Anthelmintic resistance in South Africa: Surveys indicate an extremely serious situation in sheep and goat farming

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ABSTRACT

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Surveys to determine the prevalence and degree of resistance of *Haemonchus* spp. of sheep and goats to the available anthelmintics in South Africa indicate that small ruminant production is entering a crisis situation.

Three surveys employing the faecal egg count reduction (FECR) test to determine resistance were conducted in some of the main sheep-producing areas in the summer rainfall region of South Africa, where *H. contortus* is the principal worm species in sheep.

After analyzing the data recorded in the surveys by six different methods, including the RESO test at two different levels of confidence, the results obtained in the least stringent one (geometric mean reduction of the worm egg counts of drenched, vs untreated group of sheep) are reported in this paper, so that if any bias was obtained it would be in the favour of the anthelmintic.

In Mpumalanga and KwaZulu-Natal there was anthelmintic resistance in *Haemonchus* spp. on all the 52 farms surveyed. Sixteen percent of the strains of *H. contortus* were < 60 % susceptible to three of the four anthelmintics tested, and 8 % of the strains were < 40 % susceptible to all four of the anthelmintics. FECR tests of sheep in six localities in the Lebowa district of Northern Province indicated that even in previously disadvantaged communities where anthelmintic treatment is less intensive, anthelmintic resistance is developing, and is possibly at the level at which the situation on commercial sheep and goat farms in South Africa was 25 years ago.

From the data it appears that the level of anthelmintic resistance of *H. contortus* in South Africa is possibly the highest that has so far been recorded in the world and that strains of it are emerging that may soon not be controllable by treatment with any of the existing anthelmintics. Farmers in the summer rainfall region, if not the whole country, must be alerted to the immediate need for testing the parasite burdens of their sheep for susceptibility to preparations in all four groups of anthelmintic compounds currently available. Alternative methods of integrated worm control, including biological, must be sought and implemented with urgency, to reduce further selection for resistance and to induce reversion of the resistance that has already developed.

Keywords: Anthelmintic resistance, goats, *Haemonchus* spp., sheep, South Africa

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INTRODUCTION

Waller (1997) made the following statement: "Since the first reports of resistance to the broad spectrum anthelmintics were made some three decades ago, this phenomenon has changed from being considered merely as a parasitological curiosity to a state of industry crisis in certain livestock sectors."

From the results obtained in numerous trials for determining the spectra of resistance of individual

South African strains of helminths, it is evident that anthelmintic resistance is widely disseminated in South Africa. The worms affected are *Haemonchus contortus* (Berger 1975; Van Wyk & Malan 1988), *Trichostrongylus colubriformis* (Van Wyk, Bath, Gerber & Alves 1990), *Ostertagia* spp. (Van Schalkwyk, Geyser & Rezin 1983) and *Moniezia expansa* (Visser, Van Schalkwyk & Kotze 1987), as well as *Libyostrongylus douglassi* in ostriches (Malan, Gruss, Roper, Ashburner & Du Plessis 1988) and Cyothostominae in equids (Van Wyk & Van Wijk 1992). Detailed results of anthelmintic resistance surveys conducted in South Africa have, however, not been published previously.

This paper reports the results of three South African surveys conducted from 1992–1996.

MATERIALS AND METHODS

Faecal worm egg counts (FECs)

Faeces were collected from the rectum of each sheep and kept in cool boxes containing ice bricks until examined in the laboratory by means of a modified McMaster method (Reinecke 1973).

Class of sheep sampled

As far as possible, untreated weaner lambs were selected for the surveys described below, but when too few such lambs were available for the anthelmintic test (see below), lambs or adult sheep dewormed more than 6 weeks previously were used.

Selection of the farms

The criteria for selecting farms in the various surveys (Fig. 1–4) were: More than 200 sheep, mean FECs per gram of faeces exceeding 1 000, and farmer willingness to cooperate (Table 1).

Farms were selected in the following provinces, five of which are in the summer rainfall area: Mpumalanga, Gauteng, Northern Province, KwaZulu-Natal, Free State and Eastern Cape Province (Table1).

In the Ermelo district of Mpumalanga (Survey 1, Fig. 2, Tables 1 and 3–5) 50 farms were randomly selected, using a grid system, so that the results could be extrapolated statistically for the entire district. A hand-drawn grid consisting of 450 numbered blocks was laid over a map of the district, and the required number of blocks selected using tables of random numbers. One farm was listed per selected block, by identifying each farm underlying a specified corner of the block concerned. Of the 50 farms selected, 18 had to be excluded from the survey owing to non-compliance with the stipulated criterion of > 200 sheep, and six owing to FECs < 1 000. In this district there are approximately 475 farms, which run 200 or more sheep (E. van Vollenhoven, personal communication 1998). Thus, the survey included approximately 5,5 % of the farms which were eligible for the survey.

The farms in the other surveys were not selected similarly, but comprised about 25–30 % of the "eligible" sheep farms in the different districts concerned.

Faecal egg count reduction (FECR) test

This entails comparing the FECs of groups of sheep either treated with drugs from each of the anthelmintic groups, or left untreated as controls.

On the farms where FECR tests were planned, drenching of anthelmintics was discontinued, and at intervals FECs were monitored in groups of 10 sheep, until the mean counts were > 1 000. Thereafter the FECR test was conducted within a period of 2 weeks.

Treatment groups and allocation of animals to groups

Five treatment groups of sheep were constituted on every farm, the animals in four of which each received treatment with one of four specified anthelmintics (see below), while those in the fifth group served as untreated controls. Animals were apportioned to each of the groups in random sequence: the first five sheep encountered in a crush each received one of the five treatments and thereafter the same sequence of treatments was retained until the required number of 15 sheep per group had been attained. In a few cases where there were not enough animals, some of the groups contained fewer than 15 sheep, but not less than ten per group.

Immediately after each animal was allocated to its group it was weighed, a coloured plastic identification band was applied to a foreleg for group identification, a faecal sample was collected from the rectum for both an FEC and a differential larval count (see below), and (where applicable) the dose of anthelmintic it was to receive was calculated and thereafter administered orally using hypodermic syringes. The drug was deposited behind the bridge of the tongue and before each sheep was released it was closely observed to determine whether or not it had swallowed the dose. Control sheep did not receive a placebo.

