THE EFFICACY OF IVERMECTIN (MK-933) FOR TREATMENT AND PREVENTION OF INFECTION OF PARELAPHOSTRONGYLUS TENUIS (METASTRONGYLOIDEA) IN CERVIDS

By

STEVEN KENNETH OLSEN

Bachelor of Science

Utah State University

Logan, Utah

1980

Submitted to the Faculty of the Graduate College
of the Oklahoma State University
in partial fulfillment of the requirements
for the Degree of
MASTER OF SCIENCE
December, 1982

THE EFFICACY OF IVERMECTIN (MK-933) FOR TREATMENT AND PREVENTION OF INFECTION OF PARELAPHOSTRONGYLUS TENUIS (METASTRONGYLOIDEA) IN CERVIDS

Thesis Approved:

Thesis Adviser

Dean of Graduate College

PREFACE

This study is concerned with the ability of ivermectin (MK-933) to eliminate patent infections of Parelaphostrongylus tenuis in white-tailed deer (Odocoileus virginianus) and to prevent development of infection by P. tenuis in white-tailed deer and in fallow deer (Dama dama). Fallow deer were chosen in this study to represent neurologically susceptible cervids.

A few limitations were encountered in designing this study. The number of animals were limited to a portion of the annual supply of white-tailed deer fawns born in the Deer Disease Research facility or brought to it by the Oklahoma Department of Wildlife Conservation. Fallow deer were chosen for their ease of availability, smaller size, relative ease of handling, and cost compared to elk or other large cervids that are known to be neurologically susceptible to the parasite. All animals were given a reasonable amount of space, food, water and veterinary medical care; even so, there were unexplained deaths, a common occurrence among captive wild animals used for research purposes.

Histopathologic examination was used for verification of infections and was limited to cellular reaction to eggs and larvae in the lungs or to adults on the meninges. Dr. D. Whitnack assisted in these interpretations.

The author expresses appreciation to his major advisor, Dr. A. Alan Kocan, for his guidance and assistance throughout this study.

Appreciation is also extended to other committee members, Drs. J. C. Fox and Sidney A. Ewing, for their invaluable assistance and recommendations.

A note of thanks is given to Dr. K. H. Olsen for his assistance and editing. Thanks are also extended to Judy Tyson for her superb typing.

In addition, appreciation is extended to the Oklahoma Department of Wildlife Conservation for the facilities and supply of research animals and to the Merck, Sharp and Dohme Research Laboratories, Rahway, New Jersey, for the drug used in this study. This study was supported in part by the Oklahoma State University College of Veterinary Medicine and the Oklahoma Department of Wildlife Conservation, Federal Aid in Wildlife Restoration Act, Pittman Robertson Project W-130-R.

TABLE OF CONTENTS

Chapter		Page
I.	INTRODUCTION	1
II.	LITERATURE REVIEW	3
	The Parasite	3
	The Drug	6
III.	MATERIALS AND METHODS	9
	Group I	10
	Group II	10
	Group III	11
IV.	RESULTS	12
	Group I	12
	Group II	16
	Group III	16
V.	DISCUSSION	18
VI.	SUMMARY	21
LITERATURE CITED		22

LIST OF TABLES

Table Page

I. The Number of Larvae Observed in 20 Gram Fecal Samples from Treated and Untreated White-tailed Deer with Ten-Month-Old Patent Infections of Parelaphostrongylus tenuis Treated with 0.2 mg/kg of Ivermectin Subcutaneously 14

II. The Number of Larvae Observed in 20 Gram Fecal Samples from Treated and Untreated White-tailed Deer with Five-Month Old Patent Infections of Parelaphostrongylus tenuis Treated with 0.4 mg/kg of Ivermectin Subcutaneously 15

CHAPTER I

INTRODUCTION

The meningeal worm Parelaphostrongylus tenuis (= Pneumostrongylus tenuis Dougherty 1945) is a parasite of white-tailed deer in eastern North America (Prestwood and Smith 1969). Although this parasite seldom produces clinical signs in white-tailed deer, natural infections of P. tenuis in the following cervids typically result in neurologic disease: moose (Alces alces) (Anderson 1965), caribou (Rangifer tarandus terraenovae) (Behrend and Witter 1968), reindeer (Rangifer tarandus tarandus) (Anderson 1971), wapiti (Cervus canadensis) (Carpenter et al. 1973), black-tailed deer (Odocoileus hemionus columbianus) (Nettles et al. 1977a) and fallow deer (Dama dama) (Kistner et al. 1977 and Nettles et al. 1977b). The clinical signs usually seen in these animals consist of circling, often associated with blindness, nystagmus and holding of the neck in abnormal positions and ataxia, stiffness and posterior weakness that often develops into paraplegia. The parasite appears to be endemic in the eastern part of North America and restricted to physiographic regions where white-tailed deer and the intermediate hosts, certain species of terrestrial gastropods, exist (Prestwood and Smith 1969 and Kocan et al. 1982).

