ELSEVIER

Acta Tropica 68 (1997) 301–312

ACTA TROPICA

Failure of pyrantel in treatment of human hookworm infections (*Ancylostoma duodenale*) in the Kimberley region of North West Australia

James A. Reynoldson [a,*], Jerzy M. Behnke [b], Louise J. Pallant [a], Marion G. Macnish [a], Francis Gilbert [b], S. Giles [c], R.J. Spargo [c], R.C. Andrew Thompson [a]

[a] *World Health Organisation Collaborating Centre for the Molecular Epidemiology of Parasitic Infections and Institute for Molecular Genetics and Animal Disease, Division of Veterinary and Biomedical Sciences, Murdoch University, Murdoch 6150, Western Australia*

[b] *Experimental Parasitology Research Group and Behaviour and Ecology Research Group, Department of Life Science, University of Nottingham, University Park, Nottingham NG7 2RD, UK*

[c] *Health Department of Western Australia, Western Australia*

Received 6 January 1997; received in revised form 21 July 1997; accepted 28 July 1997

Abstract

A survey of 108 individuals from a coastal Aboriginal community in north Western Australia revealed that two species of gastrointestinal protozoan parasites (*Giardia duodenalis*—39.8%, *Entamoeba coli*—40.7%) and five gastrointestinal helminths (*Hymenolepis nana*—54.6%, Hookworm [*Ancylostoma duodenale*]—30.6%, *Enterobius vermicularis*—6.5%, *Trichuris trichiura*—2.8%, *Strongyloides stercoralis* 1.9%) were present. A total of 29 individuals infected with hookworm were offered treatment with either pyrantel pamoate at a single dose rate of 10 mg/kg body weight or albendazole (single 400 mg dose). Seven days after treatment stool samples were examined. Pyrantel had no significant effect against hookworm. In contrast, albendazole cleared hookworm infections completely and reduced the prevalence of *Giardia*. The former result suggests that locally *A. duodenale* is resistant to pyrantel and despite its relatively low cost and wide availability, should not be considered a drug of choice at this dose rate in the treatment of hookworm infections (*A. duodenale*) in endemic regions. © 1997 Elsevier Science B.V.

* Corresponding author. Tel.: +61 8 93602227; fax: +61 8 93104144; e-mail: reynolds@numbat.murdoch.edu.au

PII S0001-706X(97)00106-X

Keywords: *Ancylostoma duodenale*; *Giardia duodenalis*; Australian Aboriginal community; Chemotherapy; Albendazole; Pyrantel

1. Introduction

Hookworm infections are known to still exist among communities in the northern western regions of Australia, particularly among Aborigines (Meloni et al., 1993; Prociv and Luke, 1995a,b; Hopkins et al., 1997). Recent studies indicate that the species endemic in the region is *A. duodenale* (Hopkins et al., 1997). The current standard treatment by local health authorities for these parasites in this region is pyrantel at a single dose of 10 mg/kg body weight, a dose also used frequently in the past (Rossignol, 1990; Migasena and Gilles, 1991). Public health workers in the region have used pyrantel frequently for the treatment of hookworm infections but there has been a growing suspicion that treatment with this anthelmintic has been less effective than it should have been, as compared with reports in the literature (Farid et al., 1977)

To resolve the uncertainty about the efficacy of pyrantel in the treatment of *A. duodenale* infections locally, we conducted a trial, comparing its efficacy with that of albendazole, a drug reported to be highly effective against hookworm infections (Pene et al., 1982; Ramalingam et al., 1983; Rossignol and Maisonneuve, 1983) and which has a different mode of action (Lacey, 1990).

2. Materials and methods

2.1. Study site and subjects

The study was carried out in a remote, coastal Aboriginal community of about 350 people in the Kimberley region of North Western Australia. This community was surveyed in 1993 when a prevalence of infection with *Ancylostoma duodenale* of 80.3% was detected (Hopkins et al., 1997).

