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From the preliminary results in Table 2 a number of tentative conclusions can be drawn. It can be seen that a Levamisole drench is an effective option on many of the properties. A Combination (BZ & Lev) drench is effective on many properties also probably as a result of the Levamisole active efficacy. There is a high percentage of Ivermectin (Full dose) failure across the properties – one possible reason for this could be the high volume of Ivermectin used within the merino and mid micron sectors over recent years. It has been speculated that this high level of Ivermectin (full dose) usage was a result of early BZ drench failure (undiagnosed) in the mid micron and merino sectors. When Ivermectin was introduced it was highly effective and as a consequence was a popular choice with farmers. Confirmation that the Half Dose Ivermectin method developed in Australia is a robust early warning signal of a full dose failure. Even with high levels of Ivermectin failure, no Abamectin failure was detected.

Table 3 shows the anthelmintic resistance results from individual species pooled across farms where resistance was confirmed. From Tables 2 and 3, for example, it can be seen that 79% of the farms tested had Benzimidazole resistance confirmed (Table 2), and of those 95.7% had identified *Nematodirus* resistance (Table 3), with failure to *Ostertagia* and *Trichostrongylus* also found for BZ's. For the Levamisoles and Combination (BZ and Levamisole), the only species for which resistance was confirmed was *Trichostrongylus*, which for the Combination was probably related to the Levamisole failure against *Trichostrongylus*. For the Ivermectin (Half Dose), drench failure was confirmed against *Trichostrongylus, Ostertagia* and *Nematodirus*, with Ivermectin (Full Dose) failure dominated by *Ostertagia* species.

TABLE 3: Preliminary summary of anthelmintic resistance by species.

Parasite Species	White	Clear	Dual Combination (BZ & Lev)	Ivermectin Half Dose	Ivermectin Full Dose	Abamectin
			Percentage Split %			
Ostertagia	13	0	0	47.4	50	0
Trichostrongylus	8.7	20	100	10.5	0	0
Nematodirus	95.7	0	0	32	0	0
Hamonchus	0	0	0	0	0	0
Cooperia	0	0	0	0	0	0
Chabertia	0	0	0	0	0	0
Unconfirmed	65.2	80	0	52.6	50	0

Lessons from the National Anthelmintic Resistance Surveys

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INTRODUCTION

Anthelmintic resistance is an issue that has been of growing interest in New Zealand over the last 2-3 decades. For many it was seen as an over-hyped issue of little significance, particularly where researchers were using it to justify various potential research projects. For farmers it was a problem that might arise some immeasurable time in the future whereas good parasite control was required now. The results from the national surveys and other more local surveys have focussed attention on drench resistance. The larger picture is clear. Anthelmintic resistance is now an issue, to some degree, for most sheep farmers and the majority of beef farmers. It should also be recognised there is widespread benzimidazole (BZ) resistance in horse cyathostomes and concerns about macrocyclic lactone (ML) resistance in *Parascaris equorum* and *Oxyuris equi* in horses. Deer gastrointestinal nematodes have also been demonstrated to show evidence of ML resistance (Hoskin et al., 2005).

It is pertinent to review the impact of parasites on production animals in New Zealand. Clinical parasitism i.e. the appearance of animals that are obviously affected by worms, certainly still occurs, but the general view is that it is now less common, particularly deaths, than several decades ago. In contrast, unless an animal has been very recently effectively drenched, subclinical parasitism is ubiquitous.

The often quoted figure is that one third of New Zealand's sheep production is dependent on anthelmintic-based control of nematode infections (Brunsdon 1988). This was based on New Zealand studies where undrenched lambs experienced an average mortality of 23%. In addition, 10% was added to this to account for lost production in survivors. However, this same paper admitted that 10% is very conservative and cited Wallaceville trials where mean liveweight gains in undrenched lambs were reduced by 43% over their first year of life. Quite clearly effective parasite control is essential for both animal welfare and production reasons.

At the other end of the spectrum is subclinical parasitism. Determining when that reaches a level to warrant concern is difficult. Recently, some elegant work in the United Kingdom by Forbes et al (2004) has shown why mature well-fed dairy cows treated with eprinomectin produce more milk/milk solids (likely to apply to other long-acting ML products). Treated cows grazed for 50 minutes longer per day and idling time was reduced These responses were achieved in healthy well-fed animals with presumably mature immune responses to gastrointestinal nematodes. Pasture larval levels and egg counts in untreated cows were low. They demonstrate that even small challenges to parasitism of adult animals can limit production. To what extent then should we be endeavouring to control parasites? The low price of anthelmintics has allowed farmers to move to control more and more of this sub-clinical parasitism and capture the associated production advantages, but generally without too much regard for the sustainability of this approach. Anecdotal evidence suggests that apparently a significant percentage of healthy adult dairy cows are drenched in New Zealand during lactation to harness this extra milk production

In New Zealand our principle focus for parasite control is to limit the impact of parasitism in young ruminants. For most, this is achieved by limiting their intake of infective larvae rather than allowing them to become parasitised to the point that treatment is necessary. Allowing young animals to accumulate significant burdens has likely epidemiological consequences in terms of pasture larval levels for the remainder of that season. This desire to limit pasture larval levels exposes a fundamental problem. van Wyk (2006) explains the importance of refugia for limiting the development of anthelmintic resistance. This concept requires that there be a proportion of the worm population unexposed to treatment. Resolving the quandary of achieving a balance between the low numbers of infective larvae needed for effective parasite control, but continuing to maintain a realistic source of unselected parasites is difficult. Nevertheless, it is a key point for achieving sustainable and effective parasite control.

