinfection rates throughout the treatment period, allowing complete elimination of targeted single-host parasites in wild-caught rodents such as APR.

In conclusion, fenbendazole was effective in reducing the number of APR shedding most parasites in phase 1. Similarly, piperazine and pyrantel pamoate were most effective in

reducing the number of APR shedding gastrointestinal parasites, usually after a single treatment, in phase 2. Although a statistically significant reduction in the number of animals with patent gastrointestinal parasite infections was common in most cases, clinically significant reduction (greater than 90% reduction in number of animals with patent infection) of parasites was rare. That the orally administered medications were the most effective suggests that when the dose can be better controlled (that is, by decreasing variability of self-administration and resultant potentially inconsistent exposure to medication), treatment efficacy might be increased with consistent administration. Moreover, complete elimination necessitates continued monitoring of fecal flotations and repeated treatments of positive APR. A single 30-mg/kg subcutaneous dose of praziquantel was effective to eliminate patency of cestode infections in most animals. Subsequent to the current study, APR at our institution were treated with a combination of oral pyrantel pamoate and fenbendazole with praziquantel (30 mg/kg SC) according to the results of fecal flotation. Further study is necessary to determine effective treatments for other parasites that may be present in wild-caught APR from other colonies or other ranges.

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References

1. **Benjamini Y, Hochberg Y.** 1995. Controlling the false-discovery rate: a practical and powerful approach to multiple testing. Jl Stat Soc B (Methodological) **57:**289–300.
2. **Billeter SA, Borchert JN, Atiku LA, Mpanga JT, Gage KL, Kosoy MY.** 2014. *Bartonella* species in invasive rats and indigenous rodents from Uganda. Vector Borne Zoonot Dis **14:**182–188.
3. **Bowman DD, Legg W, Stansfield DG.** 2002. Efficacy of moxidectin 6-month injectable and milbemycin oxime–lufenuron tablets against naturally acquired *Trichuris vulpis* infections in dogs. Vet Ther **3:**286–289.
4. **Cooper RG**. 2008. Care, husbandry, and diseases of the African giant rat (*Cricetomys gambianus*). J S Afr Vet Assoc **79:**62–66.
5. **Derouin F, Roffi J, Diallo PB, Dedet JP.** 1978. [Value of *Cricetomys gambianus* in the study of experimental trypanosomiasis from *Trypanosoma gambiense*. Methods for mass preparation of antigen and purification of serum exoantigen.] C R Seances Soc Biol Fil **172:**388–392 [[Article in French]].
6. **Desikan P.** 2013. Rapid diagnosis of infectious diseases: the role of giant African pouched rats, dogs, and honeybees. Indian J Med Microbiol **31:**114–116.
7. **Dipeolu OO, Akinboade OA.** 1981. Transmission of *Anaplasma marginale* from a naturally infected wild African giant rat (*Cricetomys gambianus*, Waterhouse) to a calf in Nigeria. Vet Parasitol **8:**337–339.
8. **Dipeolu OO, Akinboade OA, Ogunji F, Bobade PA, Kasali OB.** 1981. Observations on African giant rats (*Cricetomys gambianus*, Waterhouse) experimentally infected with salivarian trypanosomes. Bull Anim Health Prod Afr **29:**393–397.
9. **Ekeh FN, Ekechukwu NE.** 2009. Ecto and gut parasitic fauna of the African giant rat (*Cricetomys gambianus*) in a semiurban tropical community. Anim Res Int **6:**1082–1085.
10. **Hutson CL, Lee KN, Abel J, Carroll DS, Montgomery JM, Olson VA, Li Y, Davidson W, Hughes C, Dillon M, Spurlock P, Kazmierczak JJ, Austin CC, Miser L, Sorhage FE, Howell J, Davis JP, Reynolds MG, Braden Z, Karem KL, Damon IK, Regnery RL.** 2007. Monkeypox zoonotic associations: insights from laboratory evaluation of animals associated with the multistate US outbreak. Am J Trop Med Hyg **76:**757–768.
