Sustainable control of internal parasites in ruminants

Animal Industries Workshop
Lincoln University
Sustainable control of internal parasites in ruminants

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Edited by:
G K Barrell
Animal & Veterinary Sciences Group
Lincoln University

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## Contents

Foreword  
*A S Famlton*

Glossary: Common terms  

**Summary table:**  
Anthelmintics for use in ruminant animals in New Zealand  

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Author(s)</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control of parasitism: the global perspective</td>
<td><em>Q A McKellar</em></td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Internal helminth parasites of ruminants in New Zealand</td>
<td><em>W E Pomroy</em></td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>Internal parasites of cattle in New Zealand: Gastrointestinal nematodes and lungworm</td>
<td><em>W A G Charleston</em></td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>Internal parasites of deer in New Zealand</td>
<td><em>P C Mason</em></td>
<td>41</td>
</tr>
<tr>
<td>5</td>
<td>Internal parasites of goats in New Zealand</td>
<td><em>P C Mason</em></td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td>Life cycles and development of nematode parasites of ruminants</td>
<td><em>A S Famlton and R W McAnulty</em></td>
<td>67</td>
</tr>
<tr>
<td>7</td>
<td>Effects of nematode parasitism on ruminant animal performance</td>
<td><em>A R Sykes</em></td>
<td>81</td>
</tr>
<tr>
<td>8</td>
<td>The diagnosis of gastrointestinal parasitism in ruminants and investigating anthelmintic resistance</td>
<td><em>P B McKenna</em></td>
<td>93</td>
</tr>
<tr>
<td>9</td>
<td>The use and optimisation of anthelmintics</td>
<td><em>Q A McKellar</em></td>
<td>107</td>
</tr>
<tr>
<td>10</td>
<td>Anthelmintic resistance</td>
<td><em>P J Waller</em></td>
<td>129</td>
</tr>
<tr>
<td>11</td>
<td>Long-acting and controlled-release anthelmintics</td>
<td><em>I A Barger</em></td>
<td>141</td>
</tr>
<tr>
<td>No.</td>
<td>Title</td>
<td>Author(s)</td>
<td>Page</td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>12</td>
<td>Immunity to nematodes in ruminants</td>
<td>R G McFarlane</td>
<td>149</td>
</tr>
<tr>
<td>13</td>
<td>The selection of sheep for natural resistance to internal parasites</td>
<td>J C McEwan, S A Bisset and C A Morris</td>
<td>161</td>
</tr>
<tr>
<td>14</td>
<td>Effects of diet on gastrointestinal nematode infection in ruminants</td>
<td>M F J van Houtert</td>
<td>183</td>
</tr>
<tr>
<td>15</td>
<td>The effect of dietary protein on the establishment and maturation of nematode populations in adult sheep</td>
<td>J Donaldson</td>
<td>193</td>
</tr>
<tr>
<td>16</td>
<td>Models as a guide to sustainable worm control</td>
<td>I A Barger</td>
<td>203</td>
</tr>
<tr>
<td>17</td>
<td>Biological control of parasitism</td>
<td>P J Waller</td>
<td>215</td>
</tr>
<tr>
<td>18</td>
<td>Cestode parasites of ruminants in New Zealand</td>
<td>W E Pomroy</td>
<td>225</td>
</tr>
<tr>
<td>19</td>
<td>Trematode parasites of ruminants in New Zealand</td>
<td>W A G Charleston</td>
<td>237</td>
</tr>
<tr>
<td>20</td>
<td>Integrated control systems for the management of internal parasites in ruminants</td>
<td>A M Nicol and P G Everest</td>
<td>263</td>
</tr>
</tbody>
</table>
Foreword

Internal parasites have been a problem for animals, probably since the dawn of evolution. However, domestication and the constraints we impose on animals, particularly ruminants, by restricting selection of forage and grazing range, load the dice very much in favour of the parasites. This is a continuing problem of most livestock we have to deal with.

This text should inform the reader that this is not a situation which has quick solutions or easy answers, but despite this, progress in the control of parasites is being made. Knowledge of the parasites and of the host animals' responses to parasitic challenge will help us to keep pace with this progress. Also it is intended that the Animal Industries Workshop should go some way to explaining the principles of sustainable control.

The total reliance we placed on the 'miracle' worm drenches which became available from the early 1960s has resulted in our neglect of other management factors which, if utilised, should reduce our total dependence on these 'wonder' drugs. With the development of resistance to these drugs by the parasites and the spectre of meat and milk residue problems, the time is now opportune for re-examination of control measures.

The purpose of the workshop and this book, which is derived from papers presented during the workshop, is to present up-to-date information which can be used to inform and upskill all concerned with the management of parasite problems.

International specialists such as Quintin McKellar, Peter Waller and Ian Barger have contributed their considerable knowledge and understanding of the anthelmintics available, how they work, how anthelmintic resistance can arise and of the place long acting preparations and mixed anthelmintics have in control programmes. Other writers have addressed factors such as the extent of parasitism in New Zealand livestock, the life cycles and infectivity of these parasites in livestock, and the effects of nutrition in influencing the outcome of infection. Selection of resistant animals within breeding programmes and the acquisition of natural and artificial immunity are also included.
Management practices to control gastrointestinal parasitism each have limitations and this is discussed, as is the use of computer models.

These papers show that the situation is not hopeless, but the sustainable control of internal parasites of ruminant animals will require sensible drug usage, genetic selection of resistant livestock and use of alternative grazing and possibly nutritional management strategies.

A S Hamilton
Co-ordinator
1997 Animal Industries Workshop
Lincoln University
Glossary

Common terms

**Acquired immunity** Where the individual develops specific immunity to an infectious agent. The immune system 'memory' leads to an enhanced response if the animal is subsequently exposed to infection.

**Acute infection or disease** An infection or disease that is rapid in onset and runs a short course (hours to a few days).

**Anthelmintic** Any drug that is used to kill helminth parasites (nematodes, cestodes or trematodes). Commonly known as a drench.

**Antibody** A protein that can bind to a specific antigen. It is produced by the immune system in response to infection. The presence of specific antibodies in the host indicates that its immune system has recognized and responded to the antigen.

**Antigen** Any substance that will stimulate an immune response.

**Cestode** A tapeworm, member of the Class Cestoda.

**Challenge** A challenge is exposure to an infective agent. This can be by way of an oral dose with a known number and species, or from grazing infective pastures (field challenge).

**Chronic infection or disease** Describes an infection or disease of long standing. (Opposite of acute.)

**Definitive host** The host animal in which a parasite reaches the adult, sexually mature stage. Also known as the final host.

**Direct life cycle** A parasite life cycle that only requires the definitive host for its completion.

**Drench resistance** Where an anthelmintic correctly used fails to remove the existing worm burden from a host.

**Endoparasite** A parasite which lives within the body of the host.

*Sustainable control of internal parasites in ruminants*
**Epidemiology** The study of the distribution, causes and dynamics of an infection or a disease in a population.

**Faecal egg count** A count of helminth eggs in faeces, usually expressed as eggs per gram (epg).

**Faecal Egg Count Reduction Test (FECRT)** A test based on comparing faecal egg counts before and after treatment to assess the effectiveness of an anthelmintic. Used to detect and monitor anthelmintic resistance.

**Fluke** See trematode.

**Genotype** The inherited characteristics of an organism.

**Host resistance** The ability of the host to resist either the establishment, development, persistence or the reproduction of parasites.

**Host specificity** The degree to which a parasite is able to mature and reproduce in one or more host species.

**Immunity** A state of resistance to the effects of parasites.

**Incidence** The number of new cases of an infection or a disease that occur over a given period of time.

**Indirect life cycle** One that normally requires two different hosts for its completion - one host in which larval stages develop (the intermediate host), and another (the definitive host) in which the parasite matures.

**Infestation** Invasion by parasites; synonymous with infection.

**Larval culture** A method to identify the species of parasites infecting a host. Faeces are collected and eggs are cultured until L3 stage, when they can be identified.

**Multiple resistance** Where a nematode isolate is resistant to two or more drench families.

**Nematode** A member of the Class Nematoda. Sometimes called roundworms.

**Parasitologist** A quaint person who seeks truth in strange places.

**Phenotype** The observed physical characteristics of an organism.
**Prepatent period** Period of time that elapses between the infection of the host (e.g. uptake of infective larvae) and the appearance of products of reproduction of the parasite (usually eggs or larvae).

**Prevalence** The proportion of animals in a population (e.g. herd or flock, or larger group) that is infected by a particular parasite or affected by a disease at any given time.

**Resilience** The ability of an animal to be productive despite infection with parasites.

**Roundworm** See nematode.

**Strongyle** A nematode belonging to the Order Strongylida. Includes trichostrongyles and related nematodes that commonly occur in the gut of grazing animals.

**Subclinical infection or disease** Presence of infection or disease without clinical signs.

**Susceptible** Lacking resistance, e.g. an animal that can be readily infected with or affected by a parasite or disease, or an organism (such as a parasite) that can readily be killed by a drug. Young, stressed animals and breeding ewes in the peri-parturient period are good examples of susceptible animals.

**Trematode** A parasite belonging to the Class Trematoda. Commonly known as flukes.

**Trichostrongyle** A nematode belonging to the family Trichostrongylidae, including *Haemonchus, Ostertagia, Trichstrongylus* and *Cooperia*.
**Summary table:** Anthelmintics for use in ruminant animals in New Zealand  (as at June 1997, errors and omissions excepted)

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<tr>
<th>Trade name</th>
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<th>Administration</th>
<th>Ingredient</th>
<th>Company</th>
<th>Species</th>
<th>Withholding times</th>
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<td>CDSG</td>
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</tr>
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<td>oxfendazole</td>
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<td>C</td>
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</tr>
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<tr>
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<td>S</td>
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</tr>
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<td>Cydectin Pouron</td>
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</tr>
<tr>
<td>Dectomax</td>
<td>C2</td>
<td>inject</td>
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<td>Pfizer</td>
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<td>21 d (D)</td>
</tr>
<tr>
<td>Double-Strength Ox-Fen</td>
<td>W</td>
<td>oral</td>
<td>oxfendazole</td>
<td>Ancare</td>
<td>CSDG</td>
<td>10 d</td>
</tr>
<tr>
<td>Duotin</td>
<td>C2</td>
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<td>MSD Agvet</td>
<td>C</td>
<td>49 d</td>
</tr>
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<td>W/C1</td>
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</tr>
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<td>C1/O</td>
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</tr>
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Key:
- W = white drenches
- C1 = clear drenches (levamisole and morantel)
- C2 = Clear drenches (avermectins/milbemycins)
- O = Other drenches (mostly narrow spectrum against flukes, tapeworms or Haemonchus)
- C = cattle
- D = deer
- S = sheep
- G = goats
- nil = no withholding time
- d = days
- h = hours
Control of parasitism: the global perspective

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Anthelmintics and constraints in their use

The pharmacology and clinical efficacy of anthelmintics are discussed in Chapter 9. The most obvious and inevitable constraint on their use has been associated with the development of resistance by nematodes to all the major classes of drugs used. The widespread anthelmintic resistance prevalent in some geographical areas of the world has not, however, resulted in farmers abandoning livestock production. Where the situation has become critical, specific strategies have been implemented using knowledge of the epidemiology of the parasites to reduce the number of anthelmintic treatments required and using specific narrow spectrum products such as the salicylanilides where *Haemonchus contortus* is a problem. Furthermore, it is now accepted that the use of a combination of anthelmintics with different modes of action but similar body residence time (such that ingested parasites are exposed to both drugs) is likely to extend the 'life expectancy' of both drugs compared to their use independently. This may be because the ability of the organism to develop two genetically unrelated adaptive processes is limited. Combination products should be used on properties before resistance has been selected for by either of the individual components. Several strategies which improve the efficacy of individual anthelmintic drugs may also improve their efficacy against resistant nematodes (Chapter 9), however this is likely to represent a relative improvement in efficacy and will only delay the inevitable since with further selection it is likely that the parasite population will become solidly resistant to the anthelmintics used. Anthelmintic resistance is discussed in greater detail by Waller in Chapter 10. Other features of anthelmintics currently constrain their use and future constraints may be imposed as a consequence of ill-informed public perception rather than scientific fact. In particular residues
of anthelmintics in food derived from treated animals and the ecotoxicological implications of anthelmintic excreted from treated animals deserve consideration.