Anthelmintics

The anthelmintics used in the surveys are listed in Table 2. Albendazole, levamisole, ivermectin and rafoxanide were selected to represent the benzimidazole, imidasothiasole, macrocyclic lactone (macrolactone) and salicylanilide groups of anthelmintics (Arundel 1985), respectively.

TABLE 1 Summary of the surveys

Survey (province[a]/district)	Year	Farms (n)	How selected
Mpumalanga			
Ermelo district	1995/6	26	Strict randomizing, using a grid system for statistically valid extrapolation to the entire district[b]
KwaZulu-Natal districts			
Underberg	1995/6	9	Included most farms with sufficient sheep and consenting farmers
Mount Currie	1995/6	12	
Estcourt	1995/6	5	
Various (MP, GP, FS, KZN, NP, EC)	1992/3	28	Consenting farmers

[a] Province: MP – Mpumalanga
GP – Gauteng
FS – Free State
KZN – KwaZulu-Natal
NP – Northern Province
EC – Eastern Cape Province (Van Wyk & Van der Merwe 1993)

[b] Of the 50 farms randomly selected using a grid system, 18 did not qualify according to the criterion of > 200 sheep per farm and 6 because mean FECs were < 1 000 per gram; no farmers were unwilling to co-operate

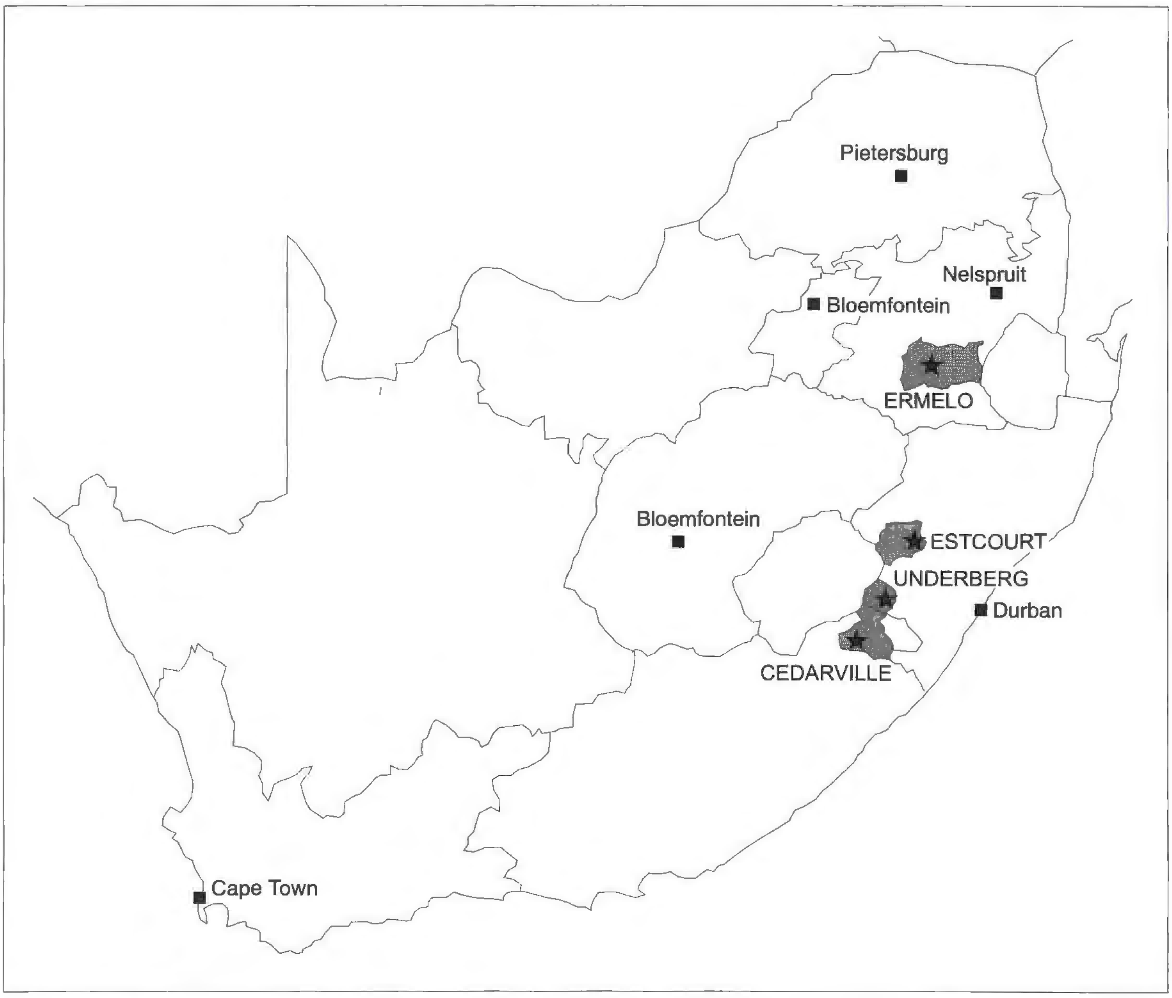

FIG. 1 Localities of Surveys 1 and 2 in South Africa

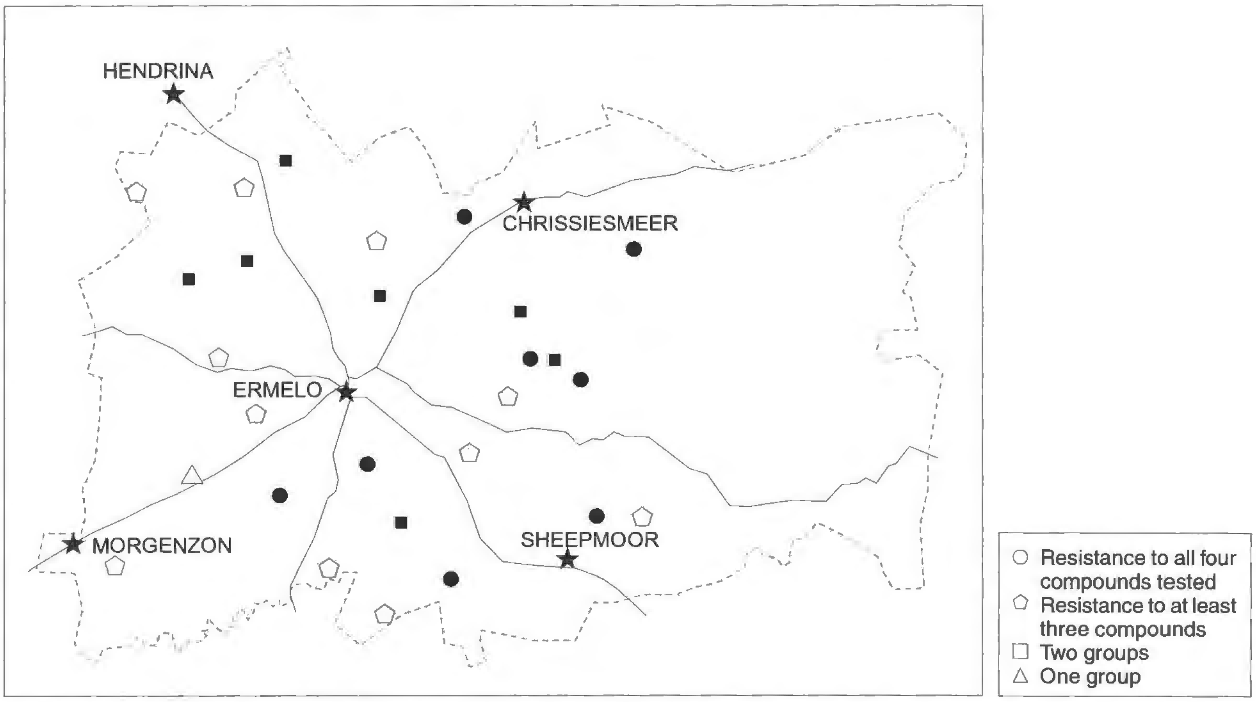

FIG. 2 Survey 1: Map of the Ermelo district (Mpumalanga), showing the distribution of the farms included in the survey

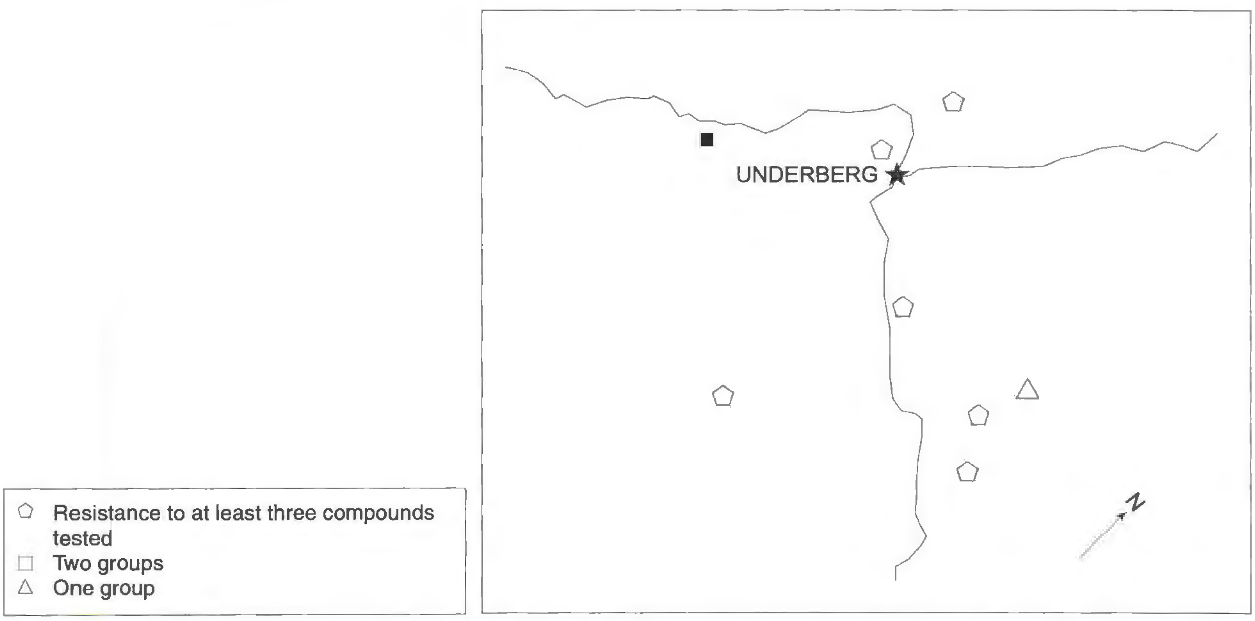

FIG. 3 Survey 2a: Map of the Underberg region (KwaZulu-Natal), to show the distribution of the farms

Differential larval counts

On the day of treatment a single bulk faecal sample was cultured for recovering and differentiating third-stage larvae (L3), followed on the day the post-treatment FECs were done, by a separate bulk sample for each of the test groups (Reinecke 1973).

Evaluation of the FECR test results obtained in the survey

The results were subjected to six methods of analysis, including the RESO statistical method (Anonymous 1989) at two levels of stringency (both the lower 95 % and the 90 % confidence limits of the