11. **Institute for Laboratory Animal Research.** 2011. Guide for the care and use of laboratory animals, 8th ed. Washington (DC): National Academies Press.
12. **Mahoney A, Weetjens BJ, Cox C, Beyene N, Reither K, Makingi G, Jubitana M, Kazwala R, Mfinanga GS, Kahwa A, Durgin A, Poling A.** 2012. Pouched rats' detection of tuberculosis in human sputum: comparison to culturing and polymerase chain reaction. Tuberc Res Treat **2012:**1–5.
13. **Macnish MG, Morgan UM, Behnke JM, Thompson RCA.** 2002. Failure to infect laboratory rodent hosts with human isolates of *Rodentolepis* (=*Hymenolepis*) *nana.* J Helminthol **76:**37–43.
14. **Majewska AC.** 1994. Successful experimentation infections of a human volunteer and Mongolian gerbils with *Giardia* of animal origin. Trans R Soc Trop Med Hyg **88:**360–362.
15. **Malekani JM.** 2009. *Cricetomys* farming for improving animal production in developing countries. [Cited 25 March 2014]. Available at: http://www.orskovfoundation.org/files/communityprojects_congo002.pdf
16. **Massussi JA, Massussi JA, Mbida Mbida JA, Djieto-Lordon C, Njiokou F, Laveissiére C, van der Ploeg JD.** 2010. Diversity and spatial distribution of vectors and hosts of *T. brucei gambiense* in forest zones of Southern Cameroon: epidemiological implications. Acta Trop **114:**44–48.
17. **Mbaya AW, Kumshe HA, Luka J, Madara AM.** 2011. Parasitic infections of the African giant rat (*Cricetomys gambianus*) in the semiarid region of northeastern Nigeria. NigerVet J **32:**21–25.
18. **Mgode GF, Weetjens BJ, Nawrath T, Lazar D, Cox C, Jubitana M, Mahoney A, Kuipers D, Machang'u RS, Weiner J, Schulz S, Kaufmann SH.** 2012. *Mycobacterium tuberculosis* volatiles for diagnosis of tuberculosis by *Cricetomys* rats. Tuberculosis (Edinb) **92:**535–542.
19. **Mogbo TC, Akunne CE.** 2014. Ecological survey of earwigs (*Hemimerus talpoides*) as ectoparasites of wild African giant rat (*Cricetomys gambianus*) in Awka, Nigeria. Am J Zool Res **2:**22–24.
20. **Okoye IC, Obiezue RNN.** 2008. A survey of the gut parasites of rodents in Nsukka ecological zone. Anim Res Int **5:**846–847.
21. **Olayemi A, Nicolas V, Hulselmans J, Missoup AD, Fitchet-Calvet E, Amundala D, Dudu A, Dierckx T, Wendelen W, Leirs H, Verheyen E.** 2012. Taxonomy of the African giant pouched rats (Nesomyidae: *Cricetomys*): molecular and craniometric evidence support an unexpected high species diversity. Zool J Linn Soc **165:**700–719.
22. **Olude MA, Ajayi OL, Adebayo AO, Akande FA, Olugbogi EI.** 2010. Intestinal intussusception due to concurrent infections with *Hymenolepis nana* and *Dentostomella translucida* in an African giant rat *(Cricetomys gambianus*), a case report. Sci World J **5**.
23. **Plumb DA.** 2015. Plumb's veterinary drug handbook, 8th ed. Ames (IA): Blackwell Publishing.
24. **Poling A, Weetjens B, Cox C, Beyene N, Durgin A, Mahoney A.** 2011. Tuberculosis detection by giant African pouched rats. Behav Anal **34:**47–54.
25. **Poling A, Weetjens B, Cox C, Beyene NW, Bach H, Sully A.** 2011. Using trained pouched rats to detect land mines: another victory for operant conditioning. J Appl Behav Anal **44:**351–355.
26. **Reiczigel J, Rózsa L.** [Internet] 2005. Quantitative parasitology, 3.0. Budapest. Distributed by the authors. [Cited 13 April 2015]. Available at: http://www.zoologia.hu/qp/
27. **Ryan J.** 1989. Evolution of cheek pouches in African pouched rats (*Rodentia: Cricetomyinae*). J Mammal **70:**267–274.
28. **Traversa D.** 2011. Are we paying too much attention to cardiopulmonary nematodes and neglecting old fashioned worms like *Trichuris vulpis*? Parasit Vectors **4:**1–11.
29. **Vassiliades G.** 1966. [A new coccidium, *Eimeria moreli* n. sp. (Protozoa: Eimeriidae) of the Gambia rat (*Cricetomys gambianus*)]. C R Acad Sci Hebd Seances Acad Sci D **262:**2473–2475.[Article in French]
30. **Zajac AM, Conboy GA.** 2006. Veterinary clinical parasitology, 7th ed. Ames (IA): Blackwell Publishing.