Residues
Residues of anthelmintics or their metabolites in tissues or milk of treated animals are an inevitable consequence of the use of the drugs. Drugs are normally excreted in an exponential fashion from animals so that although concentrations may decline fairly rapidly initially following treatment, the time taken for the molecules remaining towards the tail of the concentration time curve to be excreted may be extremely long. The development of exquisitely sensitive methods for the detection of drugs in tissues means that small concentrations of drug persisting for long periods may be detected. The public desire for 'no residue' is an almost impossible goal in conventionally managed food animals. As a consequence of this, most drug regulating authorities require a minimum withdrawal period between administration of a drug to an animal and collection of milk for human consumption or slaughter of the animal for food production. In order to determine the withdrawal period most authorities estimate how much of the drug could be consumed by a person without causing harm and what maximum concentrations present in various tissues of the animal could be consumed by a person without exceeding the amount which would not cause harm. Various safety factors and exaggerated assumptions are made to ensure that even someone with very peculiar dietary intake could not exceed the maximum 'permitted' consumption.

The first step in determining the withdrawal period is to establish a no effect level (NOEL) in animal models (usually rodent and dog). Animals are fed successively increasing concentrations of drug in a chronic (e.g. lifetime or 90 day) regimen. The maximum concentration which produces no adverse (clinical or pathological) effect in the animal is the NOEL. The concentration determined for the most susceptible species is used for extrapolation to man. A safety factor is then applied which normally assumes that man is ten times as sensitive as the test animal and that there is a ten times difference in sensitivity between the least and most sensitive person i.e. a $10 \times 10 = 100x$ safety factor is applied. This figure is termed the acceptable daily intake
(ADI). The drug is then administered by the normal treatment regimen (dose and frequency) to the target animal species and treated animals killed at time points thereafter. Tissues from the treated animals are analysed for the drug (and any potentially hazardous metabolites). The amount of edible tissue which could be eaten (liver, kidney, muscle, fat) by an average person is determined and when the total amount of drug in all the edible tissues at the determined ingestion rate falls below the ADI this is the likely withdrawal period.

It is apparent from this that the consumer is ‘protected’ by gross overestimations of the potential risks associated with residue consumption. It may also be apparent that where a drug is both extremely safe (i.e. has a very high NOEL) and is also extremely potent against target parasites (e.g. avermectins and milbemycins) it may be possible that effective concentrations of drug will persist longer than the time taken to achieve residues below the ADI. This is indeed the case and some products have justifiable claims for persistence of anthelmintic activity beyond the meat withdrawal time. Other products may have shorter than anticipated withdrawal times for pharmacokinetic reasons, e.g. morantel (as the tartrate) is minimally absorbed from the gut and therefore presents little residue potential and oxyclosanide remains tightly bound to blood proteins and is largely removed from the body if animals are bled out properly - thus conferring shorter meat withdrawal than plasma concentrations would suggest. This of course assumes that the blood is not to be used for human consumption. Also the avermectin, eprinomectin, has partitioning properties which preclude the drug crossing the blood-milk barrier to any great extent. It also has a relatively high ADI and thus is able to justify a nil milk withdrawal period.

Ecotoxicologial impact of anthelmintic therapy

Since most of the anthelmintics currently used are not completely metabolised to inactive moieties within the host, chemicals with biological activity are excreted in the urine or faeces of treated animals. This may present little ecotoxicological concern when the chemicals have narrow spectrum of activity for the target parasites for which they are licensed. However, as the spectrum of activity of the antiparasitic agents has increased - particularly those with

*Sustainable control of internal parasites in ruminants*
activity against arthropods (endectocides) - so the potential for affecting non-target organisms has increased. Furthermore, the development of sustained release technology used to deliver anthelmintics means that the proportion of excreta produced by individual animals containing anthelmintic (or metabolite) residues has also increased. Several factors affect the impact which antiparasitic chemotherapeutics have on the environment. Firstly the activity of the excreted chemicals on organisms in the locus of the excreta is critical. If the chemicals have no deleterious activity on the exposed fauna then it is likely that the ecotoxicological effects will be minimal. Secondly, the amount of active chemical which enters the environment will be proportional to its effect. This will depend upon the amount administered, the route or delivery system of administration, the extent of metabolism to inactive moieties and the rate and extent of excretion of chemicals which present a hazard. Thirdly, the temporal nature of excretion is important. Drugs with short *in vivo* residence times are likely to affect a small proportion of excreta. However chemicals with long residence time or those administered in an excipient or device which extends their residence time may affect faecal deposits over a prolonged period of time. Fourthly, the stability of the chemical in the excreta is important since chemicals which are rapidly biodegraded are likely to present a hazard for a short period only. Finally the contribution which other factors such as climate and animal disruption make to removal of contaminated excreta is important.\(^{(3)}\)

When all these factors are taken into consideration it becomes apparent that the greatest potential for ecotoxicological hazard associated with currently licensed anthelmintic drugs lies with the avermectins and milbemycins delivered in sustained release systems. The endectocides have greatest environmental impact on dipteran flies and coleopteran beetles. The avermectins and milbemycins do have different spectra of activity and it is possible that members of the group may be found with minimal ecotoxicological effect while retaining their excellent antiparasitic activity. This is partially true for moxidectin which exerts relatively low mortality on non-target insects.\(^{(4)}\) However, moxidectin is not completely innocent since effects have been seen on larvae of *Musca autumnalis*, *Orthopagaus gazella*, *Onitis alexis* and *Haematobia irritans*.\(^{(5,6)}\) Although there may be a hazard associated with the use of endectocides in livestock it must be considered in the context
of their use. Sustained release devices are likely to be used only in a particular management group of animals (usually young susceptible stock). Other animals contribute substantially to the overall faecal excretion of the herd or flock. Since older animals produce more faeces it is apparent that a very large proportion of excreta entering the environment will be from untreated animals. This faeces will act as a refugia for susceptible non-target organisms and will greatly reduce any extensive effect associated with the use of the products.

**Alternative control strategies**

Anthelmintics are undoubtedly going to remain the backbone of endoparasite control strategies for the foreseeable future. The development of controlled release device (CRD) technology has in some systems largely overcome the inconvenience of repeated treatments throughout a grazing season. However CRD have by their nature generally long meat withdrawal periods and greater potential for ecotoxicological hazard than single administration strategies. Consequently alternative strategies have been investigated for parasite control.

**Vaccination**

Immunity does develop over time with exposure to most of the important gastrointestinal and lung nematodes of cattle and sheep. Although such immunity may take some time to develop and is generally not absolute, it does provide a rationale for investigations into methods of artificially stimulating immunity which will prevent the pathogenic response to parasites and will minimise production losses.

The only nematode vaccines which have been commercialised successfully for ruminants so far are those produced by irradiation and thus attenuation of living bovine lungworm *Dictyocaulus viviparus* and ovine lungworm, *D. filaria*. Irradiated larvae of other nematode species require to be given in large numbers and generate moderate protection only. Furthermore such vaccines are expensive to make and have limited shelf life. The economically important gastrointestinal nematode parasites of sheep and cattle have proved extremely difficult to culture *in vitro* and thus it has been impractical to harvest appropriate protective antigens by this means. However, the development of recombinant DNA production systems for antigen generation has meant that
appropriate trial antigens can be produced. The most critical requirement of the generated antigen is that its conformational assembly of protective epitopes produces an immune response which recognises native antigen after challenge with the parasite.\(^9\) A vaccine for *Taenia ovis* was the first recombinant vaccine registered for commercialisation. It stimulates protective IgG antibodies to *T. ovis* oncosphere antigens\(^10\) and oncospheral antigens have been shown to confer protection against several other cestode species. The development of gastrointestinal nematode and trematode vaccines has proved more difficult. The most promising approach has been to use parasite gut antigens which stimulate serum antibody production in the host. Perhaps not surprisingly this approach has been more successful for the blood sucking nematodes such as *H. contortus* which ingest sufficient antibody from plasma to cause their demise than for the mucosal browsers such as *Nematodirus* spp. and *Trichostrongylus* spp.\(^11\) Some protection has been induced against *Fasciola hepatica* by vaccination with *F. hepatica* derived glutathione S-transferase.\(^12\) However the modest nature of this response may reflect the poor acquired immunity which develops to this parasite in naturally exposed sheep and cattle.

Since most disease associated with nematode parasites in ruminants is a consequence of mixed infections with different parasite species, it is likely that commercially successful vaccines will have to confer multivalent protection. Furthermore suitable adjuvants or delivery systems will have to be found which permit single or at most double initial vaccine strategies with single annual boosters. Also it is likely that the most appropriate subjects for vaccination, that is the young lambs, will be those which respond least well to vaccination. Despite the obstacles to parasite vaccine development the goal is attractive and modelling studies suggest that even vaccines with efficacies below 100% may provide a high degree of epidemiological control of parasitism within a flock.\(^13\)

**Biological control**

Living predators or pathogens of parasitic helminths may exert a controlling effect on the numbers of parasites in the environment thus preventing production losses in host livestock.\(^14\) Several successful biological control
programmes exist for insect pathogens. The lady beetle was successfully introduced into California to control the cottony-cushion scale on citrus trees and, although not involving a predator, the release of sterile males of the New World screwworm has proved extremely effective biological control. The female screwworm mates once only and if she mates with a sterile male her eggs are infertile. Release of large numbers of sterile males has resulted in eradication of this screwworm from areas of USA, Mexico and Libya. Effective commercial biological control programmes for parasitic helminths of livestock are not yet available. Earthworms and dung beetles are known to reduce numbers of some parasitic nematodes on pasture, however the nematode trapping fungi appear to be more promising candidates for biological control of nematode parasites. Nematopathogenic fungi may act by trapping nematodes in sticky networks of vegetative hyphae and then penetrating the nematode cuticle and digesting it. Plant nematodes may be infected by fungal spores or vegetative hyphae may invade cyst or root knot nematodes. Sufficiently high concentrations of fungi are difficult to achieve by spreading spores on pasture, however targeted activity may be obtained by including 'digestion resistant' fungi in the diet of the host animal and thus delivering high concentrations in faeces from which the free living nematode larvae develop. The fungus *Duddingtonia flagrans* has been selected for field studies. This fungus produces large numbers of thick walled chlamydospores which act as sticky nets and has been shown to survive passage through the gastrointestinal tract of sheep and cattle. Control of *Ostertagia ostertagi*, *Cooperia* spp. and *Trichostrongylus colubriformis* has been demonstrated for this fungus.

**Genetic resistance by the host to parasitic infection**

Genetic variation exists among animals in their resistance to parasitic disease. This variation may allow the selection of animals with greater resistance to parasitic disease and, where this does not affect other production characteristics, an economic benefit may be derived. Genetic variation exists between breeds and within breeds and, while the former may be exploited by breed replacement, the latter requires identification of the desirable trait and specific breed selection for that trait. The use of breed substitution has been advocated in areas of Kenya where *H. contortus* is a major constraint on sheep production. Replacement of imported breeds with the indigenous red Maasai which excrete...
about one tenth of the faecal egg output given a similar challenge [compared with the Romney breed\(^{17}\)] may provide both an immediate production advantage (associated with resistance of the individual) and an epidemiological advantage, since egg output and thus pasture contamination will be reduced. The selection of individuals within a breed which have greater resistance to nematode parasitism is also a practical goal. Breeding of the Australian Merino for improved resistance to \(H.\ contortus\) has produced flocks in which anthelmintic therapy can be reduced.\(^{18}\) Characteristics have also been identified in the Scottish Blackface which will permit selective breeding for resistance to \(Ostertagia\ (Teladorsagia)\ circumcincta.\(^{19}\) Further quantitative genetic analysis of the nematode population in Scottish Blackface sheep has demonstrated that there is a strong genetic association between host animals and average worm length and fecundity but no genetic influence on nematode numbers. Thus the major manifestation of resistance is in the control of worm egg output. Fortunately there is a very strong positive genetic correlation between low egg output and improved growth rate implying that the important genes for growth are also those that influence parasite resistance.\(^{20}\) Clearly as with breed substitution, within breed selection will provide production benefits (because of the association of resistance and growth) and epidemiological benefits associated with reduced pasture contamination. Genetic resistance will provide an extremely useful way of minimising the requirements for anthelmintics. It will, however, take time for breeding programmes to establish selected flocks and it will be assisted if appropriate accurate markers for genetic resistance can be found to aid the selection process.

