Parasite Control in Farm Animals – Present and Future

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Introduction

Parasitic worm infections can cause serious clinical disease, welfare problems and loss in production in farm animal species. As animal production has become more intensive the threat of parasitic disease has increased. Farmers are now very reliant on strategic, and in many cases "blanket", use of anthelmintic drugs to maintain health and production levels.

Over the last 40 years a number of very effective anthelmintic drug treatments have been discovered and made available to farmers to successfully control parasite disease. However, resistance to these drugs is becoming increasing prevalent, particularly in sheep, and there is little prospect of new drugs coming onto the market in the near future. Therefore there is an urgent need to re-evaluate parasite control measures to ensure animal production is sustainable. This paper discusses the emerging problem of anthelmintic resistance and strategies to aid parasite control. The paper will focus on the main research programmes that are currently being undertaken by the Veterinary Sciences Division and the Agricultural Research Institute of Northern Ireland to investigate strategic control of internal parasites in sheep. This work is jointly funded by DARD and *AgriSearch*.

Anthelmintics and Resistance in Gut-worms

The first, effective broad-spectrum anthelmintic (thiabendazole) was introduced in the early 1960's. Since then the use of effective anthelmintics has formed the essential corner stone in parasite control to allow intensive farm production to be viable and profitable. However, this is now under significant threat from resistance of parasites to these anthelmintics, which is considered by some to be the biggest treat to livestock farming throughout the world, particularly the sheep sector (Waller, 2003).

Anthelmintics used to prevent or treat gut-worm infections in domestic animals, in general, fall into 3 major groupings depending on their chemical structures and modes of action:

- Group 1-BZ are the benzimidazoles or "white drenches"
- Group 2-LM includes levamisole and morantel
- Group 3-ML are the macrocyclic lactones, which include doramectin, ivermectin and moxidectin

A recent Scottish survey, involving 90 sheep farms, found 64% of all flocks (81% of lowland flocks) had evidence of resistance to BZ drugs (Bartley *et al*., 2003).
In sheep, resistance to LM and ML drugs does not appear to be as prevalent. However there have been a number of reports since the mid-1990s of resistance to LM drugs, principally levamisole (Hong *et al*., 1994; Coles and

Simkins, 1996; Coles *et al*., 1998) and ML drugs (Sargison *et al*., 2001; Yue *et al*., 2003).

What is of greatest concern is the fact that multiple resistance (i.e. resistance to all three groups of drugs) can occur and when it does, it can render farm animal production unsustainable. This has already occurred in many parts of South Africa, Australia, North America and particularly South America (Waller *et al*., 1997; Taylor, 1999). There have been three recent reports of multiple resistance in the UK, two in Scotland (Sargison *et al*., 2001; Bartley *et al*., 2004) and one in Devon (Yue *et al*., 2003), where the advice given to the farmer was to cull his entire flock and plough-up the pastures. The situation on N. Ireland sheep farms is unknown but anecdotal evidence from diagnostic/surveillance submissions to the laboratories at the Veterinary Sciences Division and discussions with veterinary surgeon and farmers would suggest that the situation is likely to be, at least, on a par with mainland UK.

Although resistance to gut-wormers in cattle is much less prevalent it would also appear to be on the increase (Coles, 2002; Anziani *et al*., 2004). Currently the goat industry appears to be under an even greater treat than the sheep industry, with widespread, multiple resistance reported throughout the world (see review by Waller, 1997; Mortensen *et al*., 2003).

The reason why drug resistance has become such a problem is complicated. Although most drugs when initially marketed are very effective, no drug can be guaranteed to kill 100% of the worms present. Those worms left behind form a greater proportion of the parasite population and as drug resistance is heritable a greater number of the next generation of worms will have the resistant genes. This potential problem has long been recognised and farmers are advised to alternate or rotate drugs, annually, from the different groups of anthelmintics. However, this advice has largely been ignored (Coles, 1997) and drugs from the same group of drugs are used, often over-used, on the same farm for years. In addition, widespread under-dosing appears to have contributed significantly to anthelmintic problems in the field (Taylor, 1999). In an Australian survey 86% of estimated lamb weights were below the correct weight (Besier and Hopkins, 1988). If lambs are under-dosed, as a result of either underestimation of weight, inaccurate calibration of drenching guns or poor drenching technique then there is a much greater likelihood of resistant worms surviving (O'Brien, 1998; Silvestre *et al*., 2002).