2.2. Quantification of hookworm infections

Fresh stools were obtained from individuals who participated in the study and examined on the same day by $ZnSO_4$ flotation, using standard techniques, for the presence of parasite eggs/cysts. These were identified and quantified subjectively using a scoring system from 0–4 to reflect numbers of transmission stages observed per field of vision through the microscope (at $\times 10$ objective) on standard glass slides. Stools from individuals who were thus diagnosed with hookworm infection were then re-examined and quantified by the Kato–Katz technique (Katz et al., 1972). Hookworm eggs were identified and some random positive samples were cultured to distinguish hookworm species. The intensity of infection was calculated

as eggs/g faeces (EPG) and then adjusted for stool consistency and age, according to WHO guidelines (World Health Organization, 1961).

2.3. Treatment with anthelmintic

Pyrantel pamoate (Combantrin) was obtained through the Kimberley Public Health Unit and was administered at a dose of 10 mg/kg according to the manufacturer's instructions. This is the dose normally used in the community and in previous studies (Haswell-Elkins et al., 1988; Mani et al., 1993). Albendazole (Zentel) was obtained from SmithKline Beecham (Australia) and given as a single dose of 400 mg. Pregnant women and children less than 2 years of age were excluded from the study. All participants who were initially treated with pyrantel were offered treatment with albendazole when the study had been completed.

2.4. Study design

In April 1996, with the co-operation of the school and health authorities, children in the community school were surveyed for intestinal parasites. Adults were encouraged to provide stools for analysis via the community health centre. Adequate data for analyses were obtained from 106 subjects. Those individuals who were found to be positive for hookworm infection were offered treatment with either pyrantel or albendazole, the choice made randomly within age and sex-matched cohorts. Only those administering treatment, but not the subjects themselves, were aware of the treatment allocations. A week later, treated subjects were asked to provide a second (post-treatment) stool sample for examination.

Each participant (or parent/guardian) was asked to sign a consent form after the objectives of the trial had been explained at public meetings and individually when clarification was sought. The trial was approved by the Murdoch University Human Ethics Committee and permission to conduct the study given by the community Chairperson and Health Committee.

2.5. Statistical analyses

The results of the trial are presented as prevalence values for all parasites and as quantitative EPG data for hookworm infections. Semi-quantitative score-data on relative infection levels with *Giardia* were also analysed. The effect of treatment on change in the intensity of *Giardia* infections was tested by the Kruskal Wallis one-way analysis of variance by ranks (treatment on difference between the pre-treatment scores and post-treatment scores) because non-normally distributed data was involved.

For quantitative adjusted EPG data, mean $\pm$ S.E.M. are presented for each treatment group and by sex at both pre- and post-intervention surveys. We also give the clearances which represent the number and percentage of individuals who were positive for hookworm eggs pre-treatment but showed no hookworm eggs post-treatment. The EPG data were analysed by GLIM (a statistical system for

generalised linear interactive modelling; GLIM 4, PC version, Royal Statistical Society 1993) as described previously using a model with negative binomial errors (Crawley, 1993; Behnke et al., 1994). For the full data-set from the pre-intervention survey we entered EPG values for the 33 individuals whose stools were examined by the Kato–Katz method and 0 for all remaining individuals whose stools did not yield hookworm eggs by the $ZnSO_4$ flotation method. Host sex and age were entered as factors in the analysis. Likewise, the EPGs for the 29 hookworm-positive subjects who participated in the trial were analysed by GLIM with treatment and host sex as factors. Age was not entered as a factor because the sample size was too small.

Small sample size and a large number of zero counts presented problems for GLIM, since the data no longer conformed to a negative binomial distribution and iterations diverged. Therefore, we used non-parametric statistical analyses as explained in the results section. To allow for the within-subject design, we analysed changes in faecal egg counts between pre- and post-intervention surveys of the full trial, rather than comparing the results from the two surveys with each other.

3. Results

3.1. Pre-intervention survey

Of the 106 subjects for whom sex and age were recorded, 48 were males and 58 females. Most participants (80.2%) were pre-school or aged 14 or younger. Twenty of these were in the age range 2–4 years. The older subjects were mainly women. Thus 15 females and only 6 males were over 15, and there were two subjects over 60 (one of each sex).