This disease has been a concern for wildlife workers for many years. Problems arise when infected animals move or are transported to

areas nonendemic for P. tenuis. This may establish infections in susceptible animals not previously exposed to meningeal worm if the proper intermediate hosts are present. Also, non-infected and susceptible animals may become infected when they move or are transported into areas where P. tenuis is endemic. These two factors are important for state relocation programs and for the increasing number of drive-through game parks. Introduction of infected white-tailed deer into a susceptible cervid population may have as disastrous results as moving a susceptible population to an area where P. tenuis is endemic. A drug capable of prevention of infection or elimination of P. tenuis from infected animals would be a valuable tool for preparing exposed animals destined to be moved into non-endemic areas or for preventing infection in susceptible animals exposed to the parasite. The drug ivermectin, the 22, 23-dihydroavermectin B_1 derivative of avermectin, has been proven to be an effective anthelmintic against many parasites of sheep, cattle, horses and dogs (Campbell 1981, Egerton et al. 1981, Herd et al. 1981 and Campbell and Blair 1978, Blair and Campbell 1978, 1979 and 1980). This study is designed to test this new drug's ability to eliminate and to prevent infection of P. tenuis in white-tailed deer and to prevent infection in fallow deer, the latter chosen in this study to represent neurologically susceptible cervids.

CHAPTER II

LITERATURE REVIEW

The Parasite

The meningeal worm Parelaphostrongylus tenuis inhabits the cranial subdural space, cranial venous sinuses, and the spinal subdural space of white-tailed deer (Odocoileus virginianus). Except in heavy infections this parasite rarely causes neurologic disorders in white-tailed deer (Prestwood 1970). Verminous neurologic disease, the clinical signs manifested from damage to the neural parenchyma of the spinal cord or brain by larval or adult worms, has been reported in caribou (Rangifer tarandus terraenovae) (Behrend and Witter 1968), moose (Alces alces) (Anderson 1965), reindeer (Rangifer tarandus tarandus) (Anderson 1971), wapiti (Cervus canadensis) (Carpenter et al. 1973), black-tailed deer (Odocoileus hemionus columbianus) (Nettles et al. 1977a) and fallow deer (Dama dama) (Kistner et al. 1977 and Nettles et al. 1977b). Neurologic disease resulting from experimental infections with the meningeal worm has been produced in caribou (Anderson and Strelive 1968), moose (Anderson 1964), mule deer (Odocoileus hemionus hemionus) (Tyler et al. 1980), wapiti (Anderson et al. 1966), and domestic goats (Capra hircus) (Anderson and Strelive 1969).

In white-tailed deer, adult worms lay eggs on the meninges or in the circulatory system. These eggs are carried to the lungs by the

blood where emboli develop around them. The eggs embryonate and the larvae break out into the alveoli, pass up the respiratory tract, are swallowed, and pass from the host in the feces (Anderson and Davis 1971).

Once in the environment the larvae penetrate slugs and snails. Various species of terrestrial gastropods have been experimentally infected, but those of the species Deroceras laeve and Zoinitoides nitidus are probably the most important in transmission of P. tenuis in the wild (Lankaster and Anderson 1968). Other species, Triodopsis albolabris and Mesodon thyroidus, also serve as effective intermediate hosts. Development of P. tenuis larvae to the infective stage requires at least three weeks at 25°C (Anderson 1963) and probably longer at lower temperatures. The number of larvae contained in naturally infected gastropods is usually only four or five per individual (Lancaster and Anderson 1968). Deer and other cervids are infected by accidentally ingesting gastropods containing infective P. tenuis larvae. The larvae are released from the gastropod tissues in the abomasum of the deer by action of digestive juices and then penetrate the ventral curvature of the abomasum, enter the peritoneal cavity and reach the spinal cord in about ten days (Anderson and Strelive 1967). The worms develop in the dorsal horns of the spinal cord in twenty to thirty days from after they migrate through the dorsal nerve roots into the subdural space where they reach sexual maturity. The prepatent period is from eighty-two to ninety-one days (Anderson and Davis 1971).

