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A specially weighted osmotic pump for the adminis­tration of ivermectin to cattle at a controlled zero order rate was subsequently developed (Pope, Wilkinson, Egerton & Conroy, 1985). A trial was conducted at the MSD Research Centre, Hennops River, to evaluate the efficacy of ivermectin administered by this system at approximate dosage rates of 20, 40 and 60 μg/kg/day against induced infestations of Amblyomma hebraeum on cattle.

**INTRODUCTION**

The administration of systemically active compounds as a sustained release injection, bolus or implant would be expected to give better long-term control of parasites than that obtained from single oral or parenteral treatment. Drummond, Whetstone, Ernst & Gladney (1972) found that a number of insecticides, administered daily in the feed of cattle, controlled ticks, but that this method of treatment was difficult to implement practically.

Ivermectin is active against a wide range of internal and external parasites, including some tick species, at extremely low dosages (Campbell & Benz, 1984). The dose required is low enough to make it an excellent can­didate for systemic tick control by administration via a controlled release system.

Minimum effective daily dosages of ivermectin for several species of ticks, including Amblyomma americanum, A. cajennense, A. maculatum, Dermacentor andersoni, D. variabilis and Rhipicephalus sanguineus, as well as the single host ticks D. albipictus and Boophilus microplus, have already been determined in the labora­tory (Drummond, Whetstone & Miller, 1981; Lancaster, Kilgore & Simco, 1982; Nolan, Schnitzerling & Bird, 1981).

Under field conditions in South Africa (Schröder, Swan, Soll & Hotson, 1985) and Zambia (Pegram & Lemche, 1985), multiple injections of ivermectin at in­tervals of 1 or 2 weeks reduced numbers of Boophilus decoloratus, Hyalomma truncatum, Rhipicephalus appendiculatus, Amblyomma hebraeum and Amblyomma variegatum present on naturally-infested cattle.

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**MATERIALS AND METHODS**

Sixteen Friesland and Friesland Cross steers, with a body mass of approximately 200 kg, were ranked by mass within breed and allocated to replicates of 4 ani­mals each. Animals within a replicate were randomly allocated to one of the following treatment groups: untreated control; 1 ALZET* 2ML4 mini osmotic pump filled to release ivermectin at 4 mg/day, equivalent to approximately 20 μg/kg/day; 2 ALZET 2ML4 pumps (approximately 40 μg/kg/day) or 3 ALZET 2ML4 pumps (approximately 60 μg/kg/day).

Cattle were housed either in specially designed cattle crates with anti-grooming stanchions or tethered in stalls to prevent grooming or interference with tick infesta­tions.

Four areas (2 on each side of the midline) on the backs of the animals were shaved. Specially designed linen and leather bags were glued to these areas using contact ad­hesive. The 'free' end of the bag was fitted with a 'Velcro' strip which facilitated daily opening and closing of the bag for inspections. Bags were attached at least 1 day before infestation with ticks to allow fumes from the contact adhesive to dissipate. Before infestation, ticks were assessed for mobility to ensure that all were viable.

Twenty adult male A. hebraeum were placed in each of the 2 bags on the left of each animal on Day 2. Twenty female A. hebraeum were placed in each of these bags on Day 7. This ensured sufficient time for male attachment and pheromone production prior to the plac­ing of females.

This process was repeated for the other 2 bags with the same numbers of males and females being placed on Days 7 and 12 respectively. A total of 320 ticks of each sex was thus used for each of the 4 treatment groups.

Male and female A. hebraeum of 3 different strains were used: an Onderstepoort 'heartwater free' strain, a South African Bureau of Standards (SABS) organophos­phate sensitive strain and an SABS organophosphate re­sistant strain. Equal allocations of these 3 strains were made to bags within replicates to ensure that compari­sions among treatment groups would be balanced for tick strain.

The number of ticks that failed to attach or those that fed and dropped was recorded for each bag daily. Live, unattached ticks were left in the bags and dead and engorged ticks were removed. On Day 32, all unattached ticks were removed, sexed, and assessed for viability.

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Received 20 November 1986—Editor

* Trademark of ALZA Corp., USA
† Trademark of Velcro, South Africa
and stage of engorgement. All fully engorged female ticks were removed daily, mass-measured, placed in individual mass-measured glass vials and incubated at approximately 28 °C and 86% relative humidity. Thereafter, the dates of onset of egg laying, completion of egg laying and onset of egg hatching were recorded.

Spent, female ticks were removed from the vial approximately 46 days after the onset of egg laying, and the vial and eggs mass-measured to enable calculation of the mass of eggs laid.

For each animal, where possible, a sample of eggs from 2 ticks placed on Day 7 and from 2 ticks placed on Day 12 was mass-measured and the number of eggs counted to enable estimation of the number of eggs/g.

Each vial was examined approximately 9 weeks after completion of egg laying and the percentage hatch of eggs visually estimated.

**Evaluation of data**

The proportion of dead males, dead females and engorged females recovered was calculated for each bag on each animal and transformed, using the double arcsine procedure (Miller, 1978).

The mean retransformed proportion was multiplied by the number placed to calculate the mean number of each type recovered.

The egg mass:tick mass ratio and proportion hatch were transformed using the angular transformation (Snedecor & Cochrán, 1980).

Egg size (eggs/mg) was estimated for up to 4 ticks for each animal, if available. These values were averaged for each animal and multiplied by the mass of eggs laid to estimate the total number of eggs laid by each tick.

The index of reproduction (IR) was calculated for each tick by multiplying number of eggs laid by proportion hatch. The number of eggs and IR were transformed to the natural logarithm of (value +1).