**References**


5. Webb JD, Burg JG, Knapp FW. Moxidectin evaluation against *Solenopotes capillatus* (Anoplura:Linognathitidae) *Bovicola bovis* (Mallophaga: Trochodectidae) and *Musca*


Internal helminth parasites of ruminants in New Zealand

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This chapter reviews the internal helminth parasites which have been identified in farmed ruminants in New Zealand and discusses their relative importance. It is solely concerned with helminths where they occur as adults in ruminant hosts. Various checklists of parasites of ruminants in New Zealand have been produced and should be consulted for more details, particularly for details of rare parasites. A point of confusion with nematodes in ruminants is the existence of major and minor morph types for the same species, particularly in the genus *Ostertagia*, with each morph type traditionally having been given its own species name. In this review, the name used is that for the major morph type (see Table 2.1) with the names of minor morph types and the more common synonyms also being indicated. In recent years there is a view that *Ostertagia circumcincta* is incorrectly included in that genus and should be in the genus *Teladorsagia* as *T. circumcincta*. In New Zealand, this new classification is rarely used and for this reason in this review this parasite will be considered to remain in the genus *Ostertagia*.

Life cycles

It is difficult to generalise about the life cycles of so many parasites. However, most nematodes infecting ruminants in New Zealand are in the superfamilies Trichostrongyloidea and Strongyloidea (see Table 2.1) and share the same basic life cycle. Typical strongylid eggs (about 80 X 40 μm) appear in faeces with the developing embryo in the multicelled morula stage. Development to first stage larvae occurs in the egg after which they hatch. First stage larvae feed on bacteria, grow and moult to second stage larvae which also feed, grow and moult to second stage larvae. However, this last moult is incomplete and the third stage larvae maintain the separated cuticle of the previous stage.
as a sheath around them. The result is they cannot feed but this sheath does offer increased protection against adverse conditions. Being unable to feed means they must rely on stored metabolites for energy. Movement is temperature-dependent and as it increases their movement increases but so does the consumption of stored reserves. At steady temperatures from 20-30°C larvae will only survive for a few weeks but at about 5-10°C larvae are inactive and will survive for months. Larvae are not necessarily killed by frost but cannot tolerate repeated freezing/thawing conditions. Most require several degrees of frost before ice crystals form in them. After ingestion by the host, larvae move downstream to their preferred site where they associate with the gland crypts to a varying extent to develop and moult before returning to the lumen to complete development. *Oesophagostomum* spp. will penetrate into the lamina propria to develop but most other species in ruminants stay above the basement membrane of the epithelium. With the exception of *H. contortus*, trichostrongylid nematodes are mucosal browsers mainly feeding on mucus and other secretions of the host. *H. contortus* is adapted to actively seek blood vessels in the mucosa and suck blood and hence is much more pathogenic. Both strongyloid genera in ruminants have a buccal capsule, which is quite large in *Chabertia ovina*, and both are plug feeders.

Development to sexually reproducing adults for most trichostrongylid species generally takes 2 to 4 weeks after infection and slightly longer for strongyloid species. All trichostrongylids (and probably strongyloids) have the ability to become inhibited, usually as the 4th larval stage, for variable periods. This is a mechanism for the nematode to survive adverse climatic conditions outside the host. This phenomenon is best known with cattle where the synchronous emergence of previously inhibited *Ostertagia* larvae results in Type II ostertagiosis. Such synchronous emergence resulting in disease is not recognised with other species or with *Ostertagia* in sheep and goats.

Metastrongyloids have indirect life cycles requiring the involvement of an intermediate host which, for the species infecting ruminants are molluscs (slugs and snails). Similarly, the principle cestode genus of ruminants in New Zealand, *Moniezia*, requires an intermediate host (oribatid pasture mites). All trematodes require intermediate hosts which for *Fasciola hepatica* are *Lymnaea* spp. snails and for *Calicophoron calicophorum* is the freshwater snail *Gyraulus kahuika*. 

Pomroy: Parasites of ruminants in New Zealand
Importance of parasites

The decision to classify parasites as of major, intermediate or minor importance is largely based on their role in causing disease in New Zealand. This combines components of their prevalence, intensity of infection and individual pathogenicity. Parasites may also be classified as of importance if they have significance from a public health, meat hygiene or international trading perspective. For sheep and cattle the classification used for gastrointestinal nematodes in this review (Table 2.1) generally follows that of Charleston. \(^7\)

**TABLE 2.1:** Internal helminth parasites of ruminants in New Zealand: distribution in the primary host and their importance.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Sheep</th>
<th>Goat</th>
<th>Cattle</th>
<th>Red deer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abomasum</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Apteragia quadrispiculata</em> (Nt)</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
<td>2</td>
</tr>
<tr>
<td><em>Haemonchus contortus</em> (Nt)</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><em>Ostertagia circumcincta</em> (including <em>O. trifurcata</em> and <em>O. pinnata</em>) (Nt)</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><em>Ostertagia leptospicularis</em> (= <em>O. crimensis</em>; including <em>O. kolchida</em>) (Nt)</td>
<td>3</td>
<td>nf</td>
<td>2?</td>
<td>2</td>
</tr>
<tr>
<td><em>Ostertagia ostertagi</em> (including <em>O. lyrata</em>) (Nt)</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>nf</td>
</tr>
<tr>
<td><em>Spiculopteragia asymmetrica</em> (Nt)</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
<td>2</td>
</tr>
<tr>
<td><em>Spiculopteragia spiculoptera</em> (Nt)</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
<td>2</td>
</tr>
<tr>
<td><em>Trichostrongylus axei</em> (Nt)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Small intestine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Bunostomum trigonocephalum</em> (Ns)</td>
<td>3</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Bunostomum phlebotomum</em> (Ns)</td>
<td>nf</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td><em>Calicophoron calicophorum</em> (T)</td>
<td>3</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td><em>Capillaria bovis</em> (N)</td>
<td>3</td>
<td>3*</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><em>Cooperia curticei</em> (Nt)</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td><em>Cooperia oncophora</em> (including <em>Cooperia surnabada</em> [= <em>C. mcmasteri]</em>) (Nt)</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>nf</td>
</tr>
<tr>
<td><em>Cooperia pectinata</em> (Nt)</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
<td>3</td>
</tr>
<tr>
<td><em>Cooperia punctata</em> (Nt)</td>
<td>3</td>
<td>nf</td>
<td>2</td>
<td>nf</td>
</tr>
<tr>
<td><em>Morziezia expansa</em> (C)</td>
<td>2?</td>
<td>2*</td>
<td>3*</td>
<td>3*</td>
</tr>
<tr>
<td><em>Nematodirus abnormalis</em> (Nt)</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
<td></td>
</tr>
<tr>
<td><em>Nematodirus filicollis</em> (Nt)</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td><em>Nematodirus helvetianus</em> (Nt)</td>
<td>3</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td>Organ</td>
<td>Sheep</td>
<td>Goat</td>
<td>Cattle</td>
<td>Red deer</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------</td>
<td>------</td>
<td>--------</td>
<td>----------</td>
</tr>
<tr>
<td><em>Nematodirus spathiger</em> (Nt)</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td><em>Strongyloides papillosus</em> (N)</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
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<tr>
<td><em>Trichostrongylus capricola</em> (Nt)</td>
<td>3</td>
<td>2</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Trichostrongylus colubriformis</em> (Nt)</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>nf</td>
</tr>
<tr>
<td><em>Trichostrongylus longispicularis</em> (Nt)</td>
<td>nf</td>
<td>nf</td>
<td>2</td>
<td>nf</td>
</tr>
<tr>
<td><em>Trichostrongylus vitrinus</em> (Nt)</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>nf</td>
</tr>
</tbody>
</table>

**Large intestine**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Sheep</th>
<th>Goat</th>
<th>Cattle</th>
<th>Red deer</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chabertia ovina</em> (Ns)</td>
<td></td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><em>Oesophagostomum radiatum</em> (Ns)</td>
<td>nf</td>
<td>nf</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><em>Oesophagostomum venulosum</em> (Ns)</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><em>Skjiabinema ovis</em> (N)</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Trichuris discolour</em> (N)</td>
<td>nf</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
</tr>
<tr>
<td><em>Trichuris globulosa</em> (N)</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Trichuris ovis</em> (N)</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><em>Trichuris parvispiculum</em> (N)</td>
<td>nf</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
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</tbody>
</table>

**Lungs**

<table>
<thead>
<tr>
<th>Organ</th>
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<th>Goat</th>
<th>Cattle</th>
<th>Red deer</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Dictyocaulus filaria</em> (Nt)</td>
<td>2</td>
<td>2</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Dictyocaulus viviparum</em> (Nt)</td>
<td>nf</td>
<td>nf</td>
<td>1</td>
<td>1**</td>
</tr>
<tr>
<td><em>Muellerius capillaris</em> (Nm)</td>
<td>3</td>
<td>1</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Protostrongylus ryfescens</em> (Nm)</td>
<td>3</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
</tr>
<tr>
<td><em>Varestrongylus sagittatus</em> (Nm)</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
<td>3</td>
</tr>
</tbody>
</table>

**Liver**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Sheep</th>
<th>Goat</th>
<th>Cattle</th>
<th>Red deer</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Fasciola hepatica</em> (T)</td>
<td></td>
<td>2?</td>
<td>2?</td>
<td>2?</td>
</tr>
</tbody>
</table>

**Body tissues**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Sheep</th>
<th>Goat</th>
<th>Cattle</th>
<th>Red deer</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Elaphostrongylus cervi</em> (Nm)</td>
<td>nf</td>
<td>nf</td>
<td>nf</td>
<td>2</td>
</tr>
</tbody>
</table>

1 = major importance; 2 = intermediate importance; 3 = minor importance
N = nematode; C = cestode (= tapeworm); T = trematode (= fluke)
t = Trichostrongyloidea; s = Strongyloidea; m = Metastrongyloidea
* - the actual species of this genus not recorded in this host
** - in deer the species of Dictyocaulus is probably distinct and has been named as *D. eckerti* by some
nf = not found

For sheep this generally concurs with that of Vlassoff and McKenna(3) although their classification was only into two categories. In the latter report *Cooperia curticei* was classified as important whereas Charleston(7) classified it as of intermediate importance and that is the classification used here. For cattle,
Bisset\(^4\) generally concurs with Charleston\(^7\) but further points out that *Ostertagia leptospicularis* (together with its minor morph type *Ostertagia kolchida*) has been implicated in clinical disease in young cattle.\(^6\). However, in our laboratory *O. leptospicularis* is rarely seen which is consistent with earlier observations of Brunsdon.\(^9\) In this review, *O. leptospicularis* has been included as a parasite of intermediate importance for cattle. The status of *Nematodirus helvetianus* is of interest. Brunsdon\(^9\) found an average burden of 13,580 (range 700-40,000) in 67 bovine small intestines submitted for routine diagnostic purposes. However, in our laboratory we rarely see *Nematodirus* eggs in cattle faecal samples, have only ever recovered small burdens of adult parasites and have not heard of any clinical problems with this species in cattle in recent years in New Zealand. Consequently it is considered to be a minor parasite which is in agreement with Charleston.\(^7\)

There has been little research on *Dictyocaulus viviparus* in cattle in New Zealand but it is considered to be common and is periodically recorded as a cause of clinical disease. Consequently, it is listed as a major parasite of cattle in New Zealand. However, although *Dictyocaulus* filaria is also a common parasite of sheep in New Zealand, it is rarely recorded as a cause of clinical disease and in this review is ranked as a parasite of intermediate importance which generally agrees with Vlassoff and McKenna\(^3\) who did not rate it as important. *Bunostomum* spp. have only been reported with a low frequency in either cattle or sheep and when seen are generally present in only low numbers\(^3,9\) and hence are considered to be minor parasites.

The significance of *Moniezia expansa* for sheep is the subject of some ongoing debate and its significance is reviewed in more detail in Chapter 18. It is included as a parasite of intermediate importance on the basis of the recent report by Southworth \textit{et al}\.\(^{10}\) where it was shown to have an effect on growth rates in young lambs. This classification may change as more information becomes available. The species of *Moniezia* that has been found in cattle in New Zealand is in some doubt\(^4\) but, regardless of this, it has never been recorded at the same intensity of infection as *M. expansa* in sheep and is included as a minor parasite.