LESSONS FROM THE SURVEYS

Current practice is clearly exerting significant selection pressure for the development of anthelmintic resistance. Therefore if we continue as we are then widespread and severe drench resistance is inevitable for an increasing number of farmers. Change is essential and will happen by choice to avoid a worsening problem or by necessity when all drenches fail. There are already a small number of situations where multiple resistance to all drenches has been noted. There will be new anthelmintics developed, but none will be available in the near future and farmers should plan to make use of the existing families of chemicals for at least the medium term. When they do arrive they will significantly more expensive.

It is clear that regular use of anthelmintic continues to be the main form of parasite control for both sheep and beef cattle. The surveys have identified limited use of stock rotations, interchange of cattle and sheep, crops etc to achieve parasite control. The number of treatments given to young sheep (< 1year old) can be followed over several surveys from the early 1980s and include Brunsdon et al (1983) at 6.3, Macchi et al (1999) at 6.2, Sharma et al (2005) at 6.1 and the present survey at 5.5. The number of two-tooth treatments has also remained similar over this same period at about 1.4-1.8. Even though the number of treatments is not necessarily a particularly accurate way to gauge selection pressure it shows the consistent use of anthelmintics over the years.

Despite advice to farmers to "not drench unnecessarily" it is clear that most farmers believe that regular use of anthelmintics, especially in young sheep is necessary. This is also reflected in the number of farmers who followed a planned drench programme in their young sheep, most often a standard preventive programme of 5-6 treatments at 4 weekly intervals starting at weaning.

Of more concern is the increase in ewe treatments. Sharma et al (2005) reported 1.8 per year and the current survey estimated 1.5 per year. Although this is only marginally higher than the figure quoted by Brunsdon et al (1983) of 1.2, it is disguised somewhat by the change to long-acting products for ewe treatments, especially prelambing that were reported in this survey and that of Sharma et al (2005). This implies that the number of days that drenches will be active in adult sheep per year has increased substantially when most advice has been to limit anthelmintic use. As suggested from first principles, treating ewes at this time of the year, especially with a persistent product, is likely to accelerate selection for anthelmintic resistance and the regular use of such products should be considered with caution. This does not imply that a production advantage would not follow from their use, although evidence on this is contradictory, but it does suggest that this advantage will likely come with an increased risk for the selection of anthelmintic resistance. It does not mean they should never be used, as there will be situations where their advantages outweigh the potential risk, i.e., young lambing hoggets in poor condition. It may also be possible to mitigate the risk by other means such as manipulating stock rotations.

In cattle, the high level of resistance reported by Rhodes et al., (2006), especially in *Cooperia,* but also in *Ostertagia,* was surprising to some. We have the interesting situation where some companies selling anthelmintics are endeavouring to downplay the importance of *Cooperia,* in contrast to recent years where efficacy against this genus was used, by the same companies, as a marketing advantage. We are now in the situation where we are dependent on levamisole for high efficacy against *Cooperia* on most farms. Given that levamisole struggles somewhat against *Ostertagia* (Prichard 1983), this implies that combination treatments are the treatment option for most wanting good control. To suggest that *Cooperia* won't become resistant to levamisole is a very optimistic wish. The fact it hasn't to date is more likely to reflect the more limited use of this chemical in the last two decades, although it was extensively used in the 1960s and 1970s. The information from the survey would indicate that many farmers are using drench in their cattle (and sheep) which is less than fully effective. The corollary to this is that production is being lost and there may even be overt animal health issues despite regular drenching – clinical investigations have shown this on a number of farms. The paucity of drench testing in cattle needs to change so that farmers are monitoring their situation and adjusting their treatment options accordingly. Whilst the amount of drench testing in sheep is currently limited which is also a concern, it is almost non-existent in cattle and deer.

We have less historical information about drench use in cattle. Observations of drench company recommendations, often supported by solid field studies, have shown the advantages in regular treatments over a few sporadic treatments. Two decades ago it would have been usual for beef weaners to receive only one treatment at weaning. Now the mean number in their first year is about 5, which is not that many less than for young sheep. Added to that is the high usage of ML products with some persistent activity and it is apparent that exposure of worms to this action family, and hence selection pressure, is likely to be higher than for sheep! Also, added to this are the drenches given to older cattle – a high proportion get one treatment in their second year and many get 3 or more!