The potential threat to the UK sheep industry has now been recognised by Government who recently reviewed parasite control and published new recommendations (http://www.defra.gov.uk/animalh/diseases/control/parasite_control.htm)

Recommendations for gut parasites include:

- Quarantine treatment for bought-in animals with both an ML and a LM drug, sequentially
- Good drenching technique to ensure correct dose volumes are used and that oral drenches are fully swallowed. Withholding feed for 12-24 hours

prior to drenching should be considered, where practical, to improve efficacy

- Need to rotate chemical groups of anthelmintics (this does not apply to “quarantine treatments”)
- Testing flocks using pre-drenching faecal egg counts (FECs) to determine most suitable time to treat
- Correct use of safe pastures. In particular sheep must not be drenched directly on to “safe” pasture as this practice is highly selective for anthelmintic resistance
- Elimination of unnecessary dosing particularly of ewes. Fit ewes should not be dosed pre-tupping and ewes do not always need to be treated around the lambing period

The Use of Faecal Egg Counts as a Parasite Management Tool

One of the most practical recommendations to control anthelmintic resistance is the specific targeting of anthelmintic dosing to when animals actually need it, thereby ensuring efficient and cost-effective use of the drug. In addition, strategic use of anthelmintics should obviously be a goal for all farmers to ensure costs are minimised and profitability maximised. Many factors should be considered before deciding when to dose animals, including age of animals, grazing and dosing history, performance/condition and clinical signs of scour/illness. Faecal egg counts (FECs) give a reasonable estimate of worm burdens in young ruminants, especially lambs (Mc Kenna, 1981) and have been used in conjunction with other considerations, already mentioned, to decide when to dose young ruminants.

A parasite control system, Fecpak (Fecpak International Ltd., New Zealand), incorporating on-farm FECs has been recently introduced to the UK and Ireland. Farmers, advisors or vets can use a "Fecpak" kit to carry out on-farm FECs. This kit provides everything needed to do FECs including equipment, detailed information on the correct method of collecting and testing faeces samples, guidelines for decision making, and up-to-date information *via* a newsletter.

FECs can be carried out on samples from individual animals but most frequently a "mob" sample, consisting of samples from 20 sheep (i.e. from 20 dung pats) combined, is tested to provide average faecal counts for a flock or group of animals.

It is claimed that the "Fecpak" system takes the guesswork out of parasite control and provides timely supplementary information to the farmer. It can be used to:

- Monitor the trends and level of parasitism in sheep
- Ensure good timing of anthelmintic treatment
- Monitor the effectiveness of specific anthelmintic treatments
- Build worm burden profiles during problem times of the year and also identify fields where heavy worm contamination has occurred
- Monitor the effectiveness of grazing management and other management decisions

The potential use of the “Fecpak” system within any parasite control strategy was acknowledged by Vipond (1998) but caution was recommended until the system was evaluated under laboratory and field conditions in the Untied Kingdom. Therefore a major research programme was initiated in 2002 by the Veterinary Sciences Division and the Agricultural Research Institute of Northern Ireland to investigate the potential use of the “Fecpak” system on commercial farms throughout Northern Ireland (McCoy *et al*., 2004). A total of five lowland sheep farms, located throughout Northern Ireland were involved in the study. All farms were involved in an easycare research programme in conjunction with the research team at Hillsborough to investigate the potential for grass-based lambing systems to reduce feed costs and labour requirements relative to conventional indoors lambing systems (Carson *et al*., 2004). The use of FECs as a tool to potentially reduce the labour input associated with dosing sheep was also considered to be an important component of easycare systems of sheep production. On each of the farms involved in the study (including the ARINI flock), FECs were monitored in ewes and lambs using both the "Fecpak" system and the standard laboratory, McMaster technique carried out in VSD. Faecal samples were collected from the rectum of 20 –25 lambs on each farm immediately pre-dosing and at 10 to 14 days after dosing. At each sampling point, faecal samples were also taken from 20 lamb dung pats (“mob” sample) by each producer according to “Fecpak” instructions. Faecal egg counts were carried out on the following samples:

- 20-25 individual dung samples analysed at Veterinary Sciences Division using McMaster technique
- “mob” sample collected by farmer and analysed at Veterinary Sciences Division using McMaster technique
- “mob” sample collected by farmer and analysed at Veterinary Sciences Division using “Fecpak” technique
- “mob” sample collected by farmer and analysed by farmer using “Fecpak” technique

The FEC’s obtained by each method were then compared. In the laboratory, the FECs from the “mob” samples were found to be comparable to the mean FECs from the 20-25 lambs, suggesting that a “mob” sample is fairly representative of the flock or group. In the laboratory, the FECs in the “mob” samples were similar when using either the “Fecpak” system or the standard McMaster laboratory method, confirming that in the hands of experienced operators the “Fecpak” system compares well to the McMaster technique.