Except with heavy infections, white-tailed deer, the meningeal worm's probable natural hosts, normally do not manifest the typical clinical signs of meningeal worm infections seen in abnormal hosts

which consist of circling, often associated with blindness, nystagmus, and holding of the neck in abnormal positions; ataxia, stiffness and posterior weakness that often develops into paraplegia. Anderson and Strelive (1967) noted that the recovery of adult worms from the central nervous system in white-tailed deer is noticeably less than the number of larvae given them. This is in contrast to the case in moose and wapiti where an unusually high percentage of the larvae ingested reach the nervous system (Anderson 1964 and Anderson et al. 1966). It is thought that these hosts are unable to activate their defense mechanisms as rapidly or as effectively as white-tailed deer, thus allowing a greater percentage of larvae to survive the migration to the central nervous system (Anderson and Strelive 1967). This susceptibility to neural invasion accounts for only part of the severity of clinical signs seen in moose, wapiti, caribou, reindeer, fallow deer, mule deer, black-tailed deer and domestic sheep and goats. There is evidence that damage in these animals is due to P. tenuis larvae which consists of extensive trauma to the spinal cord (Anderson 1964). In contrast, it is suggested the neurologic signs seen in heavily infected white-tailed deer is not due to trauma to the neural parenchyma from wandering P. tenuis larvae, but to large masses of adult worms in the venous sinuses and the reaction they provoke by mechanically interfering with blood flow (Prestwood 1970).

Histologically, lesions in the dura mater of heavily infected white-tailed deer consist of thickenings of the dura mater, focal accumulation of lymphocytes and numerous eosinophils. Commonly, eggs and larvae are found surrounded by connective material and giant cells. Prestwood (1970) found pigment in the meninges and cerebral

cortex. This strong cellular response is in contrast to the cellular response in animals that show clinical signs from P. tenuis. For example, in black-tailed deer, occurrence of aggregates of eosinophils in the spinal cord is common (Nettles et al. 1977), while in mule deer eosinophils are occasionally found with lymphocytes and plasma cells. In wapiti, histological lesions consisted of lymphocyte infiltration interspersed with a few macrophages, eosinophils, and sometimes multinucleated giant cells which indicate a weaker cellular response than shown by white-tailed deer. Kistner et al. (1977) noted that in fallow deer histological lesions were characterized by marked thickening and chronic inflammation of the dura mater, subdural hemorrhage, marked lymphocyte infiltration and mineralization. No eosinophils were seen. This also contrasts with the reaction seen in the white-tailed deer.

The Drug

Chabala et al. (1980) states that ivermectin is the 22,23-dihydroavermectin B_1 derivative of avermectin: a macrocyclic lactone produced by a species of actinomycete, Streptomyces avermitilis. The avermectins are especially effective when given orally or parenterally against many immature and mature nematode and arthropod parasites of sheep (Campbell 1981, Wescott and Leamaster 1982), cattle (Egerton et al. 1981, Nolan et al. 1981), dogs (Campbell and Blair 1978, Blair and Campbell 1980), horses (Donham 1981, Herd, Yazwinski 1981a, and Yazwinski 1981b,) and swine (Barth et al. 1980).

The avermectins paralyze worms, but in a different manner than some of the more common anthelmintics, (organophosphates, bephenium, thenium, pyrantel piperazine and levamisole).

The organophophates paralyze by inhibiting the acetylecholinesterase needed for deactivation of choline, bephium and thenium by mimicing choline by binding to its recepters, pyrantel by depolarizing the cell membranes, piperazine by hyperpolarizing the cell membranes and levamisole by stimulating the nerve ganglion directly (Campbell 1981). In nematodes the neurotransmitter involved with sending inhibitory signals from the interneurons to the motor neurons is gamma-aminobutyric acid, or GABA. The avermectins act as GABA agonists (Campbell 1981). They potentiate the GABA effect at the synapse. It is believed that this is done by stimulating the pre-synaptic release of GABA and enhancing its binding to the post-synaptic receptors. This inhibitory neurotransmitter functions to open the chloride channels on the postsynaptic side allowing chloride ions to flow in and induce the "resting" condition. The excitatory neurotransmitter, acetylcholine in the case of nematodes, triggers the influx of sodium ions into the motor-neuron. In the presence of avermectins, the chloride channels are open when they should be shut; chloride ions flow even when only sodium should be entering. Thus the motor-neuron remains negatively charged and signals are not registered by the recipient cell. The motor-neuron and muscle cell retain their capacity for action but do not receive the signal and thus the muscle cell does not function.

Ivermectin has been shown to be effective as an anthelmintic. Egerton et al. (1979) reported that dosages of .05 and 0.1 mg/kg produced a ninety-six to ninety-nine percent reduction in worm burdens of Haemonchus contortus, Trichostrongylus axei, T. colubriformis and Oesophagostomum columbianum in sheep. Similar results were seen in the case of cattle (Egerton et al. 1980, Egerton et al. 1981). Even at low

dosages (0.025 mg/kg) there was nearly one-hundred percent activity against Dictyocaulus viviparus and Oesophagostomum. At dosages of 0.2 mg/kg ivermectin was highly effective against seven species of gastrointestinal parasites, as well as lungworm. Ivermectin has even been noted to show strength against inhibited fourth stage larvae, drug-resistant strains and lungworm.

Blair and Campbell (1980) showed that ivermectin was effective with an oral dosage of 0.05 mg/kg in preventing heartworm in dogs by acting against the microfilaria. This dosage level did not affect the adult heartworm, a desirable feature in animals with patent infections. Ivermectin is highly effective against Ancylostoma caninum at the same dosage (Blair and Campbell 1978).