The pre-intervention survey revealed that 87% of the 108 subjects examined carried at least one species of parasite. The prevalence of single species and multiple species infections is given in Table 1. The most common parasite was *H. nana*, although *G. duodenalis*, *E. coli* and hookworm all showed prevalences in excess of 30%. The most common polyparasitism was for two species (32.4%) but three-species infections were also common and one subject had five of the seven species of parasites identified in the study.

Quantitative egg counts were carried out on the 33 subjects who were identified as hookworm positive. The age-intensity profile is illustrated in Fig. 1. The overall mean intensity of infection was 250.1 ± 64.4 EPG ($n = 106$), comprising 307.8 ± 95.2 ($n = 58$) among females (36.2% prevalence) and 180.5 ± 83.7 ($n = 48$) among males (prevalence of 25%). Table 2 shows the analysis of factors affecting the intensity of infection with *A. duodenale* stratified by age and gender. The intensity of infection significantly varied between the sexes ($P < 0.025$). Statistical analysis revealed that there were significant effects of age and an interaction between age and sex (Table 2). Across the age cohorts, prevalence varied from 20 to 35.5% (Fig. 1(a)). Fig. 1(b) shows that the age/sex interaction arose because the EPG values for male subjects fell in the male cohorts aged 15 and older, whereas the older female cohorts continued to harbour infection.

3.2. Effect of treatment on protozoan and helminth parasites

Of the 33 hookworm-infected subjects, only 29 provided post-treatment stool samples. The distribution of these 29 subjects by treatment, sex and age is summarised in Table 3. The groups were reasonably well matched for numbers of each sex and for age, except that the only adults in the trial were women, none of the male subjects complying fully with treatment and provision of post-treatment samples. Despite this difference, there was no overall significant difference in age between the two treatments.

Table 4 summarises the prevalence of intestinal infections, other than hookworm (all of these subjects were positive for hookworm), among the 29 subjects and by treatment, both before and after drug administration. The prevalence of some species was higher than that detected in the pre-treatment survey of 108 subjects, notably *Giardia* showed a higher prevalence (58.6 vs. 39.8%). *E. coli* was less prevalent before treatment but rose to 53.3 and 64.3% in the pyrantel and albendazole treatment groups respectively at the post-treatment survey. Prevalence was low for the remaining species of parasites. Pyrantel had no detectable effect against any of the parasites listed in Table 4. In contrast, there was a noticeable reduction in the prevalence of *Giardia* after treatment with albendazole and there was a significant difference between the treatment groups in the change in intensity of *Giardia* (Kruskal Wallis one-way analysis of variance by ranks, $H = 7.091$, $P = 0.008$).

Table 1
Prevalence of gastrointestinal protozoan and helminth parasites and polyparasitism among the subjects sampled prior to treatment ($n = 108$)

Species	Initial prevalence
Protozoan	
Giardia	39.8
Entamoeba coli	40.7
Helminth	
Hymenolepis nana	54.6
Hookworms	30.6
Enterobius vermicularis	6.5
Trichuris trichiura	2.8
Strongyloides stercoralis	1.9
Single and multiple infections	
One species only	29.6
Two species concurrently	32.4
Three species concurrently	18.5
Four species concurrently	5.6
Five species concurrently	0.9

Table 2
Statistical analysis of the factors affecting the intensity of infections with *A. duodenale*, taking both sex and age of host as factors, through a two-way analysis of variance with negative binomial errors

Source of variation	Change in deviance[a]	Scale parameter	Degrees of freedom	Scaled deviance[b]	*P*
Age	32813	1779	4	18.445	<0.001
Sex	9451	1600	1	5.907	<0.025
Sex × Age interaction	16567	1522	4	10.855	$0.05>P>0.025$

[a] Change in deviance following the removal of the combination specified in 'source of variation' column from the full factorial model. We begin by removing the age and sex interaction from the model. Then we remove the main effects each in turn, replacing them before and removing the next in the order from the base of the table towards the top.
[b] Scaled deviance is a measure of the contribution of the factor specified under the column labelled 'source of variation' to explaining the variation in the data. It is calculated by fitting an analysis of variance with negative binomial errors through GLIM and is distributed as χ^2. For the full factorial model the scale parameter was 1412. For full details see Behnke et al. (1994).