There was no significant difference between the laboratory and farmer “Fecpak” results in *Nematodirus* egg counts (Table 1). *Nematodirus* infections cause problems in lambs in early spring and eggs present in the faeces are relatively large and easily recognised. However, there was a highly significant difference in strongyle worm egg counts (n= 24 pairs, $P<0.001$), as all flock owners over-estimated worm burdens with FECs often 10 times higher and sometimes over 100 times higher compared to those counted in the laboratory (Table 1). Strongyle infections cause problems in lambs throughout the summer and autumn and the eggs in faeces are relatively small. While imprecise sample preparation may have contributed to this over-estimate it would appear from our investigations that the main problem was the inaccurate identification of worm eggs. *Strongyloides* infections occur during the summer months and are generally of little pathogenic importance. However, they produce eggs similar in size to strongyle eggs and these eggs appeared to have contributed to the over-estimation of FECs carried out by the farmers. Other structures present, such as pollen and coccidial oocysts may also have contributed to the over-estimation of FECs.

The significance of FECs and the subsequent parasite control actions to be taken depend on many factors including the age of animal, grazing history, current performance and growth rates, previous treatments, the time since last treatment, withholding times and the presence of intercurrent disease. However, in many cases the FECs would be a major factor in deciding when to dose. The results of the study suggest that farmers using "fecpak" need to be competent and confident in using the system and together with their veterinary surgeons consider all factors before deciding when to dose. The results of the Fecpak study suggest that the "fecpak" system could be useful in skilled hands but could also be dangerous in unskilled hands (McCoy *et al*., 2004).

Table 1. Faecal strongyle egg counts (eggs per gram of faeces; epg), using the "Fecpak" system performed by laboratory staff ("Laboratory Fecpak") and by flock owners ("Farmer Fecpak") from mob faeces samples collected from lambs on five sheep farms

Flock	**Laboratory Fecpak** *Nematodirus* (epg)	**Farmer Fecpak** *Nematodirus* (epg)	**Laboratory Fecpak** Strongyle (epg)	**Farmer Fecpak** Strongyle (epg)
A	30	0	60	14340
A	0	0	0	4800
A	10	0	280	5730
B	360	150	140	1260
B	100	60	250	840
B	0	0	10	210
B	0	60	30	1140
B	50	90	100	1500
C	570	0	20	870
C	0	0	0	0
C	200	360	50	930
C	0	0	50	480
C	20	90	120	480
C	0	0	50	240
C	0	0	320	780
D	640	780	40	4920
D	590	210	440	6300
D	0	60	150	4500
D	50	150	230	5520
D	0	90	220	3870
D	0	30	60	4050
E	210	300	80	330
E	0	180	10	360
E	100	120	160	570

One farmer (Farm F) did not submit his on-farm "fecpak" results.

The "Fecpak" study also permitted the evaluation of the efficacy of anthelmintics and the prevalence of drug resistance on the farms participating in the study. The McMaster technique was used to compare pre- and post-dosing FECs. Results suggested that some resistance was present on two of the three farms using BZ drugs. No resistance was detected on farms using ML drugs. It is also interesting to note that the dosing guns, used on two of the five trial farms, were discovered to be supplying inaccurate amounts of anthelmintic. This finding highlighted the need for farmers to check the calibration of their dosing equipment in order to avoid seriously inaccurate administration of anthelmintics, which in-turn contributes to the development of anthelmintic resistance.

Overall, farmers, as a matter of urgency, need to adopt management strategies to prevent or limit drug resistance and its potential impact on the industry. If anthelmintic resistance is allowed to progress unchecked then there is the very real likelihood that farm animal production will be unsustainable on many farms. This nightmare situation has already arrived on a few farms in England and Scotland. There is an urgent need to investigate parasite resistance to anthelmintics in farm animals in N Ireland to ensure that good farm management practices are employed on farms to not only slow down the development of resistance but also decrease the dependence on anthelmintic drugs.