Two papers by Yazwinski et al. (1981a and 1981b) demonstrated ninety-seven percent to one-hundred percent efficacy of ivermectin against mature and immature Parascaris equorum and Oxyuris equi, respectively, at a dosage of 0.2 mg/kg.

In most work with gastrointestinal parasites ivermectin was given orally (Blair and Campbell 1978, Blair and Campbell 1979 and 1980). In horses researchers gave ivermectin I.M. in the neck for both gastrointenstinal parasites and larvae of Draschia and Habronema. In sheep, ivermectin has been administered subcutaneously (Westcott and Leamaster 1982) and good results were seen against most gastrointestinal parasites including Dictyocaulus, a lungworm. Oral dosages ranged from 100 mg/kg to 0.1 mg/kg. Intramuscular and subcutaneous doses were much smaller, ranging from 0.2 mg/kg to 0.01 mg/kg, with good results throughout the range. Even with the high dosages, signs of drug toxicity were not seen (Blair and Campbell 1979).

CHAPTER III

MATERIALS AND METHODS

Gastropods of the species Triodopsis albolabris were kept at room temperature in terrariums containing vermiculite and were given lettuce ad libitum. Snails were infected with P. tenuis larvae by exposing them to feces from experimentally infected white-tailed deer. After a three week development period for the larvae, the snails were cut with scissors and placed in a solution of one percent pepsin and one percent hydrochloric acid and allowed to digest for one hour to collect infective third stage larvae. The larvae were then counted and the inoculum standardized.

The white-tailed deer used in this experiment were kept at the Deer Disease Research facility near Lake Carl Blackwell, Payne County, Oklahoma. The Oklahoma State University College of Veterinary Medicine maintains this ten acre facility in conjunction with the Oklahoma Department of Wildlife Conservation. All deer were caught by hand or immobilized with succinylcholine chloride and exposed to seventy-five larvae by passing a small tube down the esophagus into the rumen and administering the larvae with a syringe.

All deer were parasite free before the experiment. All larvae found in feces and eggs and larvae found in the lungs by histologic examination were therefore identified as P. tunuis. Identification of larvae and adult P. tenuis was also done on the basis of experience.

Group I

Group I consisted of six white-tailed deer with patent infections. Four deer had ten-month-old infections and two had five-month-old infections. Three of the first four (ten-month-old infections) were given 0.20 mg/kg of ivermectin subcutaneously, and one of the latter two (five-month-old infections) was given 0.40 mg/kg, also subcutaneously. Twenty grams of feces were examined every other day starting twenty to sixteen days before treatment and continued until larval counts reached zero or until approximately sixty days post-treatment. These fecal samples were placed in a Baermann apparatus with 500 ml of warm water and allowed to set for twenty-four hours. Thirty ml of fluid was drawn from the apparatus and examined 10 ml at a time in a gridded petri dish under a dissecting microscope for the presence of larvae. The number of larvae was counted and totaled for each sample. All animals were euthanitized and removed to the necropsy facilities. At necropsy all deer were examined for the presence of P. tenuis adults in the cranial spaces by removing the skull cap and brain, incising and reflecting the dura mater, and observing for the thread-like worms on the meninges. The meninges were observed for petechial hemorrhages, granulation, or any other change in normal tissue. Samples of lung tissue were taken and sectioned histologically to observe eggs and tissue reaction. Additionally, liver, spleen and other tissues were preserved in ten percent formalin for future reference.

Group II

Group II consisted of four white-tailed deer. These deer were exposed to infective larvae as previously described. Twenty-four hours

after exposure to seventy-five larvae three deer were given 0.20 mg/kg of ivermectin subcutaneously. The fourth deer was given seventy-five larvae, but did not receive the invermectin treatment. Beginning day ninety post-treatment, fecal samples were taken every other day, placed in a Baermann apparatus, left for 24 hours, and then 30 ml of water was drawn and examined for larvae. The deer were necropsied at day one-hundred nineteen after exposure and the cranial and spinal spaces were observed for the presence of adult P. tenuis as well as for petechial hermorrhages, granulation or other lesions. Additionally, liver, spleen and lung tissues were preserved in ten percent formalin for future reference.

Group III

Group III consisted of two fallow deer and one white-tailed deer. All three deer were exposed to seventy-five larvae as in Group I. Twenty-four hours after exposure to the larvae one fallow was treated with 0.20 mg/kg of ivermectin. Eight hours later the untreated fallow deer died of unknown causes, but the treated fallow was kept and observed for neurologic signs. Fecal samples were examined after day ninety post-exposure on the white-tailed deer to determine the viability of the larvae.

The ivermectin (MK-933) used in this experiment was obtained from the Merck, Sharp and Dohme Research Labororatories, Rahway, New Jersey. All injections were given subcutaneously on the right hind flank.