The liver fluke *Fasciola hepatica* has an uneven distribution in New Zealand which is linked to the distribution of the snail intermediate hosts. Where it occurs it may be responsible for loss of productivity in sheep, cattle and goats.
although there have been no concerted investigations into this aspect of fasciolosis in New Zealand. It is described in more detail in Chapter 19. Due to its tendency to become more common in recent years it is considered to be a parasite of at least intermediate importance ranging to very important in some areas, which is a somewhat different conclusion to that of Bisset\(^4\) who considered it to be of no widespread economic importance. The only other trematode of sheep and cattle in New Zealand is the rumen fluke \textit{Calicophoron calicophorum} which is generally considered to be unimportant\(^4\) except for rare clinical cases associated with the migration of large numbers of immatures from the small intestine back up to the rumen.

In general, goats and sheep share the same helminth fauna but there is less information on goats from which to judge the relative significance of different species. The inability of goats to develop the same degree of immunity to nematodes as adult sheep means that some nematodes, such as \textit{Muellerius capillaris}, are significant in goats but not in sheep and can cause extensive lung lesions. \textit{Nematodirus} spp. eggs are seen less commonly from goat faeces than from sheep grazing the same pasture (WE Pomroy unpublished) but nonetheless burdens have been recorded that are not dissimilar to those in sheep\(^{11,12}\) so both species have been listed as major parasites of goats in this review. In the only report of \textit{Dictyocaulus filaria} from goats in New Zealand, they had slightly lower burdens than sheep but no statistical comparison was made\(^{11}\) and thus it has been given the same intermediate significance as in sheep. The species of \textit{Moniezia} found in goats is not known but is likely to be \textit{M. expansa}. Its importance in goats has never been investigated and it is considered unimportant. \textit{Trichostrongylus caprlicola} was found to be the dominant member of this genus from feral goats in one survey in the Wairoa district\(^{13}\) but seems to be of less significance in farmed goats\(^{14}\) and it has been rated as of intermediate importance.

The most important helminth of deer is \textit{Dictyocaulus}. Which species this represents is the subject of some recent research. Traditionally it has been considered to be \textit{D. viviparus} as in cattle but studies of lungworm from fallow deer in Germany has shown they are a different species which has been named \textit{Dictyocaulus eckerti}.\(^{15,16}\) It is known that \textit{Dictyocaulus} of bovine origin can infect red deer\(^{17,18}\) and vice versa\(^{19}\) but the existence of at least host-adapted strains is evident. Indeed it seems likely that the species in red
deer will also be *D. eckerti* but this has not yet been proven. There have been few studies on gastrointestinal nematodes of red deer in New Zealand and the decisions on the relative importance in Table 2.1 are based on the following: Wilson\(^{(20)}\) reported that *Spiculopteragia* was the dominant genus in 17 red deer of mixed age submitted for necropsy for a variety of reasons; Anderson\(^{(21)}\) surveyed 46 one to two year old male deer at slaughter and found that *Trichostrongylus axei* was the dominant species with up to 12,900 males being identified in one animal; C Hoskin (pers. com.) found *Spiculopteragia asymmetrica* as the most common species with *Spiculopteragia spiculoptera, Ostertagia leptospicularis* and *T. axei* to also be reasonably common. Regardless of these observations, clinical disease of red deer caused by gastrointestinal nematodes is rare and thus the species involved are generally considered to be of intermediate importance in this review. There has been a suggestion that wapiti/Canadian elk (*Cervus elaphus nelsoni*) are more susceptible to gastrointestinal parasites, particularly to those in the abomasum but there is little published information. *Elaphostrongylus cervi* is not particularly pathogenic for red deer but has been found to be widespread in New Zealand.\(^{(22)}\) It seems to be particularly prevalent in feral red deer from Fiordland, New Zealand with sufficient present at times to warrant total rejection of carcases at meat inspection\(^{(23)}\) due to host reaction around the adult worms in their predilection sites in the intermuscular connective tissue. However, it is rarely found at meat inspection of farmed deer\(^{(24)}\) as the intensity of infection is generally low and thus it is unlikely to be of any clinical consequence.\(^{(23)}\) Its presence on a farm precludes export of any deer from that farm to some countries and for this reason is considered to be a parasite of at least intermediate importance.

Examination of Table 2.1 shows that most nematodes are dominant in only one host with the exception of sheep and goats. However, many have been recorded in other ruminants but are generally found in small numbers and make little impact in terms of clinical disease or pasture contamination. The exception to this may be where quarantine drenching is being used to avoid the importation or exportation of anthelmintic-resistant strains of various nematodes. In these situations the small populations carried in these other hosts may be important. The only nematode that is considered important in all 4 ruminants is *Trichostrongylus axei*. This species is also found in the
stomachs of horses, pigs and rabbits and it has been demonstrated that isolates from each host are infective for the others.\textsuperscript{(25, 26)} However, the infectivity of larvae from one host for others has only been studied to a limited extent. Ross and Purcell\textsuperscript{(27)} observed a difference in establishment rate of a sheep isolate in calves and sheep but provided little data to support their observation. Abbott and McFarland\textsuperscript{(28)} have suggested the risk of sheep getting large infections is greater if they are grazing cattle-contaminated pasture rather than all sheep pasture. In diagnostic samples submitted to Animal Health Laboratories in New Zealand, McKenna \textit{et al.}\textsuperscript{(29)} recorded 1-3\% of sheep abomasums with burdens of \textit{T. axei} >10,000 (\textit{n}=2739; mean burden of the 49\% sheep infected was 2335) whilst in cattle Brunsdon\textsuperscript{(9)} found a mean burden of 18,904 (\textit{n}=72; percentage infected 82\%), suggesting the parasite is more numerous and common in cattle.

There have been several attempts to score the importance/pathogenicity of the common parasites of sheep in particular. The figures in these are debatable and do not take into account the prevalence or usual intensity of infection of different parasites. Gardiner and Craig\textsuperscript{(30)} reported a point system for scoring helminth infections of sheep which was later modified by Gordon\textsuperscript{(31)} and is as follows:

\begin{verbatim}
Chabertia 100 worms = 1  
Bunostomum 300 worms = 1  
Fasciola 300 worms = 1  
Trichuris 300 worms = 1  
Haemonchus 500 worms = 1  
Ostertagia 3,000 worms = 1  
Nematodirus 3,000 worms = 1  
Trichostrongylus 4,000 worms = 1  
Strongyloides 4,000 worms = 1  
immature worms (all species) 4,000 worms = 1
\end{verbatim}

Points are then combined from a mixed infection. Any figure in excess of 2 was considered economically important for young sheep and for older sheep any figure in excess of 4. Examination of these recommendations in the 1990's would suggest that they should be more conservative but the scores
do at least give one opinion of the relative pathogenicity of each parasite. A few of these scores are definitely unrealistic such as that for *Fasciola* where burdens from 50-100 adults would be likely to result in obvious production loss in young lambs.\(^{32, 33}\) A similar but slightly different scoring system for sheep was proposed by Lenghaus\(^{34}\) is:

<table>
<thead>
<tr>
<th>Parasite</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chabertia</em></td>
<td>100 worms = 1</td>
</tr>
<tr>
<td><em>Haemonchus</em></td>
<td>500 worms = 1</td>
</tr>
<tr>
<td><em>Trichuris</em></td>
<td>500 worms = 1</td>
</tr>
<tr>
<td><em>Ostertagia</em></td>
<td>)</td>
</tr>
<tr>
<td><em>Trichostrongylus</em></td>
<td>)</td>
</tr>
<tr>
<td><em>Nematodirus</em></td>
<td>)</td>
</tr>
<tr>
<td>immatures</td>
<td>)</td>
</tr>
</tbody>
</table>

Again numbers from a mixed infection are allocated fractions of a point and combined. It was suggested that any figure in excess of 2 units would affect production with 5 units capable of being fatal in lambs.

**Geographical variation**

In general there is little variation in parasite distribution throughout the country with only a few exceptions. *H. contortus* requires a relatively higher range of temperatures than other trichostrongyloid nematodes found in New Zealand. As a result, it is mainly a problem in the North Island with its importance decreasing with distance down the South Island, except for the West Coast where it may also be common.\(^{35}\) Another exception is *Nematodirus*. Clinical disease due to *Nematodirus* spp. may occur throughout the country but is particularly seen in young lambs at or around weaning only in the south of the South Island.\(^{36}\) The reason for this is not clear (see Brunsdon\(^{36}\) for a review) but is probably that the cooler conditions in this region slows down development of eggs, particularly for *N. filicollis*, so that a larger peak of infective larvae occurs on pasture in spring than occurs further north in the country. The oribatid mites which are the intermediate hosts for *Moniezia* are ubiquitous and consequently so are the parasites. The intermediate hosts of *F. hepatica* are more restricted which affects the distribution of the parasite (see Chapter 19).
References


16. Epe C, Samson-Himmelstjerna Gv, Stoye M, Schneider T. Comparative molecular


27. Ross JG, Purcell DA. The effect on infectivity and pathogenicity of cross infection of *Trichostrongylus axei* from sheep to cattle. *Veterinary Record* 84: p 49, 1969.


*Sustainable control of internal parasites in ruminants*


Internal parasites of cattle in New Zealand: Gastrointestinal nematodes and lungworm

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Introduction

Nematode infections of the gastrointestinal tract are potentially the most significant production-limiting infectious diseases of cattle. Of the many species of nematode infecting cattle in New Zealand, three are most important: *Ostertagia ostertagi*, *Trichostrongylus axei* which live in the abomasum, and *Cooperia oncophora* which lives in the small intestine. However, there are other species that are secondarily or occasionally important, including other species of *Ostertagia*, intestinal *Trichostrongylus* species, *Nematodirus helvetianus* and *Oesophagostomum radiatum*^4, 5, 11^ (and see Chapter 2). Although *Ostertagia* is regarded as the most significant of these parasites, most infections are mixed. The only nematode to be found in the respiratory system is *Dictyocaulus viviparus*, the cause of parasitic bronchitis of cattle throughout the world. Although clinical cases in New Zealand cattle are reported occasionally, very little is known of the prevalence or importance of this parasite.

In this chapter it is intended to present an overview of the epidemiology of gastrointestinal nematode infections and their effects on cattle, discuss parasite control in general terms and then in relation to specific production systems. After that, type-2 ostertagiosis and parasitism in adult cattle will be dealt with and, finally, lungworm infections.

Epidemiology and effects on production

Our knowledge of the seasonal pattern of infection with gastrointestinal nematodes is largely based on work done in the southern half of the North
Island and it has recently been reviewed by Bisset. In general terms, in the absence of parasite control the sequence of events is as follows:

Spring-born calves are infected initially with larvae that have overwintered on pasture. The initial infection gives rise to the first generation of worms, eggs from which contaminate the pasture in spring/early summer with a consequent rise in larval availability in early summer. These larvae reinfect the calves and give rise to a second and much larger generation of worms that produce the eggs which result in the major autumn/winter peak of larvae on pasture in May/June. By autumn the calves are beginning to exert some control on the numbers of eggs produced by the worms, particularly Ostertagia but also T. axei and Cooperia, and egg counts tend to fall (even though worm numbers may be high and still increasing); the reduced egg output and cooler weather decreasing larval development lead to a decline in pasture larval numbers in late winter with further dilution of those remaining by the growth of grass in spring.

Peak numbers of normally developing (as opposed to inhibited) Ostertagia and Cooperia in the calves occur in their first winter. All being well, by the time they are about a year old, they have usually developed a relatively high level of resistance to Cooperia. By 12-15 months, numbers of adult Ostertagia have also fallen to low levels (although inhibited larvae may be present). However, peak numbers of T. axei (both larvae on pasture and worms in animals) occur later, in about October, though numbers decline shortly afterwards and the peak may be quite low. It takes around 18-20 months for cattle to establish high levels of resistance to infection to all three of the major parasites.

Calves in their first year are thus the major source of pasture contamination. After about 12 months of age, faecal egg counts are generally low (<100 eggs/g), although the yearlings may contribute significant numbers of T. axei eggs to pasture in the spring.

This pattern has been largely worked out with dairy/dairy beef cattle but would be expected to apply also to cow-calf systems although quantitative differences would be likely because of later weaning, lower stocking rates and so on. Climatic differences from north to south in New Zealand will have some effect on the epidemiology of these infections; in warmer, wetter areas,
larval development on pasture would be more rapid and successful and continue for longer through the year than in colder areas.

Another factor to be considered in the epidemiology of nematode infections of cattle is the potential for prolonged survival of infective larvae in undisturbed dung pats which can serve as excellent incubators for developing larvae. Work in Victoria, Australia several years ago showed that once larvae have reached the infective stage, they can survive in significant numbers for several months, even over summer, to be released subsequently by rain.\(^1, 2\) The development and survival of larvae in cattle dung pats has not been studied under New Zealand conditions but is also likely to be prolonged in some circumstances, extending the potential infectivity of pasture.