Alternative Methods of Parasite Control

Dietary Manipulation of Worm Burdens

Nutrition, in particular protein nutrition, can have a major effect on both the resistance (i.e. the ability of the animal to limit worm establishment) and resilience (i.e. the ability of the animal to maintain performance in the face of the worm challenge) of animals to parasites (Coop and Sykes, 2002). Supplementation of feed, with protein (Donaldson *et al*., 1998) and energy (Knox and Steel, 1999) has been shown to enhance the ability of sheep to counteract parasite infections. However, practical, cost-effective nutritional regimes need to be developed to suit all types of management systems, especially low input systems.

Condensed tannins have also been shown to influence worm burdens in sheep under experimental conditions (Athanasiadou *et al*. 2000). Tannins are naturally occurring in some plant species (e.g. sulla and *Lotus* spp.) and in studies where sheep have been grazing these plants *in situ,* an increase in both the resistance and resilence to guts worms have been observed (Niezen *et al*. 1998; Molan *et al*. 2002). Tannins enhance protein metabolism and absorption in the gut (Coop and Sykes, 2002) and may also have a direct killing effect on gut parasites (Athanasiadou *et al*., 2000). However, tannins in excess can lower feed intakes (Barry and McNabb, 1999) and the efficacy varies with different species of gut worms (Niezen *et al*., 2002) and with dietary protein concentrations (Athanasiadou *et al*., 2001).

To further investigate the potential of nutritional methods to control worm burdens on farms in Northern Ireland, the effect of protein and tannin content in concentrate diets offered to lambs was investigated on six lowland farms located throughout Northern Ireland including the research farm at ARINI (Dawson *et al*., 2004). This work is part of the on-going easy-care sheep research programme undertaken in conjunction with the research team at ARINI and jointly funded by DARD and *AgriSearch*. On each of the five lowland farms involved in the study, lambs were offered no creep or a high protein creep concentrate (180 g crude protein (CP)/kg fresh), *ad libitum*, in the period from six weeks of age until weaning. At ARINI an additional treatment of low protein creep concentrate (120 g CP/kg fresh) was offered. After weaning at approximately 12 weeks of age, on each of the five farms, lambs on each of the pre-weaning treatments were re-allocated to one of two post-weaning concentrate diets offered at 500 g/d balanced for pre-weaning treatment, lamb breed and lamb live weight gain from birth to weaning. The treatments comprised a high protein concentrate (180 g CP/kg fresh) or a high protein concentrate (180 g CP/kg fresh) supplemented with 80 g tannins/kg fresh weight. At ARINI two additional treatments comprising, low protein concentrate (120 g CP/kg fresh) and low protein concentrate, supplemented with 80 g tannins/kg fresh weight were also investigated. On each of the five farms involved in the study, lambs were dosed at monthly intervals; at ARINI, lambs were dosed at six weeks of age and at weaning. At ARINI, individual faecal samples were collected from approximately 27 lambs per treatment at the start of the trial (pre-dosing) and at 65 days post-dosing (weaning). Post-weaning, faecal samples were collected at 12 days post-dosing and weekly thereafter until the end of the study. Faecal egg counts were performed on all samples using the McMaster technique. Dag scores were also measured on all lambs. Dag scores are based on visual assessment of the degree of soiling around the tail area, using a scale of 1 to 5, where 1 = no soiling and 5 = severe soiling, tail area being heavily caked in faeces.

The effect of pre-weaning treatment on lamb performance and faecal egg counts at ARINI are presented in Table 2.

Table 2. Effect of pre-weaning treatment on lamb performance, dag scores and faecal egg counts.

Pre-weaning creep treatment	Live weight at weaning (kg)	Live weight gain (birth – weaning g/day)	Dag score	Strongyle faecal egg counts (eggs/g, 65 days post-dose)
No creep	30.4^{a}	249^{a}	0.37^{a}	127.6
Low protein	34.5^{b}	294^{b}	0.51^{b}	47.2
High protein	35.5^{b}	309^{b}	0.42^{ab}	86.3
s.e.	0.61	6.4	0.040	32.27
significance	***	***	P=0.05	NS

In the pre-weaning period, lambs offered the low and high protein creep concentrate had greater live weights at weaning and live weight gains from birth to weaning compared with those on the no creep treatment (P<0.001). Protein level had no significant effect on lamb performance. Lambs offered the low protein creep concentrate had lower dag scores compared with those offered no creep (P=0.05). The was no effect of pre-weaning treatment on strongyle faecal egg counts as a long acting anthelmintic was given at 4-6 weeks of age. Pre-weaning treatment had a significant effect on performance in the post-weaning period with lambs on the no creep treatment having significantly higher live weight gains (269 g/d) compared with those offered low protein creep (236 g/d) or high protein creep concentrate (242, s.e. 8.65 g/d; $P<0.05$).