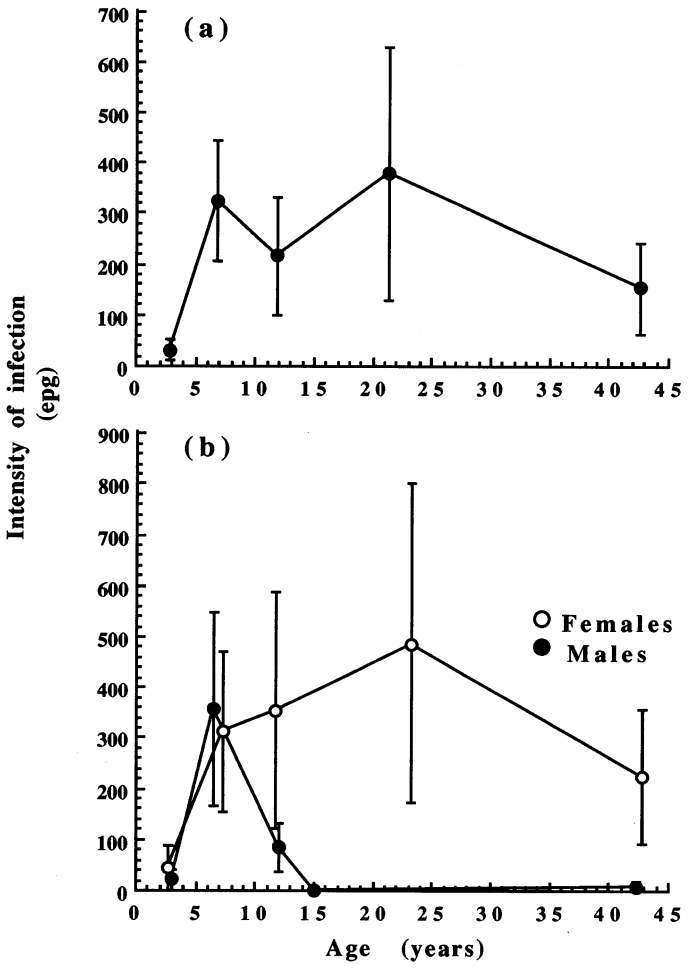

Fig. 1. Age-intensity and age-prevalence profiles for hookworm infection. Fig. 1(a) shows the mean EPG ± S.E.M. of all subjects plotted against the mean age of each cohort. The cohorts were as follows: < 4 years, $n = 10$; 4–9 years, $n = 44$; 10–14 years, $n = 31$; 15–29 years, $n = 9$; 30 years, $n = 12$. Fig. 1(b) shows the mean EPG by sex.

3.3. Effect of treatment on hookworm infections

Table 5 presents the mean adjusted EPGs and clearance of hookworm infections with treatment. Possible pre-existing differences between the treatment groups were examined through retrospective analysis of adjusted EPGs pre-treatment for the 29 subjects in the trial and the results (Table 5) indicate that there were no sex nor treatment-related effects on EPG values prior to drug administration. Hence our two groups were well matched.

Table 3
Composition of the subset of the study population, carrying hookworms at the pre-intervention survey and re-examined subsequently, by treatment, age and sex

Treatment	Sex	Number	Age		
			Mean ±	S.E.M.	Range
Pyrantel	Males	6	8.1	1.6	3.5–13.8
	Females	9	14.6	3.2	5.0–33.8
	Total	15	12.0	2.1	3.5–33.8
Albendazole	Males	4	8.7	1.3	5.4–11.9
	Females	10	11.3	3.2	2.9–39.0
	Total	14	10.6	2.3	2.9–39.0

Statistical analysis by Kruskal–Wallis one-way analysis of variance by ranks (treatment on age) gives $H = 0.21$, $P = \text{NS}$.