CHAPTER IV

RESULTS

Group I

Group I. The number of larvae observed in the feces from treated white-tailed deer #507 (0.2 mg/kg) dropped to zero eighteen days after treatment. At thirty days post-treatment the number of larvae observed increased to twenty-three, but by day thirty-five post-treatment counts dropped to zero again (Table I). At necropsy, two live male P. tenuis adults were found on the meninges. The meninges revealed large amounts of granulation, petechial hemorrhages, and a mucus coat covered a large percentage of the meninges. Histologically, the meninges revealed multiple foci of lymphocytes, increased connective tissue and granulation. Lung tissue revealed chronic pleuritis and multifocal parasite granulomas with eggs present in some of these, however, without visible larvae.

The number of larvae observed from treated white-tailed deer #508 (0.2 mg/kg) dropped to zero twenty days after treatment, increased to one and two larvae total on days twenty-six and thirty, respectively, and dropped to zero again (Table I). Upon necropsy five (three alive) male P. tenuis adults were found on the meninges. The meninges revealed slight petechial hemorrhage, some granulation, and some mucus. Histologically, lung tissue revealed multiple foci of

lymphocytes and hemosiderin-laden focal macrophages, but no eggs or larvae were seen.

The number of larvae observed from treated white-tailed deer #511 (0.2 mg/kg) dropped to zero by day twenty-one post-treatment, but a moderately high count of sixteen at forty-three days post-treatment, was observed the day before necropsy (Table I). At necropsy no adults were found on the meninges. The meninges were pearly-white with small petechial hemorrhages and granulomas. Histologically, lung tissue revealed multiple parasite lesions. Eggs were present in some of the lesions and larvae were observed in some lesions.

The number of larvae observed from treated white-tailed deer #503 (0.4 mg/kg) dropped to zero on day seventeen post-treatment no others were recovered (Table II). One male and one female P. tenuis were found on the meninges at necropsy. The meninges were thickened and contained foci of lymphocytes and macrophages. They had small granulations and minor petechial hemorrhages. No excess mucus was seen. Histologically, lung tissue revealed chronic pleuritis and small granulomas. Very few larvae and no eggs were observed in the granulomas.

White-tailed deer #516 was an untreated control. The number of larvae observed dropped to zero at day twenty-four post-treatment. Larval counts rose six days later and were increasing above seventy the day of necropsy (Table I). Two live male P. tenuis adults were observed on the meninges at necropsy. The meninges revealed no granulation or petechial hemorrhages. Histologically, lung tissue showed numerous parasite nodules, a large number of which contained eggs and larvae.

TABLE I

THE NUMBER OF LARVAE OBSERVED IN 20 GRAM FECAL SAMPLES FROM TREATED AND UNTREATED WHITE-TAILED DEER WITH TEN-MONTH-OLD PATENT INFECTIONS OF PARELAPHOSTRONGYLUS TENUIS TREATED WITH 0.2 MG/KG OF IVERMECTIN SUBCUTANEOUSLY

	NUMBER OF LARVAE OBSERVED			
Day Post-Treatment	Treated #507	Treated #508	Treated #511	Untreated #516
-20	5	3	7	22
-18	101	24	0	0
-16	8	18	407	127
-14	24	23	7	7
-12	51	48	2280	695
-10	49	94	262	517
-8	69	222	255	1522
-6	393	112	67	218
0	-	-	-	-
+1	6	22	149	-
+3	54	1687	1121	10
+5	1127	1917	788	-
+7	1149	604	615	-
+9	452	125	39	174
+14	109	76	9	340
+16	5	7	27	19
+18	0	7	50	4
+20	0	0	14	1
+21	0	0	0	2
+24	0	0	0	0
+26	0	1	0	0
+30	23	2	0	0
+32	7	0	0	1
+35	0	0	0	32
+37	0	0	0	13
+43	0	0	16	70

TABLE II

THE NUMBER OF LARVAE OBSERVED IN 20 GRAM FECAL SAMPLES FROM TREATED AND UNTREATED WHITE-TAILED DEER WITH FIVE-MONTH-OLD PATENT INFECTIONS OF PARELAPHOSTRONGYLUS TENUIS TREATED WITH 0.4 MG/KG OF IVERMECTIN SUBCUTANEOUSLY

Day Post-Treatment	NUMBER OF LARVAE OBSERVED Treated #503	Untreated #502
-16	184	2148
-14	105	-
-12	11	3092
-10	63	1809
-8	15	-
-6	42	218
-4	70	97
-2	88	368
0	-	-
+2	282	191
+5	383	168
+7	43	114
+9	2	105
+11	38	102
+13	6	107
+15	2	61
+17	0	57

White-tailed deer #502 was also an untreated control. The number of larvae observed never dropped below fifty (Table II). At necropsy six live male and four live female P. tenuis adults were found on the meninges. Grossly, the meninges revealed large amounts of mucus and large petechial hemorrhages. Histologically, the meninges were thickened and had foci of lymphocytic nodules and macrophages containing hemosiderin. There were numerous parasitic granulomas in the section of lung: these consisted of parasite eggs or larvae in the granulomas surrounded by a zone of macrophages and multinucleated cells. Eggs were more numerous than larvae.