Three time intervals were calculated for each tick that engorged and was incubated: days to engorgement, days from engorgement to onset of egg laying, and days from onset of egg laying to onset of hatching. If a tick laid no eggs or if the eggs did not hatch, the interval value was assumed to be missing. Ticks that did not lay eggs were given a zero value for mass of eggs, number of eggs and IR and a missing value for per cent hatch. Ticks that did not produce hatched eggs were assigned an IR of zero regardless of the reason (i.e., died, did not engorge, did not lay eggs, eggs did not hatch).

The means of the transformed and untransformed data were calculated for each bag on each animal; the mean for all the bags on each animal was then calculated and finally the mean for all the animals in each treatment regimen. Appropriate back transformations were applied to the treatment means.

Three animals were used to have drug remaining in the boluses when the cattle were slaughtered on Day 42. The data for these 3 animals were transformed and summarized in the bovine data, but were not included in the treatment means. The data were not statistically analyzed because there were too few replicates remaining for meaningful analysis after excluding the 3 animals.

**RESULTS**

Efficacy of sustained-release ivermectin against induced infestations of *Amblyomma hebraeum* is summarized in Table 1.

There was an increase in mortality of both male and female ticks compared to controls with increasing daily dose of ivermectin, and a decrease in the number of ticks engorging. For the ticks that engorged and were incubated, the time required for full engorgement increased with increasing dose of ivermectin. Ticks fed on ivermectin-treated cattle had a lower mass when engorged and laid smaller egg masses, both absolutely and as a proportion of engorged mass. The eggs tended to be smaller and not to hatch as well. No ticks fed on cattle treated at 60 μg/kg/day were able to reproduce successfully; although a few ticks engorged and laid eggs, none of these eggs hatched. The index of reproduction was reduced 96% at 20 μg/kg/day, >99% at 40 μg/kg/day and 100% at 60 μg/kg/day.

The 3 strains of ticks differed for some of the variables examined. The data for female ticks of each strain that fed on control cattle are summarized in Table 2.
Generally, the SABS organophosphate-susceptible and resistant strains were similar. These ticks engaged more rapidly and started laying sooner than the Onderstepoort strain. On average, their masses were approximately 1 g greater when engorged and they produced more eggs. The adjusted index of reproduction was greatest for the SABS organophosphate-resistant strain, 42 % less for the sensitive strain and 75 % less for the Onderstepoort strain.

**DISCUSSION**

Differences in fecundity and engorged mass between ticks of different origin used in this trial may be attributed to strain differences. However, photoperiod and temperature have been shown to influence significantly the mass of engorged females and reproductive index. The adjusted index of reproduction for the Onderstepoort strain, 42 % less for the sensitive strain and 75 % less for the Onderstepoort strain. Differences in fecundity and engorged mass between ticks of different origin used in this trial may be attributed to strain differences. However, photoperiod and temperature have been shown to influence significantly the mass of engorged females and reproductive index. The adjusted index of reproduction for the Onderstepoort strain, 42 % less for the sensitive strain and 75 % less for the Onderstepoort strain.

The maintenance of enzootic stability of heartwater in endemic areas requires exposure of animals to feeding Amblyomma. It is easy to control A. hebraeum by short interval dipping where alternative game hosts are not abundant (Norval, 1981). However, once control breaks down, the distribution of A. hebraeum may expand rapidly as it has in Zimbabwe (Norval, 1983a) with accompanying heartwater outbreaks (Norval, 1981, 1983b).

In South Africa, adult A. hebraeum reach peak numbers in the summer months (Baker & Ducasse, 1967; Londt, Horak & De Villiers, 1979; Schröder, 1980). Utilizing available technology (Pope et al., 1985) it is possible to provide sustained blood ivermectin levels to cattle for a period of months. Administration shortly before the onset of peak A. hebraeum activity in October in the northern Transvaal, for instance, could result in a substantially reduced reproductive potential of females during the tick season.

Because ticks must attach and engorge to some extent, the "knockdown effect" seen with some dips may not be apparent with sustained low blood ivermectin levels, and the effect of treatment may only be seen later in the season or the following season as a result of the extremely low reproductive potential of Amblyomma feeding on the treated animals.

The effect of continuous ivermectin exposure on immature ticks has not been determined. According to Nolan (1983) Boophilus microplus frequently survive to the young adult stage before succumbing to ivermectin. Soll (unpublished observations, 1986) observed that A. hebraeum nymphs engorged on both untreated control animals and animals treated with ivermectin at approximately 40 µg/kg/d but that many of those engorging on treated animals did not moult successfully. Treatment of cattle under field conditions may not only prevent engorgement of adult A. hebraeum, but also limit the number of nymphs moulting to adults which could infest animals later in the season. Larvae parasitize a wide range of alternative hosts and their specific control is probably not as critical as that of the other 2 developmental stages.

The efficacy of continuous administration of ivermectin in a sustained release formulation against A. hebraeum may facilitate control or even elimination of the tick from certain areas and may thereby alter the epizootiology of heartwater in the cattle population in those areas. This concept needs to be tested in the field with a system designed to provide ivermectin release over an extended period.

**ACKNOWLEDGEMENTS**

The authors wish to acknowledge the technical assistance of Messrs R. G. Harvey, C. J. Smith, M. G. Rathogwa and Mrs S. Meyer. We should also like to thank Dr P. Oberem of the Veterinary Research Institute, Onderstepoort, Mrs S. Ford of the SABS Research Farm, East London, for supplying infective material and Mrs J. Oliver for typing the manuscript.

**REFERENCES**


CONTROL OF INDUCED INFESTATIONS OF ADULT AMBLYOMMA HEBRAEUM WITH SUSTAINED RELEASE IVERMECTIN