The significance of gastrointestinal parasites in any cattle enterprise is mainly determined by the level of exposure to infection. If infection rates are high enough, clinical disease can result. However, it is the subclinical effects of parasitism that are by far the most important economically since they affect all animals. Nutrition is also of major importance as it affects the ability of the animal to cope with the effects of parasites or resist their establishment.

The pathogenesis of parasitic gastroenteritis is complex and many factors contribute to the disease and loss of production (see Holmes\(^19\) for a review). Most of the effects are due to induced alterations in metabolism, particularly protein metabolism. The net effect is diversion of protein synthesis away from growth and production, decreasing the efficiency of digestible energy utilisation and feed conversion. Reductions in voluntary food intake and the effects of diarrhoea on water and electrolyte balance aggravate the problem. There may also be effects on mineral metabolism and trace-element balance. It is not difficult to see how the level of nutrition can either ameliorate or exacerbate the effects of gastrointestinal parasitism.

The effects of parasitism are likely to be most severe and of greatest long-term significance in the first year of life. These animals have little or no acquired resistance, have minimal reserves to draw on and need to be making maximal skeletal and muscular growth if their lifetime production is not to be impaired. Numerous drenching trials in New Zealand have demonstrated the scale of potential losses, averaging about 15 kg live weight but ranging up to 55 kg live weight and 33% mortalities.\(^{15, 22, 25, 26, 27}\) However, in most trials,
the potential losses in the absence of parasite control are underestimated because of the need to run treated and untreated animals together where treatment groups are not replicated.

There is little published work on the effects of gastrointestinal nematodes on production of cattle in the second and later years of life, and the situation is complicated by the tendency for animals to accumulate inhibited Ostertagia larvae with the potential for causing type-2 ostertagiosis. There is some evidence that mature cattle can suffer a loss in body weight if exposed to substantial numbers of larvae on pasture. \(^{(31)}\)

Principles of control

The primary objective of all control strategies should be to minimise the exposure of cattle to infective larvae on pasture. The key is the control of parasitism in the first 12-15 months of life because animals of this age are most vulnerable and they are potentially the main source of pasture contamination. This directly affects the challenge to which older animals are exposed and the potential for type-2 ostertagiosis. The control strategies that can be used will differ with the type of enterprise concerned (e.g. dairy, bull-beef, cow-calf systems), the management options available and the preferences of individual producers. In most situations, however, anthelmintics are an important part of the control programme.

Today there are many highly effective anthelmintics available for the control of cattle parasites, and many are formulated in ways that greatly increase the convenience of their use, notably pour-on and injectable formulations, and slow-release boluses. The anthelmintics in use can be categorised into three groups according to their mode of action, the benzimidazoles, levamisole & morantel, and the milbemycin/avermectin endectocides. The last group is used most widely. This is not surprising given their high level of effectiveness against both nematodes and ectoparasites, and prolonged activity and ease of administration (particularly in some formulations). The benzimidazoles and levamisole still have place in the armoury, however, and it would be most unwise to rely on one action family of drugs to the exclusion of others. The recent introduction of a pour-on formulation of oxfendazole is an interesting development.
Whatever the drug or formulation used, its use should be in accordance with label instructions, particularly with respect to the correct dose rate, and the observance of withholding periods and other precautions or restrictions on use. It is generally agreed that preventive use of anthelmintics is preferable to reliance on treatment after problems have arisen, and this requires planning. Anecdotal evidence indicates that failures of parasite control most often arise through the lack of a planned strategy or failure to adhere to it.

Another potential cause of failure of control is anthelmintic resistance and while this is recognised as a serious problem in parasites of sheep and goats, little attention has been paid to it in cattle. Although there have been no surveys for anthelmintic resistance in cattle nematodes in New Zealand, there are several confirmed cases of resistance to benzimidazoles and others suspected. These have involved the three major cattle parasites, *Ostertagia*, *Trichostrongylus* and *Cooperia*.\(^{20, 21, 25}\) Recently, resistance to ivermectin and moxidectin in *Cooperia* spp. has been described.\(^{29, 30}\) There is probably considerably more anthelmintic resistance around than these records would suggest.

It is important to distinguish between anthelmintic resistance, which is an acquired characteristic of a population of nematodes, and inherent differences in susceptibility of different nematode species that have never been exposed to the drug concerned. Some are much easier to kill than others. Species that are inherently more difficult to kill often determine the dose of a drug that needs to be used in practice to obtain a high level of overall parasite control. These are known as dose-limiting species. A good example of this is *Cooperia*, species of which are relatively less susceptible to the avermectin/milbemycin group. These have come into prominence recently following a number of reports of lower than expected efficacy of ivermectin against *Cooperia*, particularly following topical (pour on) application, in circumstances where there had been little or no previous use of drug on the farm.\(^{7, 24, 32}\) Whether this inherent lack of susceptibility will result in a more rapid selection of truly drug-resistant populations than with inherently more susceptible species, is not known.

Anthelmintic resistance of cattle nematodes and its likely impact on the sustainability of parasite control reliant on anthelmintics warrants serious
attention. The situation is probably similar to that with sheep nematodes about ten years ago. There is a need for information on the present anthelmintic resistance status of cattle parasites and for the development of strategies to slow its development and reduce its impact. To suppose that we can ignore it and assume it will not become a significant problem would, in my opinion, be a serious mistake. The fact that there are now some combination drenches containing a benzimidazole and levamisole on the market for cattle is an encouraging sign. The use of combination drenches has been advocated as a most effective way of reducing the rate of selection for resistance. On the other hand, over-reliance on the avermectin/milbemycin group to the exclusion of others, and the patterns of anthelmintic use in some intensive rearing systems are matters of real concern.

**Parasite control in dairy calves**

This will be dealt with from the point of view of a spring-calving, factory-supply system with additional comments on town-supply herds at the end. Given the variations in management systems on individual farms, it is only possible to provide generalised recommendations that may need to be adapted to particular situations.

**Minimising initial infection**

When they start to graze, calves pick up their initial nematode infections from larvae that have overwintered. It is important to try to minimise this initial exposure by ensuring that the infectivity level of paddocks in which the calves will be kept until weaning is as low as possible. In practice this means avoiding paddocks grazed by the yearlings or other young cattle in the preceding autumn and winter. Paddocks in which cases of clinical parasitism have occurred are particularly dangerous.

**Preventive drenching**

A major attraction of the preventive drenching programme is that it can be applied regardless of the management system being used. It is, however, totally reliant on the use of anthelmintics, and its success depends on ensuring that treatments are carried out at the correct intervals and that the drench used is effective.
Calves are commonly given their first drench at weaning, which may be as early as October. If so, this is before the recommended start of the standard preventive drenching programme and the weaning drench should be regarded as additional. The published recommendation is for the first drench in the preventive programme to be given in November, followed by five further treatments at 4 week intervals\(^{(5)}\) although with the availability of drugs with prolonged activity, it may be possible to extend the interval between treatments without prejudicing the outcome.\(^{(16)}\) The objective is to minimise infection levels and pasture contamination over a 4-5 month period from late spring to about April so that growth rates are maximised and the autumn peak of larvae on pastures is largely prevented. Assuming this is the only means of parasite control being used, it is possible that, in warmer areas, a further drench may be needed to prevent a late-developing peak of larvae on pasture. There do not appear to have been any investigations of this. In addition, the situation can vary with the management system, e.g. the use of a ‘run-off’ (see below).

When they are young and relatively easily handled, calves can be drenched orally with little difficulty but this becomes an increasing problem as they grow, particularly if handling facilities are limited. This is a major reason for the popularity of pour on and injectable formulations of drugs which, for the most part, are in the avermectin/milbemycin group. Once the calves have reached 100 kg live weight, the ivermectin slow-release bolus offers an alternative approach to regular treatments.

**Grazing management**

Grazing management can play a major role in the control of parasitism in young cattle either by reducing the exposure to infection or assisting animals to cope with the effects of parasitism by improving nutrition. Conversely, some management practices can make matters worse.

**Rotational grazing** While on the main farm, calves are commonly grazed on a rotational system ahead of the milking cows. This provides good nutrition for the calves but does not generally provide adequate parasite control on its own. The likely reason for this is that although the calves may graze over the whole farm, the speed of rotation varies according to the amount of feed available. As a result some paddocks become more heavily contaminated with worm eggs than others and high levels of infection can build up. Because
of this, a preventive drenching programme should always be used in conjunction with such rotational grazing systems.

**Set-stocking of calves in small groups** Under this system, calves are set-stocked around the farm in small groups of, say, 2-3 per paddock. For practical reasons, it is generally not feasible to do this until after the calves are weaned and vaccinations completed. It is advisable to drench the animals at weaning or before they are divided up. Although there appear to have been no experimental investigations of this, it is reported that calves do very well under this system with little or no need for additional drenching. It is probable that infection levels are markedly reduced because pasture contamination from the calves is distributed evenly over the whole farm, and the adult cows periodically remove most of the herbage mass on each paddock and, with it, most of any infective larvae that have developed.

**Use of 'run-offs'** Run-off areas away from the main farm are commonly used to relieve pressure on the main grazings. The pattern of their use varies but generally they are used for yearlings and/or in-calf heifers. Dry cows may also be grazed on them during winter. The fact that these areas may be grazed consistently by young animals whose resistance to nematodes is not fully established, means that they can become heavily contaminated with nematode larvae. The extent to which this is likely to occur will, of course, be affected by the adequacy of parasite control in the calves before and after they are placed on the run-off. However, even with adequate control in the calves, a high base-level of larvae on the pasture may still arise through repeated use for young stock.

If this occurs, the resulting parasite challenge can seriously affect the growth of yearlings placed on the run-off, and this will be exacerbated if nutritional conditions are marginal or worse, particularly in winter. Obviously, if parasite control in the calves is inadequate and they shed large numbers of eggs onto the pasture, the situation will be much more serious. Maintaining good growth during the first winter is important if target weights are to be met and heifers are to become pregnant. Since, for practical purposes, the level of infection on the pasture is not measurable, at the very least careful monitoring of the animals on run-offs is essential and continued parasite control, at least through the winter, may well become a necessity either by regular treatments or by
the use of an intraruminal bolus. The importance of maintaining good nutrition in addition, cannot be stressed too much.

*Town-supply herds* with their extended calving can have particular parasite control problems if late-born calves are to be kept. Without a high level of parasite control in the spring-born calves, the numbers of nematode larvae on pasture will increase during the summer and, if they graze the same pastures, be available to the late calves when they are starting to graze. While this can be controlled by the use of anthelmintics in both early and late calves, it is likely that the late calves will need to be treated through the winter if growth rates are to be maintained, and particularly if nutrition is marginal. The importance of providing good nutrition cannot be overemphasised - anthelmintics are no substitute for food.

If the late-born calves can be grazed in the autumn and winter on pasture not contaminated by the spring calves, this will markedly reduce the risk of them acquiring significant worm burdens. However, since no pastures are parasite-free and pasture larval numbers may have built up to some extent, careful monitoring of the animals is advisable. If circumstances or experience suggest that significant challenge to the calves is likely to occur, drenching through the winter may again be necessary.

Having to drench both age-groups means the prolonged use of drenches on the farm, adding to costs and the risk of drench resistance developing. With careful planning it may be possible to overcome these problems by adapting the set-stocking system described above to reduce the need for drenching.

**Intensive bull-beef systems and contract rearing of dairy heifers**

In bull-beef systems, calves are usually reared on milk replacer with or without concentrate supplements, and weaned at around 10 weeks or at a predetermined weight. Management systems vary with some rearing calves from birth, others buying them in as weaners or yearlings. In some, animals are slaughtered at around 18 months of age; in others, not until 2-3 years. They may be 'stand-alone' enterprises or part of a mixed one. Mobs of animals may be rotationally grazed or set-stocked according to feed availability. In
some systems, forage crops are used to provide high quality feed and conserve pasture. Contract rearing of dairy heifers is similar in that groups of young cattle are intensively managed generally from about 9 months of age.

With both bull-beef and dairy heifers, maximising growth rates and attaining target weights quickly and efficiently are key issues. Checks to growth or reduced efficiency of feed conversion are clearly undesirable and to be avoided if possible. Parasite control is a major concern and tends to rely heavily on regular anthelmintic treatments. In stand-alone enterprises or where they are confined to a particular area of a farm, successive mobs of cattle are run on the same area until slaughter weights are reached or they are sold on. This monoculture of predominantly young cattle means that a high level of pasture infectivity is inevitable without effective parasite control. In these situations, there is little or no scope for using grazing management to reduce it.