The outcome of treatment is also summarised in Table 5, which presents mean EPG values for the subjects in each treatment by age and clearance. The latter indicates that only two of 15 subjects given pyrantel ceased passing hookworm eggs after treatment, compared to 100% of those subjects given albendazole. Statistical analysis of the post-intervention faecal egg counts employed non-parametric techniques, in a two step procedure, first testing for an effect of sex, then treatment. In respect of two measures; EPGs at the post-intervention survey and change in EPG between the two surveys, there was no significant effect of sex ($H = 0.379$, 0.443 respectively; $P > 0.05$), indicating that both sexes responded indistinguishably from one another. In contrast, the effect of treatment was highly significant ($H = 16.821$, 5.352; $P < 0.001$, $P < 0.05$ respectively) confirming that pyrantel exhibited a signifi cantly lower effect than albendazole which was highly effective in removing hookworms.

4. Discussion

Our findings clearly confirm the suspicions of local public health workers, that pyrantel, at a single recommended dose of 10 mg/kg, is an ineffective treatment for hookworm infection caused by *Ancylostoma duodenale* in the Kimberley region of North Western Australia. Our results are also consistent with earlier studies (Albonico et al., 1994, 1995) emphasising the uniform effectiveness of albendazole against hookworm infection and its additional beneficial effect in reducing concurrent *Giardia* and possibly pinworm infections.

The pre-treatment parasite prevalence was similar to previous reports (Hopkins et al., 1997), but the finding of a significantly higher EPG for *A. duodenale* in women compared to men was unexpected. Although this result must be interpreted with caution it may suggest an immunologically-based difference in susceptibility between males and females or the existence of behavioural factors that result in the

Table 4
Prevalence of gastrointestinal protozoan and helminth parasites (apart from *A. duodenale*), before and after treatment, among the 29 subjects who were initially infected with hookworms and participated in the trial

Species	Initial prevalence. All subjects ($n = 29$)	Treated with pyrantel ($n = 15$)		Treated with albendazole ($n = 14$)	
		Before	After	Before	After
Protozoan					
Giardia	58.6	53.3	40	64.3	7.1
Entamoeba coli	27.6	20.0	53.3	35.7	64.3
Helminth					
Hymenolepis nana	58.6	60	60	57.1	57.1
Enterobius vermicularis	10.3	6.7	6.7	14.3	0
Trichuris trichiura	3.4	6.7	6.7	0	0
Strongyloides stercoralis	3.4	6.7	6.7	0	0

build-up of heavier worm burdens in women, perhaps as a result of more frequent exposure due to their association with children who defaecate promiscuously. The frequency distribution of EPGs also indicates a highly aggregated distribution of *A. duodenale* (data not shown). Across the age cohorts, intensity appeared to stabilise in the combined data-set, conforming to a typical monotonic age-intensity profile usually associated with hookworm infections (Behnke, 1987).

Most previous studies have been primarily concerned with the effects of pyrantel against *Necator americanus*, with clearance of 75–100% at a 10 mg/kg single dose rate (reviewed in Janssens, 1985; De Clercq et al., 1997). However, clearances ranging from 78–100% have also been reported for *A. duodenale* at this dose (Farahmandian et al., 1972; Goldsmid and Saunders, 1973; Farid et al., 1977). The reasons for the poor efficacy of pyrantel are not clear at this stage. It would appear that treatment strategies in this region of Australia may be inappropriate for *A. duodenale*, possibly due to host factors or the strain of parasite in this isolated region of northern Australia. However, a more likely possibility is that *A. duodenale* has developed resistance against pyrantel as a consequence of the drug's frequent use in the community over many years.

Resistance to anthelmintics is widespread among nematodes affecting domestic animals and occurs after only a few treatments at a time when most parasites are in their hosts (Waller, 1990; Coles et al., 1994). Such resistance has long been anticipated among human gastrointestinal nematodes (Smith, 1990; Geerts et al., 1997) and recent evidence has shown that *Necator americanus* in Mali has developed resistance to mebendazole (De Clercq et al., 1997). Consequently, future control strategies in the region will rely on the use of alternative drugs to pyrantel, based principally on the strategic use of the benzimidazoles combined with public health, environmental and educational programmes.