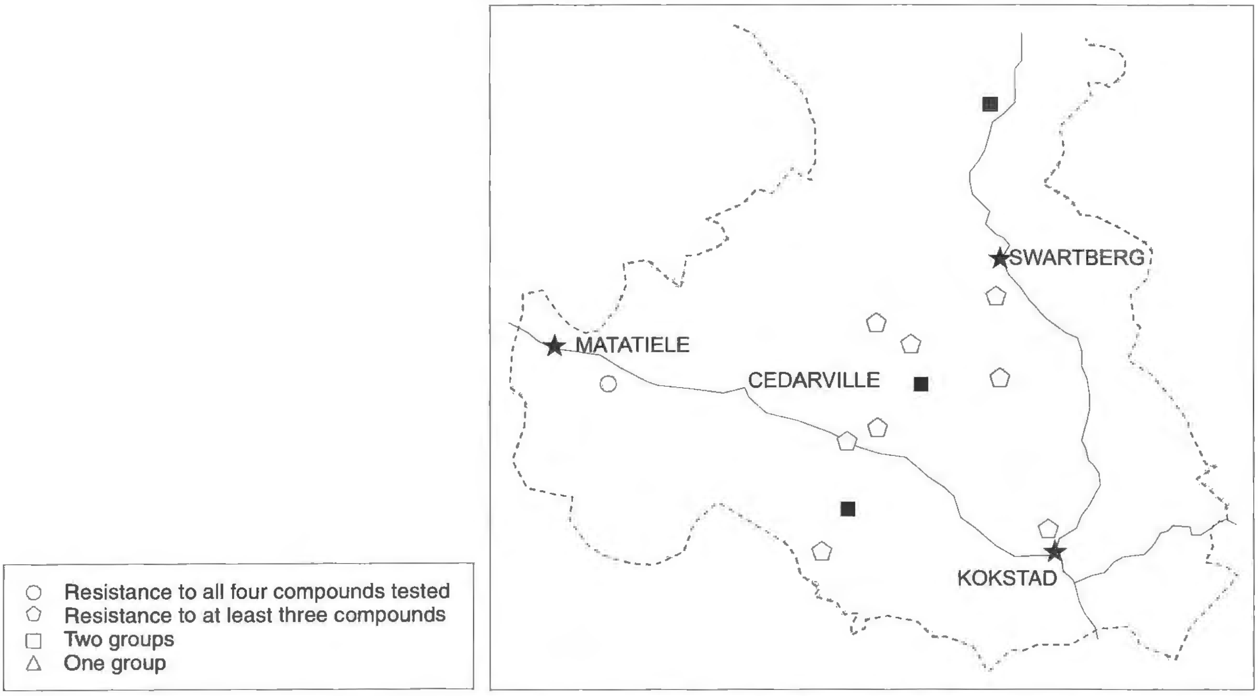

FIG. 4 Survey 2b: Map of the Mount Currie district (KwaZulu-Natal), depicting the farms tested

TABLE 2 Anthelmintics[a] drenched orally in the faecal egg count reduction tests

Active ingredient	Trade name	Company[b]	Dosage (mg kg^{-1})
Benzimidazoles			
Albendazole	Valbazen	SKB	3,8
Imidasothiazoles			
Levamisole	Ripercol	Janssen	7,5
Macrolactones			
Ivermectin	Ivomec	MSD	0,2
Salicylanilides			
Rafoxanide	Nasalcur	Hoechst	7,5

[a] In Surveys 2–5 (Table 1) all tests were done with a single batch of anthelmintic per active ingredient

[b] Hoechst – Hoechst Roussel Vet
Janssen – Janssen Pharmaceutica
MSD – Merck, Sharpe & Dohme (now Merial) products sold at that time by Logos Agvet in South Africa
SKB – SmithKline-Beecham, since taken over by Pfizer

percentage reduction < 90 %), and the following formula, using both the arithmetic and the geometric mean values of the test group FECs (Presidente 1985). The results listed are from the latter method, using the geometric mean values.

$$\text{Anthelmintic efficacy (\%)} = \left\{1 - \frac{C_1}{C_2} \times \frac{T_2}{T_1}\right\} \times 100$$

where T_1 and T_2 represent, respectively, the mean pre- and post-drenching FECs of the treated groups, and C_1 and C_2, similarly, the corresponding counts of the undrenched control sheep.

RESULTS

The results are summarized in Tables 3–6.

Differential larval counts indicated such a predominance (> 95 %) of the genus *Haemonchus* in the sheep on every farm included in Surveys 1 and 2 (Tables 1 and 3–6), that other genera could be ignored. In Survey 3 (in six provinces—Tables 1 and 3–6) individual efficacies were calculated (where applicable) for each nematode genus, according to the differential larval counts, but here also, *Haemonchus* spp. predominated.

Consequently, only the results of this worm genus are listed in this paper.

In the three surveys, from 93 % (Survey 3, in six provinces) to 100 % (Surveys 1 and 2: Ermelo and KwaZulu-Natal, respectively) of *Haemonchus* strains were less than 95 % susceptible; between 44 % and 83 % of strains were < 60 %; and between 40 % and 75 % were < 40 % susceptible to at least one of the four anthelmintics tested (Table 3).

TABLE 3 Resistance of *Haemonchus* spp. to at least one anthelmintic

Survey #	Locality	Farms (*n*)	Efficacy		
			< 95 %	< 60 %	< 40 %
			% of worm strains		
1	Mpumalanga				
	Ermelo (1996)	26	100	69	46
2	KwaZulu-Natal				
	Mount Currie (1996)	12	100	44	44
	Estcourt (1996)	5	100	80	40
	Underberg (1996)	9	100	83	75
3	Various provinces (1992)[a]	28	93	50	46
Total/mean		80	98,6	65,2	50,2

[a] Province: Mpumalanga, Gauteng, Free State, KwaZulu-Natal, Northern Province, Eastern Cape Province

TABLE 4 Strains of *Haemonchus* spp. resistant to three (or all four) anthelmintic groups

Survey #	Locality	Farms (*n*)	Efficacy[a]		
			< 95 %	< 60 %	< 40 %
			% of worm strains		
1	Mpumalanga				
	Ermelo (1996)	26	69 (19)	16 (8)	8 (8)
2	KwaZulu-Natal				
	Mount Currie (1996)	12	75 (8)	8 (8)	0 (0)
	Estcourt (1996)	5	60 (60)	0 (0)	0 (0)
	Underberg (1996)	9	78 (0)	0 (0	0 (0)
3	Various provinces (1992)[b]	28	60 (14)	11 (7)	7 (4)
Total/mean		80	64,8 (20,2)	7,0 (6,2)	3,0 (2,4)

[a] Figures in brackets: Resistance to compounds from all four groups

[b] Province: Mpumalanga, Gauteng, Free State, KwaZulu-Natal, Northern Province, Eastern Cape Province

Furthermore, on 60–75 % of all the farms, at least three of the anthelmintics tested were less than 95 % effective against the worm, with 8 % of the strains in Ermelo (Survey 1) < 40 % susceptible to all four of the anthelmintics tested (Table 4).

Levamisole was < 95 % effective on between 20 % and 27 % of the farms (with 0–8 % of the worm strains < 40 % susceptible), and thus least affected by resistance, while rafoxanide (79–96 % of worm strains were < 95 % susceptible; and 27–57 % < 40 % susceptible) and the benzimidazole, albendazole (with corresponding percentages of 75–85 % and 12–32 %) were hardest hit (Table 5). Ivermectin was intermediate: 50–92 % of strains < 95 %, and 8–27 % < 40 % susceptible.

In the resource-limited, communal grazing area of Lebowa, *Haemonchus* spp. from five of six localities were resistant to at least one compound, with those from one locality having resistance to two compounds and those from some of the others being on the border of resistance (Table 6).

Note, however, that the locality worst affected, Tompi Seleka, is a governmental farm, and hence, despite being situated in the underdeveloped Lebowa region, is not a communal grazing locality.