The move to rearing dairy beef as a virtual monoculture of young animals in recent years is heavily dependent on the availability and use of effective anthelmintics. Cattle are often sold by 18-24 months of age, just as their immune response to gastrointestinal nematodes is maturing and they are available to do some effective work by ingesting many more larvae than they potentially contaminate the pasture with in the form of eggs. Sheep may or may not be an option to cross-graze with young cattle, but in many cases this is not possible or utilised. At any rate sheep will not be contributing to the refugia of unselected cattle parasites. Intensive rearing of young dairy beef (and heifers) will be difficult as anthelmintic resistance becomes more common and pervasive. It is difficult to see how this farming system is sustainable in the medium term with our currently available tools in the form of anthelmintics. Our challenge is to develop sustainable systems to rear 600,000 to 1,000,000 young dairy bull calves each year as well as the number of dairy heifers that are also reared in similar systems

The importance of effective quarantine drenching is slowly permeating the farming industry with more than half indicating they always use them for sheep. A lesson from the survey is that that sheep bought from farms where the resistance status is not known to the purchaser are highly likely to be carrying resistant nematodes and that ML-resistant *Ostertagia* are common. We also know that ML-resistant *Trichostrongylus colubriformis* are common in goats at least, and many of these cross graze with sheep. Hence the use of MLs as a single active quarantine drench by most is potentially encouraging the introduction of these parasites to their farm and would now have to be considered inadequate where the status of the purchased animals was not known.

The genetic basis behind ML resistance is still not fully determined, but this will be at least introducing these genes onto a farm where they may not already be present. It may take a period of years before the gene frequency builds up to a point where resistance is clinically apparent, but the foundations were likely laid some time before. Thus all farmers trading in sheep and cattle need to be especially vigilant about quarantine treatments even though our knowledge about the genetics etc of most of these is incomplete. We also need to be careful where these quarantine-drenched animals then graze on their new farm. It needs to be somewhere that has a refugia of parasites and not a "clean" area that could allow the few survivors to be the only contaminating worms.

It remains intriguing that we are yet to confirm ML resistance in *Ostertagia* in cattle despite their almost continuous use for over 20 years on many farms, often with products that are injectable or pour-on which by their formulation invariably have a declining "tail" of some length. Such selection pressure would have been expected, based on first principles, to have exerted considerable selection pressure for resistance to have occurred. The national survey has identified some farms that had apparent failure of MLs against *Ostertagia,* but these are currently being retested to confirm these original findings. It is similarly intriguing that we have not identified many farms with ML-resistant *Haemonchus contortus* in sheep (none in this survey). Given its very seasonal nature in most of its range in New Zealand and its generally accepted inability to survive over winter on pasture, it might be expected there would be limited refugia and hence high selection pressure at certain times of the year. It is well known from elsewhere around the world that *Haemonchus* are more than capable of becoming very resistant to the MLs.

There is some confusion about the relationship between the number of treatments given and the selection pressure for the development of anthelmintic resistance. Good worm control achieved with fewer drenches is not necessarily a recipe for delaying the emergence of resistance. The priority needs to be on achieving a reduction in selection pressure for resistance rather than reducing drench frequency per se. Many believe there is a direct correlation between the number of drenches and development of resistance, but the situation is far more complex.

Van Wyk (2006) explores the concept of refugia which is integral to this discussion. A couple of simple comparisons can be made. A single lamb drench is likely to be less selective than a single ewe drench at the same time. The lamb will become rapidly reinfected and the survivors numerically swamped and unlikely to mate with each other. In the ewe, the immune response is such that new infections will be slow to establish and allow survivors a much longer time to mate with each other. Drenching lambs or calves and then immediately moving them to "clean" pasture where the only larvae will be from the survivors of the drench versus returning them to their original or another contaminated pasture where any survivors will be diluted out by the larvae already there is a further example where the same selection pressure is not being exerted. Another is the comparison between a drench in autumn when egg development is relatively high versus the depths of winter when any eggs from survivors are much less likely to develop. Good parasite control is often synonymous with reducing the number of infective larvae on pasture, but the dynamics of resistance is complex Good parasite control can imply high selection for resistance, but not always! For the future we need to identify high risk strategies and avoid them where possible. These include: limit drenching of adult sheep especially prelamb, don't drench and move onto "clean" pasture, effectively quarantine drench (and then ensure the animals go onto contaminated pasture).

Research on many aspects of parasite control and anthelmintic resistance is lacking. For example, it took many years to convince the funding agencies that a national survey would be a useful piece of research. We are heavily reliant on modelling to get indications about the consequences of some control practices and few of these have subsequently been studied empirically. Research in applied parasitology was dramatically reduced with the advent of modern anthelmintics as the problem was considered to be "solved". We are seriously deficient in our understanding of many basic details about the biology of worms and their interactions with their hosts. This survey has identified some likely high risk strategies with sheep, especially the use of long-acting anthelmintics in ewes pre-lambing. Some of the other identified risk factors are likely to be proxies for underlying practices that will require further research. In the absence of this research we are heavily reliant on applying first principles, and opinions formed from these, as we try to determine effective and sustainable solutions, but the complexities involved make this a haphazard process. Nevertheless parasite control must remain the focus even if anthelmintic resistance dominates the discussion. A balance needs to be negotiated between achieving good control and the sustainability of those control options.