Table 5
Changes in intensity of infection with *Ancylostoma duodenale* between pre- and post-intervention surveys and cure rates following treatment ($n = 29$)

Treatment	Mean adjusted EPG ± S.E.M.		Change (%)[a]	Clearance[b]	
	Pre-treatment	Post-treatment		No.	%
Pyrantel ($n = 15$)					
All subjects	869.6 ± 304.8	1270.4 ± 583.4	(+) 46.1	2	13.3
Males	924.0 ± 567.2	1884.0 ± 1356.6	(+) 103.9	0	0
Females	833.3 ± 369.4	861.3 ± 416.5	(+) 3.4	2	22.2
Albendazole ($n = 14$)					
All subjects	816.4 ± 231.5	0	(−) 100	14	100
Males	762.0 ± 149.0	0	(−) 100	4	100
Females	838.2 ± 324.4	0	(−) 100	10	100

[a] Negative and positive signs indicate relative reduction or increase in EPGs, respectively.
[b] Number and percentage of subjects in treatment sub-set who had eggs during the pre-intervention survey but none at the post-intervention survey.

Acknowledgements

We are grateful for the financial support of SmithKline Beecham, the National Health and Medical Research Council of Australia and the Western Australian Lotteries Commission. JMB acknowledges the travel funding from the Royal Society. We are indebted to the nurses from the community health centre and the headmaster and his staff at the community school for their co-operation and support throughout our study, and for the technical support of Russ Hobbs. The support of the Health Department of Western Australia and the Commissioner of Health is gratefully acknowledged.

References

Albonico, M., Smith, P.G., Hall, A., Chwaya, H.M., Alaw, K.S., Savioli, L., 1994. A randomised controlled trial comparing mebendazole and albendazole against *Ascaris*, *Trichuris* and hookworm infections. Trans. Roy. Soc. Trop. Med. Hyg. 88, 585–589.

Albonico, M., Smith, P.G., Ercole, E., Hall, A., Chwaya, H.M., Alaw, K.S., Savioli, L., 1995. Trans. Roy. Soc. Trop. Med. Hyg. 89, 538–541.

Behnke, J.M., 1987. Do hookworms elicit protective immunity in man?. Parasitol. Today 3, 200–206.

Behnke, J.M., Pritchard, D.I., Wakelin, D., Park, J.R., McNicholas, A.M., Gilbert, F.S., 1994. Effect of ivermectin on infection with gastro-intestinal nematodes in Sierra Leone. J. Helminth. 68, 187–195.

Coles, G.C., Borgsteede, F.H.M., Geerts, S., 1994. Anthelmintic-resistant nematodes in the EU. Parasitol. Today 10, 288–290.

Crawley, M.T., 1993. GLIM for Ecologists. Blackwell, Oxford.

De Clercq, D., Sacko, M., Behnke, J.M., Gilbert, F., Dorny, P., Vercruysse, J., 1997. Failure of mebendazole in treatment of human hookworm infections in the Southern Region of Mali. West Africa. Am. J. Trop. Med. Hyg. 57, 25–30.

Farahmandian, I., Sahba, G.H., Arfar, F., Jabali, H., 1972. A comparative evaluation of the therapeutic effect of pyrantel pamoate and bephenium hydroxynaphoate on *Ancylostoma duodenale* and other intestinal helminths. J. Trop. Med. Hyg. 75, 205–207.

Farid, Z., Bassily, S., Miner, W.F., Hassan, A., Laughlin, L.W., 1977. Comparative single/dose treatment of hookworm and roundworm infections with levamisole, pyrantel and bephenium. J. Trop. Med. Hyg. 80, 107–108.

Geerts, S., Coles, G.C., Gryseels, B., 1997. Anthelmintic resistance in human helminths: learning from the problems with worm control in livestock. Parasitol. Today 13, 149–151.