Regardless of the management system or parasite control programme that is to be used, animals that are brought in to these intensive systems should always be drenched on arrival as their parasite status is usually unknown. Almost 20 years ago it was suggested that monthly drenching from weaning to 12 months of age might be needed but actual drenching practices have not been surveyed. A drenching programme that has been widely recommended involves treatments beginning about the end of November, or when the weaners are brought in, and continuing at four or six weekly intervals until July. Some producers may continue treatments beyond this time. While the treatment interval may vary with the drug and formulation used, and could include the use of an intraruminal bolus, the aim is to minimise parasite effects through the first year by minimising pasture contamination by removing parasites before they have had time to lay many, if any, eggs.

Assuming that the treatments are properly given and that the drugs are working, such a schedule of treatments will provide a high level of parasite control. Depending on the circumstances, it is possible that not all these treatments are essential but, in practice, there is no way of telling if this is the case on the individual farm at the time. From the producer's point of view, the returns are almost certain to more than cover costs and the economic stakes are too high to risk reducing the effectiveness of parasite control. In such circumstances, reliance on regular drenching for parasite control seems

Charleston: Parasites of cattle in New Zealand
unavoidable. The sustainability of such a high level of drug use is, however, a serious concern as the risks of anthelmintic resistance developing are high. If these intensive production systems are to remain practicable and profitable, strategies to reduce these risks need to be developed urgently.

Should resistance develop on a farm, it is likely to be gradual in onset and initially there may be only subtle effects on production that are difficult to detect. Signs of control failure are most likely to be seen first in the younger animals and they are more likely to be picked up early where growth rates are being monitored regularly.

**Parasite control in cow-calf systems**

**General considerations**

In suckled beef systems, calves are usually weaned at 4-6 months of age and so are somewhat less dependent on grazing early in life than calves weaned earlier. The cattle are usually run at lower stocking rates than in dairy or intensive beef enterprises, and in conjunction with sheep. Nevertheless, good parasite control in the post-weaning period in cow-calf systems is essential as without it there are likely to be major subclinical effects on growth, as well as the potential for outbreaks of disease.

An important factor in the epidemiology of nematode infections in suckled calves is the date of weaning as this is normally when the calves are drenched for the first time. This can vary from as early as February to as late as April or May.\(^{[27]}\) When weaning is as late as April, much of the season's contamination with nematode eggs will be already on the pasture. Consequently, if the calves are grazed after weaning on pastures contaminated by them before, they are likely to be exposed to substantial parasite challenge. Drenching then becomes 'curative' or 'protective' rather than 'preventive' as the nematodes removed by the drench are rapidly replaced. In production terms this is far less satisfactory than preventing infection, (although it may reduce the selection pressure for anthelmintic resistance). Understanding this, however, enables the producer to avoid the problem by ensuring that, after weaning, the calves are grazed on pastures they have not contaminated. Theoretically, there would be advantages in starting the drenching programme earlier to reduce pasture contamination over the summer.

*Sustainable control of internal parasites in ruminants*
Another point to note is the potential for prolonged survival of infective larvae in undisturbed dung-pats mentioned earlier. This can result in paddocks remaining relatively high risk for longer than one would otherwise expect. It is the probable explanation for a case described to me by a practitioner in which a severe outbreak of parasitic gastroenteritis occurred in August on a paddock that had not been grazed by cattle (or other stock) since April.

Recommendations for parasite control

Recommendations for treatment in the six months or so after the weaning drench have ranged from one or two additional drenches upwards. Early recommendations for relatively few drenches (e.g. Brunsdon and Adam) were based on the trial data available at the time; some later trials indicated that benefits from 5-6 drench regimes were not always reflected in value at slaughter, and that a three-drench regime at 6-week intervals was satisfactory. However, all these trials were carried out before the development of the endectocides and when beef cattle comprised a comparatively small proportion of the stock on sheep/beef farms, which would have reduced the levels of infection the cattle were likely to be exposed to.

More recent trials using ivermectin in beef weaners showed that six treatments at 6-week intervals between March/April and October were more profitable than a series of four treatments ending in July, and this has become the basis for a widely recommended drenching programme. Whether continuing drenching until October is needed or would be equally profitable in all circumstances, is not certain, however. The interpretation of the above trials is complicated by the need to have untreated controls which, in this case were heavily parasitised and adding to pasture contamination. Where all the animals at risk are treated, as would be usual under farm conditions, there should be minimal pasture contamination through the autumn and winter, and no infection in the animals to carry over into the spring. On the other hand, as even small intakes of larvae may significantly affect growth, particularly at the end of winter when nutrition is marginal, some might argue that continuing drenching into the spring is justifiable on the grounds of ‘better safe than sorry’ even though profitability may be uncertain. To what extent it increases the risk of selecting for anthelmintic resistance is more problematic.
As noted earlier, the benefits of drenching will be much reduced if the animals are subjected to high levels of parasite challenge. With reasonable balance between cattle and sheep on farms, it should be possible to use grazing management to avoid this. At the very least this will improve the returns on drenching, and may reduce the frequency of drenching needed to obtain satisfactory levels of parasite control. There is relatively little interchange of parasites between sheep and cattle, and alternate grazing for blocks of time has the potential to substantially reduce the level of homologous challenge. Little has been published on such systems under New Zealand conditions but possible approaches have been discussed by Bisset and co-workers.\(^{10}\)

Some research has been done on the possibility of parasite control in sheep and cattle without the use of anthelmintics, relying entirely on grazing management. This work has been reviewed elsewhere.\(^{18}\) So far it seems that obtaining satisfactory growth and parasite control is easier with sheep than cattle in such systems. More research is needed to explain this and explore practical possibilities.

Once again it should be noted that where weaners are bought in, it is important that they are drenched on arrival as their parasite status is generally unknown.

**Type-2 ostertagiosis:**

Under New Zealand conditions, cattle generally accumulate 'inhibited' or 'arrested' *Ostertagia* larvae through the late autumn and winter.\(^{6,13,14}\) Burdens of several thousands may accumulate but as long as they remain inhibited, they appear to have very little effect on the animal. Generally, these larvae are lost over the spring and summer without any clinical signs developing. In some circumstances, however, substantial numbers of larvae resume development and emerge from the mucosa simultaneously causing severe gastritis and clinical signs of ostertagiosis. As the condition arises from the maturation of previously inhibited larvae, this is referred to as type-2 ostertagiosis.

Although cases can be dramatic and there are some serious outbreaks on record, they are sporadic and uncommon, most often in yearlings and first-calvers but sometimes in older cattle. Outbreaks may involve single animals or several in a herd. The disease may be very acute in onset with severe
diarrhoea, rapid loss of condition, dehydration and possibly death, or it may be more chronic with diarrhoea and loss of condition occurring over several weeks. What factors precipitate clinical cases is not fully understood but they are often associated with calving (perhaps more particularly in dairy cattle), or with abrupt nutritional changes (for better or worse), and sometimes movement of stock from one situation to another.\(^6,17\) While all these can be viewed as ‘stressful’ and potentially affecting host immunity, precisely how this relates to the development of clinical disease is not known.

For the treatment of type-2 ostertagiosis, the drugs of choice are the avermectin/milbemycin group as these are highly effective against both the developing *Ostertagia* and remaining inhibited larvae in the abomasal mucosa. Longer acting benzimidazoles can also be used but treatments should be repeated after 7-10 days to ensure high activity against mucosal larvae. Even with the best of treatment, animals that are already severely affected may die. Treating dairy cows in lactation has presented a problem as, until recently, all the more effective drugs either had withholding periods during which the milk should not be used for human consumption or, in the case of the avermectin/milbemycin group, were banned from use during lactation and, in some cases, within 28 days of the start of lactation. The recent introduction of eprinomectin and changed regulations for pour on moxidectin, both of which are highly effective and have a nil withholding period for milk, solves this particular problem and will make treatment of these cases much simpler.

The prevention of type-2 ostertagiosis is complicated by uncertainties about the precipitating causes of disease and its sporadic nature. It is probable that the likelihood of disease occurring will be substantially reduced by effective parasite control in calves as they are the major contributors to pasture contamination. In intensive dairy heifer and bull beef systems, the fact that the cattle are drenched regularly, at least until the end of the first winter, should mean that type-2 ostertagiosis is very unlikely to occur providing the drenching is effective.

The treatment of yearlings and older animals at the end of winter with a drug that is effective against inhibited larvae will, of course, remove any risk of the disease developing. However, since very few animals are, in fact, likely to be affected, a blanket recommendation to treat all animals regardless of
circumstances would be difficult to justify. Furthermore, it could be a potent way of selecting for anthelmintic resistance as any surviving worms are likely to be resistant and become a source of pasture contamination early in the season and contribute to the initial infection of the new season's calves.

Nevertheless, there are circumstances where preventive treatments should be given. For example, where there is a history of cases occurring in heifers or cows around calving, it may be advisable to treat before calving. In situations where parasite control in the previous year is less than good, and experience or circumstances suggest nutritional stress, treating yearlings or in-calf heifers in the spring may also be advisable. Farmers buying in stock, whether yearlings or older, especially over the winter and spring, should always treat them on arrival as their parasite status will be unknown and the transport and change in environment may well precipitate disease. In-calf heifers are likely to be particularly at risk in such circumstances.

**Routine treatment of adult dairy cattle:**

Aside from the question of the prevention of type-2 ostertagiosis, the drenching of adult cows to improve milk yield has been debated for many years. Trials of varying quality carried out both here and overseas (mainly in the 1970s) produced inconsistent results and even where increased production was observed, it was not always of economic value. The early work in New Zealand has been reviewed elsewhere.\(^{(8, 9, 15)}\) In a later extensive series of trials involving 47 herds, it was shown that treating cows at drying off and again just before calving with oxfendazole, produced a significant overall increase in milkfat production averaging 2.24 kg milkfat/cow.\(^{(8)}\) However, further analysis of the data\(^{(9)}\) showed that the size of the response was directly related to the level of parasite control in the calves. On farms where a preventive drenching programme was used for the calves, the response to treatment of the cows was minimal. Where the calves received two or fewer drenches, and particularly where the cows grazed pastures contaminated by the calves over winter, the responses averaged over 5 kg milkfat/cow.

This clearly shows that exposure of cows to heavily contaminated grazing adversely affects their production, and the importance of controlling pasture contamination by the calves. Since there are substantial advantages to be
gained in terms of growth and long-term productivity by adequate control of parasites in the calves, that is clearly where the priority should lie. If that is done, there would appear to be no advantage from routinely treating cows during the dry period with the expectation of increased milk production. Treating these animals for the purpose of preventing type-2 ostertagiosis has been discussed earlier. Whether or not there is any production advantage in treating cows later in lactation is not known.

Lungworm

Very little is known about lungworm (*Dictyocaulus viviparus*) in cattle in New Zealand. It is generally assumed, probably correctly, that infections are common but there have been no surveys of prevalence. The epidemiology of infection has not been studied either. Anecdotal reports indicate that clinical cases are seen occasionally, perhaps more commonly in later born calves. The relative lack of clinical significance of lungworm in New Zealand compared with Europe is probably attributable to the fact that here calves are at pasture from an early age and remain there for life. It is probable that light infections are acquired early on from overwintering larvae as the calves start to graze and these induce a level of resistance that is sufficient to withstand later challenges. These calves are likely to develop patent infections which will result in a rise in the availability of larvae from late spring. Later born calves may then encounter larger numbers of larvae on pasture than the early ones and this may account for the clinical signs that sometimes develop in them. Preventive drenching programmes, which commonly start at or soon after weaning, are widely used and these will also prevent the occurrence of clinical lungworm infections.

References


*Sustainable control of internal parasites in ruminants* 39


Internal parasites of deer in New Zealand

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Introduction

Six species of deer have been introduced to New Zealand and have established permanent populations in the wild. Only two of these, Cervus elaphus (red deer, wapiti and their hybrids) and Dama dama (fallow deer) are farmed to any extent, with C. elaphus by far the most numerous on farms and the main subject of this article.