The effects of the concentrate diets offered in the post-weaning period are presented in Table 3.

Table 3. Effect of concentrate treatment offered to lambing in the post-weaning period at ARINI on performance and faecal egg counts.

Post-weaning concentrate treatment	Live weight at end of study (kg)	Live weight gain (birth – end of study g/day)	Dag score	Strongyle faecal egg counts (eggs/g)
High protein	44.2	255^{ab}	0.99^{b}	406.9
High protein + tannin	43.8	245^{ab}	0.67^{a}	333.1
Low protein	43.4	228^{a}	0.48^{a}	435.1
Low protein + tannin	44.0	267^{b}	0.54^{a}	329.4
s.e.	0.64	9.9	0.100	63.55
significance	NS	**	***	NS

Neither, protein nor tannin content of the diet had any significant effect on worm burdens as measured by faecal egg counts. However, irrespective of pre-weaning treatment, lambs offered the low protein concentrate, had lower live weight gains compared with those offered the other treatments, which may be related to the protein binding effects of the tannin.

The results averaged over the five farms involved in the study, also failed to reveal significant effects of protein or tannin content of the diet on worm burdens, although significant effects on animal performance were obtained (Table 4). However, it should be noted that each of the farms were dosing regularly throughout the study.

Table 4. Effect of pre- and post-weaning treatment on lamb performance and faecal egg counts (results averaged over five lowland farms).

Pre-weaning concentrate treatment	Live weight at weaning (kg)	Live weight gain (birth – weaning g/day)	Strongyle faecal egg counts†
No creep	35	276	456
High protein creep	37	290	354
s.e.	0.3	2.9	95.2
Significance	NS	**	NS
Post weaning treatment	**Liveweight at end of study (kg)**	**Live weight gain (birth to end of study g/d)**	**Strongyle faecal egg counts‡**
High protein	44	229	1085
High protein + tannin	43	229	965
s.e.	0.3	6.5	853.8
Significance	NS	NS	NS

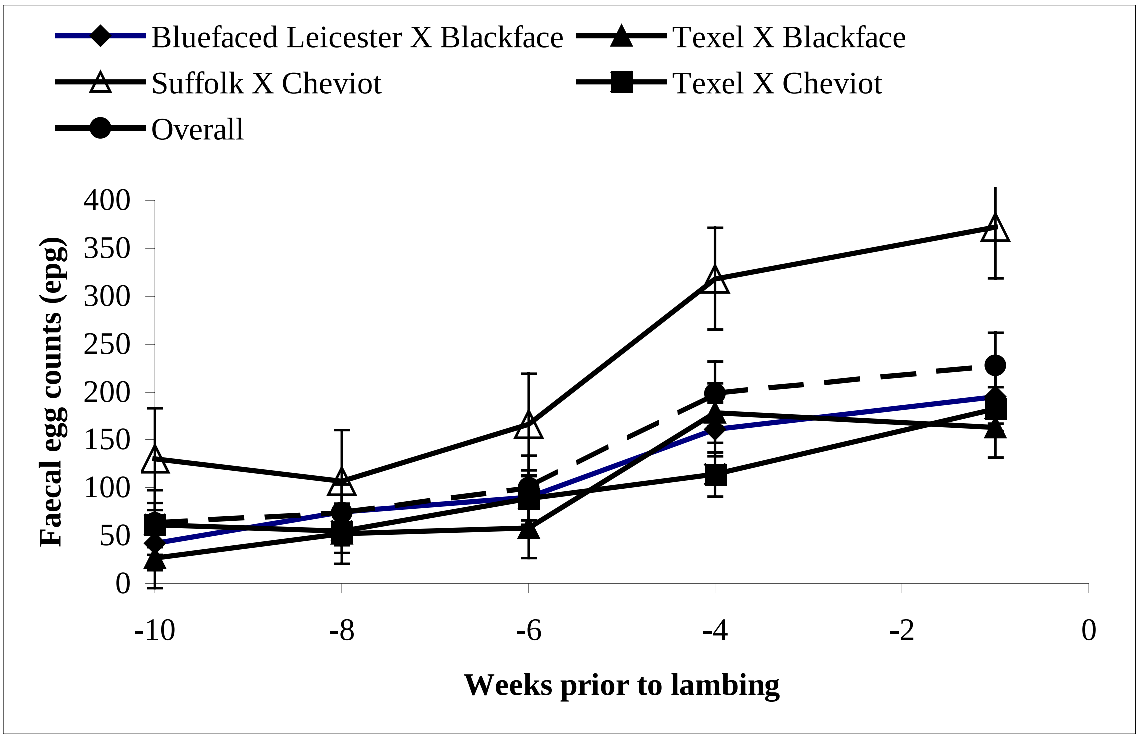
† faecal egg counts (eggs/g) based on individual samples 30 days post-dosing
‡ faecal egg counts (eggs/g) based on mob samples 20 days post-dosing