TABLE 5 Rate of failure of the individual anthelmintics tested, against the 80 strains of *Haemonchus* spp. in the five surveys

Survey #	Region and % efficacy	Strains tested (*n*)	% of worm strains[a]			
			Benz	Iver	Rev	Rfx
1	Ermelo	26				
	< 95		77	92	20	96
	< 60		20	38	8	69
	< 40		12	27	8	57
2	KwaZulu-Natal	26				
	< 95		85	77	27	92
	< 60		47	12	4	46
	< 40		32	8	0	27
3	Various provinces[b]	28				
	< 95		75	50	21	79
	< 60		39	21	11	46
	< 40		21	14	7	36
Total/mean		80				
	< 95		79	73	23	89
	< 60		35	24	8	54
	< 40		22	16	5	40

[a] Percentage of the worm strains with a geometric mean susceptibility of < 95 % to the different compounds (cf. Table 2):

Benz – benzimidazole
Lev – levamisole
Iver – ivermectin
Rfx – rafoxanide

[b] Province: Mpumalanga, Gauteng, Free State, KwaZulu-Natal, Northern Province, Eastern Cape Province

TABLE 6 FECR tests against *Haemonchus* spp. in Lebowa, a communal grazing area in Mpumalanga and the Northern Province

Locality	Anthelmintic efficacy (%)[a]			
	Lev	Rfx	Iver	Benz
Tompi Seleka[b]	95	61	96	26
Buffelsfontein	100	53	100	93
Nooitgesien	98	0	97	100
Klipspruit	100	95	99	100
Goedertrou	100	90	100	100
Vogelstruiskoppies	100	76	100	99
Mean	98,8	62,5	98,7	86,3

[a] Percentage of the worm strains with a geometric mean susceptibility of < 95 % to the different compounds (cf. Table 2):

Benz – benzimidazole
Lev – levamisole
Iver – ivermectin
Rfx – rafoxanide

[b] A government experimental farm—note that evaluation of the results with the RESO method (Anonymous 1989) indicates resistance against all four of the anthelmintics used (Van Wyk & Van der Merwe 1993)

DISCUSSION

As no adult worms, but only L3 from each locality included in the surveys were examined, the classification was done only to genus, and not species level. Nevertheless, the larval sheath morphology of the *Haemonchus* spp. encountered coincided with that of *H.contortus*, in contrast to the considerably longer free tail sheath of *H. placei* (Burger and Stoye 1968). Therefore it is probable that the overwhelming majority of the *Haemonchus* L3 were *H.contortus*.

The present surveys were conducted only in the summer, and non-seasonal rainfall regions of South Africa, which comprise more than 80 % of the important sheep-producing areas of the country. However, unpublished data emanating from trials conducted in the winter-rainfall region, where *Ostertagia* and *Trichostrongylus* spp. predominate, indicate that the situation regarding the ever-increasing worm resistance to anthelmintics is no better there than elsewhere in the country (A.P.R. Kloeck, unpublished observations 1991; R.K Reinecke, personal communication 1992).

The results obtained in the surveys not only strongly support the opinion of Waller (1997) that resistance is causing an industry-crisis in small ruminant farming, but it is also our opinion that they are the worst that have been published to date. It must also be kept in mind that South Africa was the first country in which resistance to rafoxanide (Van Wyk & Gerber 1980; Van Wyk, Malan, Gerber & Alves 1987), closantel (Van Wyk, Gerber & Alves1982), ivermectin (Carmichael, Visser, Schneider & Soll 1987; Van Wyk & Malan 1988), disophenol (Van Wyk, Malan & Randles1997) and nitroxynil (Van Wyk *et al.* 1997) was reported, as well as a helminth strain resistant to compounds from all five anthelmintic groups available for gastrointestinal nematode infection of small ruminants (Van Wyk *et al.* 1997).

When the efficacy of the four groups of anthelmintics administered to the sheep in the surveys was estimated using the arithmetic and the geometric mean values, the latter method yielded less stringent results, giving the anthelmintics a more favourable rating than the former. These differences in results concurred with those reported, amongst others, by McKenna (1997). For the present report it was decided to apply the more lenient of the six methods, to obtain a relatively conservative estimate of the present state of resistance in South Africa. On the other hand, we agree with McKenna (1997), that the arithmetic instead of the geometric mean should be used when advising farmers on the state of anthelmintic resistance and the implications for worm control on their farms. We have found it of value to calculate the results at two levels of confidence for the RESO (Anonymous 1989) method, as well as by that listed by Presidente (1985), using both the arithmetic and geometric mean FECs.

The results obtained for the prevalence of anthelmintic resistance in the Ermelo district (Survey 1; Tables 3 and 4) are statistically extrapolable to cover the entire district, and for this reason are more trustworthy as an indicator of the true prevalence and extent of resistance than those of the other two surveys. Similar levels of resistance were, however, found in the trials in Surveys 2 and 3 (Tables 3 and 4), as well as with subsequent random FECR tests on a few additional farms (J.A. van Wyk, M.O. Stenson & L.J. van Rensburg, unpublished data 1998).

Maciel, Giménez, Gaona, Waller & Hansen (1996) reported resistance in Paraguay to be "... by far the worst recorded in the world", and added: "... a large, and ever increasing, proportion of sheep farmers are rapidly approaching the time when they will have exhausted all chemotherapeutic options to control parasites." Similarly, after conducting a survey on 192 farms in Brazil, Echevarria, Borba, Pinheiro, Waller & Hansen (1996) described their resistance as constituting a crisis situation, and echoed the opinion regarding a future lack of effective anthelmintics. However, from Table 7 which compares the results obtained in South Africa with those of four Southern American countries, it is obvious that, despite using a considerably more lenient method of analysis than the RESO method (Anonymous 1989) used in the South American countries, the South African strains of *Haemonchus* tested appear to be at least as resistant as those of their most resistant counterparts in South America. While the South American results are reported only as percentages less than 95 % effective, our Table 4 shows disturbing proportions of farms where three, or even all four anthelmintics were respectively less than 60 % and 40 % effective against *Haemonchus*.