Know internal parasites of the two farmed deer species are listed in Table 4.1.(1)

Nematodes

Lungworm (Dictyocaulus viviparus)

The common lungworm of deer, Dictyocaulus viviparus, sometimes known as D. eckerti, is the most important parasite in farmed deer.(2,3,4,5) A 1981 deer farm survey indicated it is present throughout the country,(6) and this will not have changed.(7)

Dictyocaulus viviparus has a direct life cycle. Adult worms live in the air passages in the lungs; the eggs hatch in the lungs shortly after being laid, and first stage larvae are expelled from the lungs and pass down the gastrointestinal tract of the host and are shed in the faeces. These larvae develop on pasture (without feeding) to infective third stage larvae in as little as five days under optimum conditions. Deer become infected when they ingest infective larvae. These leave the intestine, migrate to the lungs and break through into the alveoli to complete the life cycle.

The minimum prepatent period (time from infection of the host until the worms start laying eggs) for D. viviparus in red deer is around 20 days.(7,8)
TABLE 4.1: Known parasites of deer in New Zealand. (Numbers refer to source reference.)

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<td></td>
<td>red/wapiti</td>
<td>fallow</td>
</tr>
<tr>
<td>Protozoa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Eimeria</em> spp.</td>
<td></td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td><em>Toxoplasma</em></td>
<td></td>
<td></td>
<td>45</td>
</tr>
<tr>
<td><em>Sarcocystis</em> spp.</td>
<td></td>
<td></td>
<td>45</td>
</tr>
<tr>
<td><em>Cryptosporidium</em></td>
<td></td>
<td></td>
<td>49</td>
</tr>
<tr>
<td><em>Neospora</em></td>
<td></td>
<td></td>
<td>46</td>
</tr>
<tr>
<td>Trematodes</td>
<td><em>Fasciola hepatica</em></td>
<td>53</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>Paramphistomatidae</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Cestodes</td>
<td><em>Taenia hydatigena</em></td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td><em>Moniezia</em> spp.</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td><em>M. expansa</em></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Lung nematodes</td>
<td><em>Dictyocaulus viviparus</em></td>
<td>53</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td><em>Elaphostrongylus cervi</em></td>
<td></td>
<td>25,26</td>
</tr>
<tr>
<td></td>
<td><em>Varestrongylus sagittatus</em></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Abomasal nematodes</td>
<td><em>Ostertagia</em>-like:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Apteragia quadrispiculata</em></td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Haemonchus contortus</em></td>
<td></td>
<td>56</td>
</tr>
<tr>
<td></td>
<td><em>Ostertagia (Teladorsagia)</em></td>
<td>56</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>circumcincta</em></td>
<td></td>
<td>56</td>
</tr>
<tr>
<td></td>
<td><em>O. leptospicularis</em></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Rinadia mathevossiana</em></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Skrjabinagia kolchida</em></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Spiculopteragia asymmetrica</em></td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>S. spiculoptera</em></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Trichostrongylus axei</em></td>
<td>56</td>
<td>7</td>
</tr>
<tr>
<td>Small intestinal nematodes</td>
<td><em>Capillaria</em> spp.</td>
<td>53</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td><em>C. mcmasteri</em></td>
<td></td>
<td>58</td>
</tr>
<tr>
<td></td>
<td><em>C. oncophora</em></td>
<td></td>
<td>58</td>
</tr>
<tr>
<td></td>
<td><em>C. pectinata</em></td>
<td></td>
<td>57</td>
</tr>
<tr>
<td></td>
<td><em>Nematodirus</em> spp.</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>Large intestinal and caecal nematodes</td>
<td><em>Oe. venulosum</em></td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Trichuris ovis</em></td>
<td></td>
<td>53</td>
</tr>
<tr>
<td></td>
<td><em>Trichuris</em> spp.</td>
<td></td>
<td>6</td>
</tr>
</tbody>
</table>
The early signs of lungworm infection in red deer are vague, including loss of condition, retarded growth and roughened coat: coughing is not a common sign. Severely affected animals will die.\(^{(3,9,10)}\) The most susceptible stock are calves during their first autumn and early winter (3-6 months old) and recently-captured individuals of all ages. By July calves are generally relatively resistant and this resistance persists in healthy animals.\(^{(6)}\) Reports of sudden deaths in heavily infested young deer continue to be reported.\(^{(11,12,13)}\)

In severe infestations the trachea and bronchi are packed with worms, and death appears to result from physical blockage of the air passages by worms. Extensive areas of consolidation and collapse of lungs, as in cattle, are not usually seen in red deer.\(^{(5,9)}\)

My original recommendations for anthelmintic control of *D. viviparus* were to drench calves every three weeks from weaning in March until early winter using one of the longer-acting benzimidazoles.\(^{(2)}\) In retrospect this appears to be an overkill for most properties, though desirable where the free-living stages flourish. Subsequently it has been possible to recommend extension of the drenching interval if the newer milbemycin/avermectin anthelmintics are used, because these have persistent activity against lungworm.\(^{(14,15,16,17,18,19,20)}\) Levamisole is not effective against lungworm in red deer.\(^{(21)}\) Adult deer do not normally require drenching for lungworm. See below for a more detailed discussion of drenching.

There is a good relationship between faecal larval counts and lungworm burdens.\(^{(7,19)}\)

Lungworm do not seem to be as important in fallow deer as in red deer, but outbreaks of clinical disease are known, such as the case where 90 of 100 fallow deer died from parasitic bronchopneumonia caused by *Dictyocaulus*.\(^{(22)}\)

**Tissue worm (Elaphostrongylus cervi)**

Tissue worm has become important to sections of the New Zealand deer industry, not because of any disease that it causes, but because its presence here has been a barrier to the export of live deer to Australia and Canada. This nematode has been the subject of a recent reviews.\(^{(23,24)}\)
Elaphostrongylus cervi was first seen in deer shot in the so-called ‘wapiti block’ in Fiordland.\(^{(25,26)}\) Since then it has been found in low numbers in farmed deer throughout the country, but there was a significant association between the presence of E. cervi and the introduction of deer from Southland/Fiordland at the time the survey was done.\(^{(6)}\)

Elaphostrongylus cervi has a two host life cycle. The life cycle is broadly as follows; adult worms are found in the connective tissue (fascia) surrounding skeletal muscles, the eggs are carried to the lungs in the blood system where first stage larvae hatch, migrate through the lung tissue into the air sacs, travel up the trachea, down the gut and leave the host in the mucous coating on the faecal pellets. Further development, to the infective third larval stage, continues in a molluscan intermediate host (slug or snail). When deer eat an infected mollusc the infective larvae are released by digestion and migrate to their preferred site. The migration route may involve a period of association with the central nervous system. The prepatent period is in the region of 120 days. Adult worms may live for several years in a deer.

No clinical signs have been described from naturally infected deer in New Zealand. Adult worms in the fascia of muscles can, however, elicit a reaction from the host; it appears as a localised green discolouration, resulting from an infiltration of eosinophils and lymphocytes, and parasitic granulomata may be formed.\(^{(25,27)}\) A diffuse interstitial pneumonia with focal emphysema and consolidation caused by first stage larvae migrating through the lungs has also been described from red deer.\(^{(28)}\)

The parasite was first described from red deer in Scotland but has not been associated with disease in that country.\(^{(29)}\) In Kazakhstan, on the other hand, it is regarded as the most pathogenic nematode on deer farms.\(^{(30)}\) These different views may reflect differences in the way deer are managed or fed in different countries.\(^{(23)}\)

No effective treatment is known, though benzimidazoles and ivermectin may temporarily suppress or decrease larval production.

**Lungworm** (*Varestrongylus sagittatus*)

A new lungworm for New Zealand, *Varestrongylus sagittatus* (syn: *Bicaulus*)
was recovered from the lungs of a farmed red deer in August 1993.\(^7\) *Varestrongylus sagittatus* is a parasite of both red and fallow deer in Europe. This species has a typical protostrongylid life cycle involving a molluscan intermediate host like *E. cervi* above. The adults are found in the lungs where they are intimately associated with the lung tissue, like *Muelleriinus* in sheep, but no further details are known of it at this time. This species is unlikely to be of any animal health significance, but as the larvae shed in the faeces look like the first stage larvae of *E. cervi*, apart from being smaller, they have the potential to make the diagnosis of *E. cervi* more difficult.

**Gastrointestinal nematodes**

In the early days of deer farming some highly elevated gastrointestinal worm burdens were seen in farmed deer.\(^31\) Such cases are now comparatively rare. In practice, gastrointestinal nematodes have been perceived to be of minor importance when compared with *Dictyocaulus*. In the past a management programme that controlled lungworm has usually controlled gastrointestinal worms as well.

Recently however, gastrointestinal worms, and the *Ostertagia*-like abomasal worms in particular, have made a comeback in importance. *Apteragia, Spiculopteragia, Rinadia* and *Skrjabinagia* (see Table 4.1) are all *Ostertagia*-type nematodes. The gastrointestinal nematodes are similar in appearance and have similar life cycles to their counterparts in sheep and cattle.

There is little information available on the relationship between faecal egg counts and gastrointestinal worm burdens in deer, but all the indications are that neither faecal egg counts nor plasma pepsinogen levels give a reliable indication of worm burden.\(^7,19,32\) In practice this means that gastrointestinal worm burdens in deer cannot currently be estimated reliably in live animals.

There is now both anecdotal and experimental evidence that comparatively low abomasal worm burdens can have a significant effect on production.\(^19,32,33,34,35\) For example, ill thrift was investigated in mixed age red hinds in Canterbury. Two thin hinds were necropsied. They were grossly emaciated, and the abomasum of each had a ‘Morocco leather’ appearance. The laboratory report confirmed parasitic gastritis. Abomasal worm burdens of these hinds were elevated, but not high in sheep terms, ranging between
1500 and 7200 adult worms and 50 and 1700 fourth stage larvae. Other deer in the mob responded to appropriate drenching.\textsuperscript{32}

A form of type II ostertagiasis has recently been reported from farmed red deer in the U.K.\textsuperscript{36} Anecdotal evidence suggests a similar condition may be found in New Zealand.

The effects of nematodes in farmed deer are similar to those in other ruminants, leading to ill thrift and in some cases death.

Wapiti and wapiti hybrids appear to be more severely affected by abomasal nematodes.\textsuperscript{34} One explanation that has been proposed is that wapiti come from North America, at the eastern end of the circumpolar range of \textit{Cervus elaphus}. When their ancestors left Asia and entered America they appear to have left their gastrointestinal parasites behind. Since then wapiti have become isolated in North America and lost their ability to cope with these nematodes. Be this as it may, wapiti do seem to be more susceptible.

Although not identified here, a similar range of species has been recorded from fallow deer in Australia,\textsuperscript{37,38} and would be expected to occur in fallow deer here.

Although plasma pepsinogen levels do not appear to be useful as an indicator of parasitism in red deer, the situation may be different in fallow deer. In an investigation in Germany, plasma pepsinogen levels in helminth free and naturally raised farmed fallow were measured at 4 weekly intervals from birth to 11 and 15 months respectively. The mean level at birth was 0.708 units tyrosine/l which decreased until 14 weeks of age in both groups. Thereafter, it levelled out at around 0.2 units tyrosine/l in the helminth free group, but gradually increased from the 18th week in the naturally raised group to around 0.8 to 1.0 units tyrosine/l in response to worm infestation, significantly higher levels than the helminth free group.\textsuperscript{39}

\textbf{‘Fading elk syndrome’}

The term ‘fading elk syndrome’ is used to describe a condition of chronic stress and ill thrift in wapiti and wapiti/red deer hybrids. The state of current knowledge was reviewed by Waldrup and Mackintosh.\textsuperscript{40} The principal sign of the condition is elevated abomasal pH which has a negative influence on
both copper uptake and the effectiveness of oral anthelmintics, and reduces digestive efficiency. They postulate that the change in abomasal pH results from parasitism of the abomasal wall by fourth stage larvae of an Ostertagia-type nematode. Early treatment with double the recommended dose rate of ivermectin pour on for cattle seems to be effective in some cases. Further work on this condition is in press.

Efficacy of anthelmintics against gastrointestinal worms

Earlier work on the efficacy of anthelmintics concentrated on the efficacy against lungworm in red deer. More recently, there has been a shift towards looking more closely at efficacy against gastrointestinal worms and incorporating wapiti and wapiti x red hybrids. This has happened because of the improved availability of wapiti type stock and because of the health problems that have occurred in some of these animals.

The summary of lungworm drenching studies in red deer in the mid 1980s put anthelmintics into three categories: \( ^{(41)} \)

- diethylcarbamazine, levamisole and cambendazole had low activity;
- mebendazole, albendazole, oxfendazole, fenbendazole and febantel had moderate to good activity; and
- oral ivermectin (200 μg/kg) had very good activity.