Group II

The one untreated white-tailed deer control was observed to have larvae present in its feces one-hundred seventeen days after exposure to seventy-five infective larvae. At one-hundred nineteen days after exposure this animal, along with the other three from this group, was necropsied; two live female and four live male adult P. tenuis were observed on the meninges. Grossly, the meninges had small petechial hemorrhages and had no granulation. Histologically, lung tissue revealed parasite granulomas with eggs and larvae within. The three treated white-tailed deer had pearly-white meninges and no adult P. tenuis were observed there. Lung tissue from each of these animals revealed normal tissue void of parasite lesions.

Group III

The one exposed, untreated fallow deer died from unrelated causes two days after exposure to infective larvae. The exposed, treated

fallow deer revealed no changes in behavior, or posture. No clinical signs were observed in this animal up to two months after exposure to larvae. The white-tailed deer used to test viability of the larvae was necropsied ninety-seven days after exposure to infective larvae, even though first stage larvae had not been observed in its feces. Two live male and one live female were found on the meninges.

CHAPTER V

DISCUSSION

The effect of ivermectin on patent infections of Parelaphostrongylus tenuis shows several things. First, there seems to be a large increase in the number of larvae observed starting soon after treatment and lasting for up to ten days (Tables I and II). No such increase in larval counts was observed in untreated control deer (Tables I and II). Because this occurs so soon after treatment it can be suggested that the drug affects the larvae present in the lungs and allows them to be swept from the lungs in greater quantities by ciliary action than if they were mobile. However, since the larvae observed in the feces were moving this phenomenon may just be normal variation in larvae found in fecal samples. Secondly, counts show that the number of larvae observed in the feces drops to zero seventeen to twenty-one days post-treatment. It is doubtful, because of the blood-brain barrier, that the adults were affected by either dosage of the drug and so an explanation of the dropping larval counts must come from the effect of the drug on larvae traveling in the bloodstream or residing in the tissues of the lungs. This is supported by the fact that in some animals, especially #511 and #516, larvae were again observed after a period of absence, indicating that adults were not affected and continued to produce eggs and larvae. Thirdly, the effects of ivermectin seems to last only for a month or a little more at a dosage

level of 0.2 mg/kg. Larval counts on animal #511 (Table I) were increasing at the time of necropsy. This is also supported by a paper by Blair and Campbell (1979) in which they report suppression of circulating larvae (microfilaria) of Dirofilaria immitis soon after treatment with ivermectin but normal levels of microfilaria returned as soon as nine weeks post-treatment. Histologic lung sections also support the fact that ivermectin lasts only a month or a little more. Along with older granulomas there is evidence of new invasions of viable eggs and larvae in treated animals. Lung tissue in untreated animals had the usual progression of old granulomas, older granulomas with eggs and larvae, and new invasions of eggs and larvae.

At the dosages given here (0.2 mg/kg and 0.4 mg/kg) there seems to be no appreciable affect on adult P. tenuis. It may be that this is due to the blood-brain barrier or it may be that ivermectin does not affect P. tenuis adults as was also the case with Dirofilaria adults no matter how high the dosage (Blair and Campbell 1979).

There was no significant difference in the number of adult P. tenuis between treated and untreated animals.

The condition of the meninges of treated animals seems no worse than that of untreated animals. This response: granulation, petechial hemorrhage, presence of mucus, may be due to dead worms. However, the difference is not extreme enough to infer that this difference is significant. In fact, one treated animal, #511, had normal meninges and no adults were seen even though larvae were seen in the feces.

The higher dosage of 0.4 mg/kg seems to have no advantage over the lower dosage of 0.2 mg/kg. It did not seem to influence the length of time before the number of larvae observed drops to zero. The large

increase in larval counts soon after treatment still occurs (Table II), but the peak is not as high as with the lower dosage.

The effect of ivermectin on newly acquired Parelaphostrongylus tenuis infections is distinct. The treated white-tailed deer failed to develop patent infections, have larvae present in their feces, or have parasite lesions, eggs, or larvae in the lung tissues. The untreated control animal developed a patent infection: larvae present in its feces and adult worms on the meninges.

Because the exposed, untreated fallow deer (control) died of unrelated causes, the effects of ivermectin in preventing P. tenuis infections in fallow deer cannot be proved from the results of this experiment. However, the literature states that fallow deer are susceptible and develop neurologic disease (Kistner et al. 1977 and Nettles et al. 1977b) and the larvae given to the treated fallow deer were proved to be viable because infection developed in the white-tailed deer control. Thus, it can be concluded from this and from the failure of the treated fallow deer to develop neurologic disease that ivermectin was effective at preventing infection, as it was in the white-tailed deer from Group II.