In a recent account of a strain of *H.contortus* resistant to eight of nine compounds tested, Van Wyk *et al.* (1997) posed the question: "How long will it be before resistance makes it impossible to control some field strains of *H.contortus* in South Africa with any of the modern anthelmintics?" At present another resistant strain under intensive investigation is known to be fully susceptible only to moxidectin, so that this and only one other compound, nitroxynil (as yet untested) perhaps hold promise for highly effective control (J.A. van Wyk, unpublished observations 1998). As both of these compounds are related to drugs to which there is already a high level of resistance on these farms, it seems likely that such worm strains will soon be uncontrollable unless new, unrelated compounds are developed, or unless exceptionally effective methods of biological control become available in the near future. In addition, considering the history of the macrolactones in South Africa (the first cases of resistance of *H. contortus* to ivermectin being recorded within 3 years after it had been registered for use in sheep in this country (Carmichael *et al.* 1987; Van Wyk & Malan 1988; Van Wyk, Malan, Gerber & Alves 1989), any single new anthelmintic group will probably bring but temporary relief to the resistance crisis, unless the present practice of excessive drenching is reduced considerably beforehand. According to Soll (1997), out of every 7 500 compounds identified by manufacturers/developers to have anthelmintic activity, only about one is eventually approved for commercial sale, and the process may take 11 years and cost more than US$100 million. McKellar (1994) estimates the costs at US$230 million. Furthermore, because the global sheep anthelmintic market is small (Soll 1997), the chances seem small that an adequate number of new, unrelated nematocidal compounds will be produced that would avert the resistance crisis.

What is disconcerting is that, despite the overwhelming evidence of serious anthelmintic resistance and catastrophic consequences it can have on ruminant production, the money made available in South Africa for investigating possible solutions to the phenomenon is rapidly dwindling. Another factor that has played a role is that we are probably paying the price of insufficient effort to transfer knowledge to farmers. As Waller, Dash, Barger, Le Jambre & Plant (1995) put it: "... results of [previous] research [has] remained virtually unused by farmers.

Although the research results, and the recommendations arising from them were published in scientific journals, the vital step of communicating [effectively] with advisory officers and farmers was not taken. Farmers were left to their own devices." The notion became established with farmers, their advisors and policy-makers, that anthelmintics could be used as the sole method of worm control. This arose from the perception that the stream of cheap, highly effective anthelmintics, which was reaching the market during the 1970s and 1980s, would never end.

As in Argentina (Eddi, Caracostantogolo, Peña, Schapiro, Marangunich, Waller & Hansen 1996) and Uruguay (Nari, Salles, Gil, Waller & Hansen 1996), South African farmers often do not perceive resistance to be a problem, despite the serious situation. This is probably because reasonably good worm control is maintained until the efficacy of the compounds drops to below about 50 %. This likelihood is supported by the reasonable clinical efficacy of older anthelmintics in South Africa, such as the old "Gow's Remedy For Wire Worm and Tape Worm" (containing arsenious oxide and nicotine), as well as the "Onderstepoort Nodular Worm Remedy" (containing copper arsenate and copper tartrate), which greatly reduced losses from worm infection, despite being only about 50 % effective against adult *H. contortus* and *Oesophagostomum columbianum*, respectively (J.A. van Wyk, unpublished observations 1971).

Whatever the reasons for the present resistance predicament, it is our opinion that the prevalence and high levels of resistance make it virtually impossible for anyone in South Africa to advise farmers effectively on worm control on any farm, without knowledge of the susceptibility status of the worm strain(s) on the farm concerned. Thus every effort should be made to convey this message to both the farmers and their advisors.

The resistance spectra on six localities in the resource-limited communal farming communities in Lebowa merit special consideration. In such situations it has been our experience that many stockowners do not consider internal parasites as important, possibly because of the latter's location in the hosts and generally small size. It also seems that many may even be unaware of the existence of such parasites. Consequently their treatment also receives a low priority rating.

The reason why *Haemonchus* has developed resistance to some anthelmintics on these communal grazing areas (Table 6) may possibly lie with one of the following: Firstly, the fact that, as in the case where the tests were conducted, some farms were appropriated from commercial farmers and added to the existing communal pastures. Secondly, the high resistance status which is present in the worms on Tompi Seleka, a Government experimental farm in Lebowa (Table 6), may have played a role. It has been noticed that on such experimental farms it is a common practice to drench animals intensively with anthelmintics, even as often as 12 times a year (J.A. van Wyk, unpublished observations 1990). One of the prime functions of Tompi Seleka and similar farms throughout the country is to breed and distribute animals of good quality to farmers to improve livestock production. In this way resistant worm strains may have been disseminated and the resistance enhanced by whatever drenching there was.

The development, prevalence and dissemination of resistance in helminths has been reviewed by several workers, amongst others, Martin (1985), Van Wyk (1990), Waller (1993; 1997) and Waller *et al.* (1995), but why did this resistance become such a particularly serious problem in South Africa?

Firstly, it seems a global problem that farmers do not realize the extent of the escalating resistance. For instance, in a survey in Uruguay, where high percentages of resistance were found (Table 7), the perception of the majority of the farmers was that the benzimidazole anthelmintics (61 % of worm strains resistant) and levamisole (29 % resistant strains) were performing satisfactorily (Nari *et al.* 1996). In our surveys in South Africa we found that very few farmers complained about resistance or appeared to be perturbed by the possibility of its development, even though some were of the opinion that "some of the compounds" were no longer as effective as previously. This even held true for the two farms in the Ermelo district, where the worst results were recorded (Table 9), as well as for the farm on which Van Wyk *et al.* (1977) recorded resistance of *H. contortus* to eight of the nine different compounds tested. The apparently continued advent of new compounds

TABLE 7 Resistance of *Haemonchus* spp. of sheep to various anthelmintics: Comparison of South Africa with four South American countries

Country[a]	Survey farms	Anthelmintic: % resistant farms[b]						
	(*n*)	Benz	Iver	Lev	Rfx	Clos	B + L	Overall
South Africa	80	79	73	23	89	–	–	98[c]
Paraguay*	37	70	67	47	–	–	–	?
Uruguay**	242	61	1	29	–	–	–	93
Brazil***	182	68	7	19	–	20	15	97
Argentina****	65	37	2	8	–	–	5	46

[a] * Maciel *et al.* (1997)
** Nari *et al.* (1997)
*** Echevarria *et al.* (1997)
**** Eddi *et al.* (1997)

[b] Benz – benzimidazole
Iver – ivermectin
Lev – levamisole
Rfx – rafoxanide
Clos – closantel
B + L – benzimidazole + levamisole
Overall – percentage of farms with resistance (< 95 % susceptibility of worm strains) to any anthelmintic
? – not listed in the relevant paper