Although the results of this research, failed to demonstrate significant effects of protein and tannin content of the diet on worm burdens, further work is on-going to establish the optimum level of tannin inclusion in the diet and offering tannin-containing concentrates from six weeks of age rather than from weaning. In addition, dosing with a worm drench will only be undertaken when faecal egg counts reach a critical level.

Breeding worm-resistant sheep

Resistance to nematodes in sheep has been shown to have a degree of heritability, using faecal egg counts as a marker (Stear *et al*., 1999; Woolaston and Windon, 2001). In a recent study Sayers *et al*. (2004) identified specific genes which were associated with nematode resistance, based on faecal egg counts, in Texel and Suffolk sheep. In addition, a study conducted by DARDNI and co-founded by AgriSearch, as part of an ongoing sheep production study, found that Suffolk X Cheviot ewes tended to have higher strongyle worm egg counts and therefore higher egg output during the periparturient period compared to other breeds (Figure 1; Carson *et al*., 2002). This could have implications for pasture contamination and worm management control in lambs. Recently both UK Texel and Suffolk sire reference schemes have starting using FECs, to compute FEC estimated breeding values (FEC EBVs) for individual rams, with the view to increasing the resistance of their offspring to gut parasites (Nieuwhof and Evans, 2002). Extension of this technique to other breeds could lead to a much improved resistance to parasites in the national flock (Carson *et al*., 2002).

Figure 1. Effect of ewe genotype on faecal egg counts



Biological Control

An exciting development in parasite control over recent years has centred on biological control of gut-worm parasites. This work has primarily involved the use of the fungus *Duddingtonia flagrans.* This fungus has the capacity to survive passage through the gut, grow rapidly in faeces and feed on hatched parasitic larvae before they are able to leave the dung-pat. Recent work has shown substantial reduction in pasture larval numbers and significant reduction in worm egg counts and worm burdens in sheep fed *D. flagrans* fungi in feed supplements (Chandrawathani *et al*., 2003; Fontenot *et al*., 2003). Additional work has also shown that *D. flagrans* is environmental benign and with large scale production of this fungus now possible, commercialisation of this control measure is near (Waller, 2003). Provided a suitable means of delivery (e.g. bolus, feed blocks, etc) can be developed then biological control offers an attractive additional control measure against parasitic disease in animals.

Copper Wires

Copper oxide wire particles (in low doses of 2-2.5 g/lamb) have been shown to lodge to the abomasum and, over a period of months, dramatically reduce the burden of abomasal worms (*Ostertagi ostertagi* and *Haemonchus contortus*) in sheep (Bang *et al*., 1990; Knox, 2002; Burke *et al*., 2004). However, treatment is ineffective against intestinal worms and care needs to be exercised when administering to sheep susceptible to copper toxicity. Despite these reservations the administration of copper oxide particles could prove, under certain circumstances, to be an extremely cost-effective means of controlling abomasal parasites.

Vaccines

Some promising antigens are currently under investigation for both gut worms (*Haemonchus contortus*, *Ostertagia* and *Trichostrongylus* spp.) and liver fluke. However, progress has been relatively slow and much work still needs to be done to understand the "host-parasite" interaction (Dalton and Mulcahy, 2001; Dalton *et al*., 2003; Geary and Thompson, 2003).

Conclusion

Anthelmintic resistance is a major threat to sheep and cattle farming. Immediate steps need to be taken to halt or, at least, slow down the development of resistance. In addition, new control measures need to be developed and incorporated as practical, cost-effective control measures to aid in the fight against internal parasites.

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