CHAPTER VI

SUMMARY

The efficacy of ivermectin on patent infections of P. tenuis in white-tailed deer is: (1) at the dosages given (0.2 mg/kg and 0.4 mg/kg) adults residing on the meninges were not affected; (2) the number of larvae observed in the feces drops to zero between sixteen and twenty-one days post-treatment but larvae are again seen in the feces after a short period of absence; and (3) ivermectin apparently lasts no more than a month-and-a-half in the body (possibly longer at higher dosages than those given here) (Blair and Campbell 1979). More research is needed to determine if higher dosages will completely eliminate the infection.

Ivermectin is effective in preventing infection of P. tenuis in both white-tailed deer and in fallow deer. It is recommended that more research be done with ivermectin in other cervids. It is also suggested that if this drug is to be used prophylactically that treatment would have to be done on a monthly basis if the animals were constantly exposed to infective larvae.

LITERATURE CITED

Anderson, R. C. 1963. The incidence, development and experimental transmission of Pneumostrongylus tenuis Dougherty (Metastrongyloidea: Protostrongyloidae) of the meninges of the white-tailed deer (Odocoileus virginianus borealis) in Ontario. Can. J. Zool. 41:775-92.

Anderson, R. C. 1964. Motor ataxia and paralysis in moose calves infected experimentally with Pneumostrongylus tenuis (Nematoda: Metastrongyloidea). Paper presented at N. E. Wildl. Conf., Hartford, Connecticut, 7 pp., Mimeo. From Biological Abstracts.

Anderson, R. C. 1965. An examination of wild moose exhibiting neurologic signs in Ontario. Can. J. Zool. 43:635-39.

Anderson, R. C. 1971. Neurologic disease in reindeer (Rangifer tarandus tarandus) introduced into Ontario. Can. J. Zool. 49:159-66.

Anderson, R. C. and J. W. Davis eds. 1971. Parasitic Diseases of Wild Mammals. Iowa State University Press, Ames, Iowa.

Anderson, R. C. and U. R. Strelive. 1967. The penetration of Pneumostrongylus tenuis into the tissues of white-tailed deer. Can. J. Zool. 45:285.

Anderson, R. C. and U. R. Strelive. 1968. The experimental transmission of Pneumostrongylus tenuis to caribou (Rangifer tarandus terraenovae). Can. J. Zool. 46:503-510.

Anderson, R. C. and U. R. Strelive. 1969. The effect of Pneumostrongylus tenuis (Nematoda: Metastrongyloidea) on kids. Can. J. Comp. Med. 33:280-286.

Anderson, R. C.; M. W. Lankaster; and U. R. Strelive. 1966. Further experimental studies of Pneumostrongylus tenuis in cervids. Can. J. Zool. 44:851-61.

Barth, D.; I. H. Sutherland; R. A. Roncalli; W. H. D. Leaning. 1980. The efficacy of ivermectin as an antiparasitic agent in the pig. Proc. 1980 Congress. Int. Pig Vet. Society. Copenhagen, Denmark. June 30-July 3, 1980. p. 275. From Biological Abstracts.

Behrend, D. F. and J. F. Witter. 1968. Pneumostrongylus tenuis in white-tailed deer in Maine. J. Wildl. Manage. 32:963-66.

Blair, L. S. and W. C. Campbell. 1978. Efficacy of avermectins against Ancylostoma caninum in dogs. J. Helminth 52:305-307.

Blair, L. S. and W. C. Campbell. 1979. Efficacy of avermectin B_{1a} against microfilaria of Dirofilaria immitus. Am. J. Vet. Res. 40:1031-32.

Blair, L. S. and W. C. Campbell. 1980. Efficacy of ivermectin against Dirofilaria immitus larvae in dogs 31, 60 and 90 days after infection. Am. J. Vet. Res. 41(12):2108.

Campbell, W. C. 1981. An introduction to the avermectins. New Zeal. Vet. J. 29:174-78.

Campbell, W. C. and L. S. Blair. 1978. Efficacy of avermectins against Dirofilaria immitus in dogs. J. Helminth. 52:308-10.

Carpenter, J. W.; H. E. Jordan; and B. C. Ward. 1973. Neurologic disease in wapiti naturally infected with meningeal worms. J. Wildl. Dis. 9:148-53.

Chabala, J. C.; H. Mrozik; R. L. Tolman; P. Eskola; A. Lusi; L. H. Peterson; M. F. Woods; M. H. Fisher; W. C. Campbell; J. R. Egerton; and D. A. Ostlind. 1980. Ivermectin, a new broad spectrum antiparasitic agent. J. Med. Chem. 23:1134-36.