[c] When analyzed by the RESO method, all three South African surveys show resistance on 100 % of the commercial farms investigated

TABLE 8 General South African inflation rate* 1961/1997, in relation to that of anthelmintics (using the launching price of thiabendazole as base)

Item	Inflation (%)
General inflation rate	2 700
"Older" groups	
Benzimidazoles	370
Closantel	463
Levamisole powder	147
Levamisole liquid	274
Rafoxanide	579
Mean	367
Macrolactones	
Ivermectin injectable	1 379
Moxidectin injectable	1 623
Mean	1 501
Mean: All compounds	691

[a] Inflation rate from 1961–1997 (S.A. Reserve Bank), and anthelmintic prices of June 1998 (Havemann, Hoechst Roussel Vet, personal communication 1998). In every case the price of the cheapest product available in South Africa in June 1998, was selected

TABLE 9 Resistance of *H.contortus* on two farms, where FECR tests were conducted after the surveys

Anthelmintic	Efficacy (%)	
	Farm 1	Farm 2
Ivermectin	9	0
Rafoxanide	0	14
Albendazole	0	22
Levamisole	34	39

such as moxidectin has tended to reinforce the belief that new compounds will continuously be found to avert a crisis. What the farmer seldom realizes, however, is that practically all of the new compounds being introduced belong to existing groups, with the result that side-resistance is likely when they are used.

Unnecessarily frequent drenching over the long term is very likely the main reason why resistance develops. Contributing to this is farmer reluctance to accept that serious resistance can develop and threaten livestock production, and, possibly more importantly, a plethora of cheap anthelmintics, which could be an asset to the farmer, yet has led to overuse.

Intensive competition between manufacturers and suppliers of anthelmintics has "fostered a 'drench gun' mentality" in many farmers (Waller 1993). This is well illustrated in South Africa by a comparison of the inflationary price rise of similarly safe and effective anthelmintics since the early 1960s (when thiabendazole first came on the market), with the general inflation rate. In Table 8 the initial price of thiabendazole (when it was launched in South Africa) is used as a basis for comparing prices of anthelmintics of broadly similar safety and efficacy in 1961 and 1997. Compared with a general inflation rate of 2700% (South African Reserve Bank), only the price of moxidectin (1 623 % "inflation") is relatively close to what is to be expected if prices of the modern, safe anthelmintics had risen accordingly; the mean price of the older groups of anthelmintics is 367% higher than that of thiabendazole in 1961, with a range of 147–579%. In other words, the mean general price rise was 7,4 times (range: 4,7–18,4 times) higher than that of the older groups of anthelmintics. Furthermore, if compared to the price rise of some other commodities needed by farmers, such as vehicles and farm implements, the difference is even larger. For instance, the rise in price of a light delivery vehicle has been more than 30% higher than that of the general inflation rate (J.A. van Wyk, unpublished observations 1997). Thus, the real price of most of the modern anthelmintics has dropped markedly over the years, encouraging farmers to rely almost exclusively on drenching for worm control. The advent of the generic compounds has dropped prices still more.

Another important contributing factor in the serious escalation of resistance in South Africa is wide dissemination by large-scale movement of animals within South Africa (Van Wyk 1990). Notably, it has happened repeatedly that whole flocks of sheep have been auctioned at stock sales, when severe multiple resistances became a threat to worm control. Another potentially dangerous system is the "Veld Ram" (field ram) clubs, where, in order to compare the performance of selected rams of various breeders under natural conditions, they are run together on common pasture for a year, whereafter the best performers are auctioned. In this type of system, of which numerous different ones already exist in South Africa, as many as 100 breeders are involved. During the period of observation, the rams in most systems are drenched frequently with anthelmintics, to eliminate the effects of helminths in the selection process. This has the potential to act as a "sieve" that concentrates the resistance genes in the helminths that have been introduced by the rams from the various breeders. Van Wyk, Van Schalkwyk, Bath, Gerber & Alves (1991) reported resistance to three anthelmintic groups on a ram club. Before rams in such a club are auctioned, they are dewormed, but their FECs are seldom monitored afterwards to verify the efficacy of the treatment. Therefore, selected worms are sold and distributed in selected sheep, or, rather, stud worms are purchased by the buyers, together with their stud rams!

CONCLUSION

The following statements by Waller (1997)—who is one of the most knowledgeable and recognized persons in this field—are repeated, as we so strongly concur: That "... the problem of anthelmintic resistance needs to be recognised globally as one of the greatest threats to grazing livestock production; ... [that] the solutions will not be found by piecemeal, *ad hoc* research directed at small sectors of the industry; ... [and that] concerted efforts, funded by the private and public sector, both nationally and internationally, are what is required."

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REFERENCES

ANONYMOUS 1989. Anthelmintic resistance. Report of the Working Party for the Animal Health Committee of the Standing Committee on Agriculture. Canberra (*SCA Technical Report Series*, no. 28).

ARUNDEL, J. 1985. The chemotherapeutic arsenal, in *Resistance in nematodes to anthelmintic drugs*, edited by N. Anderson & P.J. Waller, CSIRO Division of Animal Health, Australian Wool Corporation Technical Publication: 45–55.

BERGER, J. 1975. Resistance of a field strain of *Haemonchus contortus* to five benzimidazole anthelmintics in current use. *Journal of the South African Veterinary Association*, 46:369–372.

BÜRGER, H.-J. & STOYE, M. 1968. Parasitologische Diagnostik (Teil II), in ANONYMOUS, Therapogen Praxisdienst 3, Therapogen-Werk, MSD. Munchen:1–23.

CARMICHAEL, I., VISSER, R., SCHNEIDER, D. & SOLL, M. 1987. *Haemonchus contortus* resistance to ivermectin. *Journal of the South African Veterinary Association*, 58:93.

ECHEVARRIA, F., BORBA, M.F.S., PINHEIRO, A.C., WALLER, P.J. & HANSEN, J.W. 1996. The prevalence of anthelmintic resistance of sheep in Southern Latin America: Brazil. *Veterinary Parasitology*, 62:199–206.

EDDI, C., CARACOSTANTOGOLO, J., PEÑA, M., SCHAPIRO, L., MARANGUNICH, L., WALLER, P.J. & HANSEN, J.W. 1996. The prevalence of anthelmintic resistance of sheep in Southern Latin America: Argentina. *Veterinary Parasitology*, 62: 189–197.