Goldsmid, J.M., Saunders, R.C., 1973. Pyrantel pamoate for human hookworm infection. S. Afr. Med. J. 47, 25–26.

Haswell-Elkins, M.R., Elkins, D.B., Manjula, K., Michael, E., Anderson, R.M., 1988. An investigation of hookworm infection and reinfection following mass anthelmintic treatment in the South Indian fishing community of Vairavankuppam. Parasitology 96, 565–577.

Hopkins, R.M., Gracey, M., Hobbs, R.P., Spargo, R.M., Yates, M., Thompson, R.C.A., 1997. The prevalence of hookworm infection, iron deficiency and anaemia in an Aboriginal community in North-West Australia. Med. J. Aust. 166, 241–244.

Janssens, P.G., 1985. Chemotherapy of gastrointestinal nematodiasis in man. In: Vanden Bossche, H., Thienpont, D., Janssens, P.G. (Eds.), Chemotherapy of Gastrointestinal Helminths. Springer, Berlin, pp. 183–406.

Katz, N., Chaves, A., Pellegrino, J., 1972. A simple device for quantitative stool thick-smear technique in *Schistosomiasis mansoni*. Revt. Inst. Med. Trop. S. Paulo 14, 397–400.

Lacey, E., 1990. Mode of action of benzimidazoles. Parasitol. Today 6, 112–115.

Mani, G.G., Rao, T.S., Madhavi, R., 1993. Estimation of hookworm intensity by anthelmintic expulsion in primary schoolchildren in South India. Trans. Roy. Soc. Trop. Med. Hyg. 87, 634–635.

Meloni, B.P., Thompson, R.C.A., Hopkins, R.M., Reynoldson, Gracey, M., 1993. The prevalence of *Giardia* and other intestinal parasites in children, dogs and cats from Aboriginal communities in the Kimberley. Med. J. Aust. 158, 157–159.

Migasena, S., Gilles, H.M., 1991. Treatment of disease. In: Gilles, H.M., Ball, P.A.J., (Eds.), Human Parasitic Diseases, vol. 4, Hookworm Infections. Elsevier, Amsterdam, pp. 195–203.

Pene, P., Mojon, M., Garin, J.P., Coulaud, J.P., Rossignol, J.F., 1982. Albendazole: a new broad spectrum anthelmintic. Double-blind multicenter clinical trial. Am. J. Trop. Med. Hyg. 31, 263–266.

Prociv, P., Luke, R.A., 1995a. The changing epidemiology of human hookworm infection in Australia. Med. J. Aust. 162, 150–154.

Prociv, P., Luke, R.A., 1995b. Evidence for larval hypobiosis in Australian strains of Ancylostoma duodenale. Trans. Roy. Soc. Trop. Med. Hyg. 89, 379.

Ramalingam, S., Sinniah, B., Krishnan, U., 1983. Albendazole, an effective single dose, broad spectrum anthelmintic drug. Am. J. Trop. Med. Hyg. 32, 984–989.

Rossignol, J.F., 1990. Chemotherapy: present. In: Schad, G.A., Warren, K.S. (Eds.), Hookworm Disease, Current Status and New Directions. Taylor and Francis, London, pp. 281–290.

Rossignol, J.F., Maisonneuve, H., 1983. Albendazole: placebo-controlled study in 870 patients with intestinal helminthiasis. Trans. Roy. Soc. Trop. Med. Hyg. 17, 707–711.

Smith, G., 1990. Chemotherapy: future problems. In: Schad, G.A., Warren, K.S. (Eds.), Hookworm Disease, Current Status and New Directions. Taylor and Francis, London, pp. 291–303.

Waller, P.J., 1990. Resistance in nematode parasites of livestock to the benzimidazole anthelmintics. Parasitol. Today 6, 127–129.

World Health Organization, (1961) CCTA/WHO African conference on ancylostomiasis, Brazzaville, 22–29 August 1961. Tech. Rep. Ser. 1963; No. 225.