Egerton, J. R.; D. A. Ostlind; L. S. Blair; C. H. Eary; D. Suhayda; S. Cifelli; R. F. Riek; and W. C. Campbell. 1979. Avermectins, new family of potent anthelmintic agents: efficacy of the B_{1a} component. Antimicrob. Agents and Chemother. 15:372-78.

Egerton, J. R.; J. Birnbaum; L. S. Blair; J. C. Chabala; J. Conroy; M. H. Fisher; H. Mrozik; D. A. Ostlind; C. A. Wilkins; and W. C. Campbell. 1980. 22:23-Dihydroavermectin B_1, a new broad-spectrum antiparasitic agent. Br. Vet. J. 136:88-97.

Egerton, J. R.; C. H. Eary; and D. Suhayda. 1981. The anthelmintic efficacy of ivermectin in experimentally infected cattle. Vet. Parasit. 8:59-70.

Herd, R. P. and J. C. Donham. 1981. Efficacy of ivermectin against cutaneous Draschia and Habronema infection (summer sores) in horses. Am. J. Vet. Res. 42:1953-55.

Kistner, T. P.; G. R. Johnson; and G. A. Rilling. 1977. Naturally occurring neurologic disease in a fallow deer infected with meningeal worms. J. Wildl. Dis. 13:55-58.

Kocan, A. A.; M. G. Shaw; K. A. Waldrup and G. J. Kubat. 1982. Distribution of Meningeal Worm (Parelaphostrongylus tenuis) in White-Tailed Deer from Oklahoma. J. Wildl. Dis. In Press.

Lankaster, M. W. and R. C. Anderson. 1968. Gastropods as intermediate hosts of Pneumostrongylus tenuis Dougherty, of white-tailed deer. Can. J. Zool. 46:373-84.

Nettles, V. F.; A. K. Prestwood; and R. G. Nichols. 1977a. Meningeal worm induced neurologic disease in black-tailed deer. J. Wildl. Dis. 13:137-43.

Nettles, V. F.; A. K. Prestwood; and R. D. Smith. 1977b. Cerebrospinal parelaphostrongylosis in fallow deer. J. Wildl. Dis. 13:440-44.

Nolan, J.; H. J. Schnitzerling; and P. Bird. 1981. Evaluation of the potential of systemic slow release chemical treatments for control of the cattle tick (Boophilus microplus) using ivermectin. Aust. Vet. J. 57:493-97.

Prestwood, A. K. 1970. Neurologic disease in white-tailed deer massively infected with meningeal worm. J. Wildl. Dis. 6:84-86.

Prestwood, A. K. and J. F. Smith. 1969. Distribution of Meningeal Worm (Pneumostrongylus tenuis) in Deer in the Southeastern United States. J. Parasitol. 55:720-25.

Tyler, G. V.; C. P. Hibler; and A. K. Prestwood. 1980. Experminental infection of mule deer with Parelaphostrongylus tenuis. J. Wildl. Dis. 16:533-40.

Wescott, R. B. and B. R. Leamaster. 1982. Efficacy of ivermectin against naturally acquired and experimentally induced nematode infections in sheep. Am. J. Vet. Res. 43:531-33.

Yazwinski, T. A.; D. Hamm; T. Greenway; and W. Tilley. 1981a. Antiparasitic effectiveness of ivermectin in the horse. Am. J. Vet. Res. 43:1092-94.

Yazwinski, T. A.; D. Hamm; M. Williams; T. Greenway; W. Tilley. 1981b. Effectiveness of ivermectin in the treatment of equine Parascaris equorum and Oxyuris equi infections. Am. J. Vet. Res. 43:1095.

VITA[2]

Steven Kenneth Olsen

Candidate for the Degree of

Master of Science

Thesis: THE EFFICACY OF IVERMECTIN (MK-933) FOR TREATMENT AND PREVENTION OF INFECTION OF PARELAPHOSTRONGYLUS TENUIS (METASTRONGYLOIDEA) IN CERVIDS

Major Field: Veterinary Parasitology and Public Health

Biographical:

Personal Data: Born in Los Alamos, New Mexico, August 5, 1958, the son of Dr. and Mrs. K. H. Olsen.

Education: Graduated from Los Alamos High School, Los Alamos, New Mexico, 1976; received Bachelor of Science degree in Wildlife Science with a minor in Biology from Utah State University, Logan, Utah, 1980; enrolled in masters program in Veterinary Parasitology and completed requirements for Master of Science degree at Oklahoma State University in December, 1982.

Professional Experience: Volunteer in Parks for Bandelier National Park, New Mexico, March 1976 through August 1976; graduate teaching assistant, Oklahoma State University, Department of Veterinary Parasitology, Microbiology and Public Health, 1980-82; technician in Wild Animal Disease Lab, Stillwater, Oklahoma, summers of 1980, 1981 and 1982.