MACIEL, S., GIMÉNEZ, A.M., GAONA, C., WALLER P.J. & HANSEN J.W. 1996. The prevalence of anthelmintic resistance of sheep in Southern Latin America: Paraguay. *Veterinary Parasitology*, 62:207–212.

MALAN, F.S., GRUSS, B., ROPER, N.A., ASHBURNER, A.J. & DU PLESSIS, C.A. 1988. Resistance of *Libyostrongylus douglassi* to levamisole in ostriches. *Journal of the South African Veterinary Association*, 59:202–203.

McKELLAR, Q.A. 1994. Chemotherapy and delivery systems — helminths. *Veterinary Parasitology*, 54:249–258.

McKENNA, P.B. 1997. Use of arithmetic and geometric means in the calculation of anthelmintic efficacy. *Veterinary Record*, 141:472–473.

MARTIN, P.J. 1985. Nematode control schemes and anthelmintic resistance, in *Resistance in nematodes to anthelmintic drugs*, edited by N. Anderson & P.J. Waller, CSIRO Division of Animal Health, Australian Wool Corporation Technical Publication: 29–40.

NARI, A., SALLES, J., GIL, A., WALLER, P.J. & HANSEN, J.W. 1996. The prevalence of anthelmintic resistance of sheep in Southern Latin America: Uruguay. *Veterinary Parasitology*, 62:213–222.

PRESIDENTE, P.J.A. 1985. Methods for detection of resistance to anthelmintics, in *Resistance in nematodes to anthelmintic drugs*, edited by N.Anderson & P.J.Waller, CSIRO Division of Animal Health, Australian Wool Corporation Technical Publication: 13–27.

REINECKE, R.K. 1973. *The larval anthelmintic test in ruminants* (Technical Communication no. 106, Department of Agricultural Technical Services, Republic of South Africa).

SOLL, M.D. 1997. The future of anthelmintic therapy from an industry perspective, in *Managing anthelmintic resistance in endoparasites*, edited by J.A. van Wyk & P.C. van Schalkwyk. Workshop held at the 16th International Conference of the World Association for the Advancement of Veterinary Parasitology, 10–15 August 1997, Sun City, South Africa: 1–4.

VAN SCHALKWYK, P.C., GEYSER, T.L. & REZIN, V.S. 1983. Twee gevalle waar *Ostertagia* spp. van skape teen bensimidasool wurmmiddels bestand is. *Journal of the South African Veterinary Association*, 54:93–98.

VAN WYK, J.A. 1990. Occurrence and dissemination of anthelmintic resistance in South Africa, and management of resistant worm strains, in *Resistance of parasites to antiparasitic drugs*, edited by J.C. Boray, P.J. Martin & R.T. Roush. Round Table Conference held at the VIIth International Congress of Parasitology, Paris, August 1990: 103–113.

VAN WYK, J.A., BATH, G.F., GERBER, H.M. & ALVES, R.M.R. 1990. A field strain of *Trichostrongylus colubriformis* resistant to levamisole and morantel in South Africa. *Onderstepoort Journal of Veterinary Research*, 57:119–122.

VAN WYK, J.A. & GERBER, H.M. 1980. A field strain of *Haemonchus contortus* showing slight resistance to rafoxanide. *Onderstepoort Journal of Veterinary Research*, 47:137–142.

VAN WYK, J.A., GERBER, H.M. & ALVES, REGINA M.R. 1982. Slight resistance to the residual effect of closantel in a field strain of *Haemonchus contortus* which showed an increased resistance after one selection in the laboratory. *Onderstepoort Journal of Veterinary Research*, 49:257–261.

VAN WYK, J.A. & MALAN, F.S. 1988. Resistance of field strains of *Haemonchus contortus* to ivermectin, closantel, rafoxanide and the benzimidazoles in South Africa. *Veterinary Record*, 123:226–228.

VAN WYK, J.A., MALAN, F.S., GERBER, H.M. & ALVES, R.M.R. 1987. Two field strains of *Haemonchus contortus* resistant to rafoxanide. *Onderstepoort Journal of Veterinary Research*, 54: 143–146.

VAN WYK, J.A., MALAN, F.S., GERBER, H.M. & ALVES, R.M.R. 1989. The problem of escalating resistance of *Haemonchus contortus* to the modern anthelmintics in South Africa. *Onderstepoort Journal of Veterinary Research*, 56:41–49.

VAN WYK, J.A., MALAN, F.S. & RANDLES, J.L. 1997. How long before resistance makes it impossible to control some field strains of *Haemonchus contortus* in South Africa with any of the anthelmintics? *Veterinary Parasitology*, 70:111–122.

VAN WYK, J.A. & VAN DER MERWE, J.S. 1993. Anthelmintic resistance in South Africa: An update, in *Understanding and control of parasitic diseases of animals*. 14th International Conference of the World Association for the Advancement of Veterinary Parasitology. Cambridge, 8–13 August 1993: 371.

VAN WYK, J.A., VAN SCHALKWYK, P.C., BATH, G.F., GERBER, H.M. & ALVES, R.M.R. 1991. Die gevaar van wye verspreiding van weerstandbiedendheid teen wurmmiddels deur veldramp-prestasietoetssentra. *Journal of the South African Veterinary Association*, 62:171–175.

VAN WYK, J.A. & VAN WIJK, E.F. 1992. Weerstand van klein strongiele van 'n perdestoetery in Suid-Afrika teen die bensimidasool wurmmiddels. *Journal of the South African Veterinary Association*, 63:144–147.

VISSER, E.L., VAN SCHALKWYK, P.C. & KOTZE, S.M. 1987. Aanduidings van weerstand by lintwurms van kleinvee, in *Worm resistance workshop, Onderstepoort*, edited by J. Schröder. 24–25 August, 1987: 24–28.

WALLER, P.J. 1993. Towards sustainable nematode parasite control of livestock. *Veterinary Parasitology*, 48:295–309.

WALLER, P.J. 1997. Anthelmintic resistance. *Veterinary Parasitology*, 72:391–412.

WALLER, P.J., DASH, K.M., BARGER, I.A., LE JAMBRE, L.F. & PLANT, J. 1995. Anthelmintic resistance in nematode parasites of sheep: learning from the Australian experience. *Veterinary Record*, 136:411–413.