After further work using injectable (200 μg/kg) and pour on ivermectin (500 μg/kg) at cattle dose rates, \( ^{(16,19)} \) the guidelines for where the risk of reinfection with lungworm was high were:

- use second generation benzimidazoles at 21 day intervals,
- use oral ivermectin (200 μg/kg) at 4 weekly intervals,
- use injectable ivermectin (200 μg/kg) at 5 weekly intervals, and
- use pour on ivermectin (500 μg/kg) at 7 weekly intervals. Subsequently, moxidectin pour on (500 μg/kg) and eprinomectin pour on have demonstrated similar or better activity against lungworm.

These guidelines are still applicable, but on most farms drenching need not be as frequent. Note however, that oral and injectable ivermectin are not licensed for use in deer.
Recent work on anthelmintic efficacy becomes somewhat more complex. In most investigations lungworms continue to be susceptible to anthelmintics except in two reports:

- In the first case larvae were still found in faeces for a few days after treatment. This is not evidence of ineffectiveness because it takes up to 5 days for larvae and eggs to leave the body of the host after treatment.
- The second case immature lungworm larvae were recovered 7 days after drenching with ivermectin pour on at 1500 μg/kg (3 times the cattle dose rate). This finding cannot be explained. The persistent effect of ivermectin should have stopped reinfection occurring so quickly after treatment. This may be evidence for ivermectin resistant *Dictyocaulus*, or may indicate that the immature stages are less susceptible to ivermectin than the adults. Further investigation is needed.

While both moxidectin and ivermectin pour ons are effective against adult *Ostertagia*-like worms in the abomasum at 500 μg/kg, the dose of ivermectin (but not moxidectin) needs to be doubled to kill the fourth stage larvae (L₄) of the abomasal *Ostertagia*-like worms. In one investigation ivermectin pour on was administered to wapiti hybrids at 1500 μg/kg. Although it was stated that this is routine practice, no data were presented to support the need to increase the dose rate to this level.

Boluses were used in two investigations:

- A morantel bolus protected wapiti hybrids against ill thrift, but if deer were treated with ivermectin pour on at 1000 μg/kg at the time the bolus was given the bolus gave no added benefit.
- An albendazole bolus did not completely protect treated red deer from reinfection with nematodes, but did suppress production of live lungworm larvae and protect from loss of weight.

Most of the publications cited above indicate that relatively low burdens of abomasal worms can cause ill thrift. It is interesting therefore to see a paper from the U.K. which reported very high worm counts, but then went on to state “No adverse effects of parasitism were observed in the adult deer in any of the three years, ....” Are these the same species of worms that are causing ill thrift in adult deer in New Zealand?
The key points that emerge from all this are:

Drench efficacy varies with:

A. availability of the anthelmintic in the host and persistence of the anthelmintic.
   - white drenches
   - milbemycin/avermectin pour ons

B. target species and life history stage
   - lungworm (*Dictyocaulus*)
   - adult gastrointestinal worms: ivermectin or moxidectin pour on at 500 μg/kg, or albendazole oral or bolus (other benzimidazoles may be equally effective)
   - L4 abomasal worms: ivermectin pour on at 1000 μg/kg, moxidectin pour on at 500 μg/kg, or albendazole oral or bolus (other benzimidazoles may be equally effective)

C. reinfection risk to stock - depends on management, climate and weather

D. drench resistance (no published reports from deer, but expected)

Initially we had assumed that drenches that worked in sheep and cattle would also work in deer. We soon found out however, that this was not the case. The extreme case was levamisole, a valuable drench in sheep and cattle. We found that it was not effective against lungworm in deer because it was broken down too quickly by the deer. (7)

Deer are not sheep or cattle. The efficacy, toxicity and metabolism of any pharmaceutical product, be it a drench or some other product, has to be established independently in deer.

Our knowledge of the behaviour of drenches in sheep and cattle has grown out of a large number of trials that have been carried out over many years. Deer have not been around as a farmed animal for very long and during this time it has not been easy to get stock for trial work. Further critical investigations are needed to unravel what is occurring with drenches in deer.

**Protozoa**

**Coccidia (*Eimeria* spp.)**

Unidentified oocysts of the *Eimeria* type were recovered in small numbers
from red deer on 27 farms and fallow deer on one farm during a 1981 deer farm survey.\(^{(6)}\) They usually have no clinical effect, but may cause disease in stressed animals. A seven month old Père David’s X red deer calf that had been unthrifty since birth died.\(^{(44)}\) At necropsy the only abnormality was thickening of the large intestine, which showed acute catarrhal colitis associated with severe coccidiosis.

**Toxoplasma**

*Toxoplasma* is found throughout New Zealand. It would be expected periodically to cause problems in deer. It has been reported from feral red deer from the Rotorua area and the heart blood of an aborted deer foetus.\(^{(45,46)}\)

**Sarcocystis**

*Sarcocystis* was recovered from 25 of 75 feral red deer from the Rotorua area and transmission from red deer to dogs has been demonstrated.\(^{(47,48,45)}\) Its distribution is unknown but it could be widespread. The species concerned has not been identified. This organism has not proven to be a problem in farmed deer.

**Cryptosporidium**

*Cryptosporidium* has been reported as causing disease in young deer, primarily hand reared calves.\(^{(49)}\) *Cryptosporidium* and rotavirus are the commonest causes of diarrhoea in deer calves up to 3 weeks old and recur as causes of death and disease.\(^{(10,50,11)}\)

**Neospora spp.**

*Neospora* spp.-like lesions have been associated with an aborted deer calf in two cases.\(^{(46)}\)

**Tape worms**

**Moniezia** *spp.*

*Moniezia expansa* has been recovered from farmed red deer calves, and *Moniezia* eggs from both red deer and fallow deer.\(^{(6,51)}\) This parasite is likely to be widespread, but does not appear to cause any clinical disease.
False hydatids (*Taenia hydatigena*)

Natural infections with false hydatids cysts, or 'cysticercus tenuicollis', the larval stage of *Taenia hydatigena*, have been found in feral red deer, wapiti, fallow and farmed red deer.\(^{52,53,54,13}\) Deer become infected by ingesting eggs passed by infected dogs. The developing cysticerci migrate through the liver and mature in the abdominal cavity.

There are generally no clinical signs of infection, although at slaughter there may be haemorrhagic tracts through the liver caused by the migration of developing cysticerci. In an unusual case however, a young red deer calf which died with hepatitis cysticercosa.\(^{54}\) Prior to death the calf was described as being moribund with subnormal temperature, cold extremities, pale mucous membranes and severe abdominal pain.

Flukes

Liver fluke (*Fasciola hepatica*)

The common liver fluke *Fasciola hepatica* has been reported from feral red deer.\(^{53}\) It is a common parasite of red deer in other parts of the world and has the potential to be a problem here on farms in endemic areas. Fortunately, reports suggest that red deer can tolerate higher *F. hepatica* burdens than can cattle. Triclabendazole is effective against *F. hepatica* in fallow deer and red deer.\(^{55}\)

Paramphistomes

*Calicophoron calicophorum* (syn: *C. ijima*) has been identified from red deer, and paramphistome eggs have been found in fallow deer faeces. No treatment is usually necessary.

Concluding remarks

Although this review has concentrated on the use of pharmaceutical products to control parasites, it is important to realise that drug resistant parasites will eventually appear in deer. So, when possible it is best to use non-drug tools in parasite control programmes.
This review makes it clear that there is a lot we do not know about parasites of farmed deer and their control. Whether much more information will be available in future depends on availability of funds for the necessary research.

References
7. Mason PC. personal observation.


56. McKenna PB. Personal communication.


58. Rutherford DM. Personal communication.


Sustainable control of internal parasites in ruminants
Mason: Parasites of deer in New Zealand
Farmer opinions on goats are sharply polarised, they either love them or loathe them, seldom anything in between. While much of this is due to goat behaviour, it can also relate to their parasitology. From a parasitological point of view goats are maligned and with some cause. The reasons for this are the main content of this chapter, which sets out to describe internal parasitism in goats, the impact this can have on other domestic animals and guidelines for the control of internal parasites in goats.

The internal parasites of goats in New Zealand are listed in Table 5.1.

**Gastrointestinal worms**

Gastrointestinal worms live in the abomasum, small intestine and large intestine. As can be seen from Table 5.1 the majority of the worms listed have the same names as sheep worms. This is important, because goats and sheep do share the same worms and can transmit them to each other. Life cycles are the same as they are in sheep.

The most important worms are *Ostertagia* spp. in the abomasum, and *Trichostrongylus* spp. in the small intestine. *Haemonchus* can cause problems in goats in parts of the New Zealand where it would not be expected to be a problem in sheep. This is thought to happen because shelters provide a protected environment for the free-living stages of this worm. *Nematodirus* is a greater problem towards the south of the country.

It was commonly believed that goats do not develop ‘age resistance’ to worms in the way that sheep do. But there is evidence that goats do develop some resistance to gastrointestinal worms after 12 months of age.\(^{(1,2)}\)
TABLE 5.1: Internal parasites found in goats in New Zealand. (Unless otherwise indicated these records are from McKenna. Other sources are indicated by their reference number.)

<table>
<thead>
<tr>
<th>Nematodes</th>
<th>Abomasum</th>
<th>Common</th>
<th>Uncommon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Haemonchus contortus</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Ostertagia circumcincta</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>O. trifurcata</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>O. ostertagii</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>O. lyrata</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Spiculopteragia spiculoptera</em></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td><em>Trichostrongylus axei</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>T. vitrinus</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td><em>Trichostrongylus colubriformis</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>T. vitrinus</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>T. capricola</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Nematodirus filicollis</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>N. spathiger</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Cooperia curticei</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Bunostomum trigonocephalum</em></td>
<td>✓?</td>
<td>✓</td>
</tr>
<tr>
<td>Large intestine</td>
<td><em>Capillaria spp.</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Lungworm</td>
<td><em>Muellerius capillaris</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Dictyocaulus filaria</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Tapeworms</td>
<td><em>Taenia ovis</em> (cysts) - sheep measles</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Taenia hydatigena</em> (cysts) - false hydatids</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Echinococcus granulosus</em> (cysts) - true hydatids</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Moniezia spp.</em></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Flukes</td>
<td><em>Fasciola hepatica</em> - liver fluke</td>
<td>✓ in some areas</td>
<td></td>
</tr>
<tr>
<td>Protozoa</td>
<td><em>Eimeria</em> spp. - coccidia</td>
<td>✓ disease rare</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Sarcocystis</em> spp.</td>
<td>✓ disease rare</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Toxoplasma</em></td>
<td>✓ disease rare</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Cryptosporidium</em></td>
<td>✓ disease rare</td>
<td></td>
</tr>
</tbody>
</table>

* No clear first report of this parasite.
In a study in Canterbury, faecal egg counts of kids appear to have a good relationship to worm burdens, like lambs. Clinical parasitism (scouring, obvious ill thrift) occurred in kids when the mean faecal egg counts in a random sample of 12 kids exceeded 1000 epg. \(^{(1)}\)

**Effects of parasites on goats and interaction with nutrition.**

The implications of nutrition to the ability of ruminants to withstand gastrointestinal nematode infections have recently been reviewed in detail by van Houtert and Sykes.\(^{(3)}\) My interpretation of the key points of this review are set out below, readers wanting more detail are referred to the original review. In this field most of the work has been done with sheep. The effects in goats are likely to be the same, but as goats are more susceptible to the effects of worms than sheep then clinical effects are likely to appear earlier in goats:

- The effects of nematode worms range from subclinical through to overt clinical disease (scouring, ill thrift, loss of weight and finally death).
- Worm infections depress food intake.
- The depression of food intake may be less when diets are high in protein.
- Between 40 and 90% of lost production can be attributed to reduced food intake.
- There appears to be a repartitioning of protein away from productive functions towards repair functions.
- There is an increased energy requirement for maintenance which reduces the energy available for production.
- The absorption and retention of phosphorus are reduced by *Trichostrongylus* infections in the small intestine.
- The ability to absorb calcium may be reduced by nematode infestations.
- Increasing the protein content of the diet can decrease the effects of worms, but this protection may be related to the levels of specific amino acids present, so the benefit may vary with the type of protein in the diet.
- Some forage species may affect either nematode larval intake or nematode establishment.
- Studies suggest that in young sheep, although diet does not appreciably affect nematode establishment it may enhance the rate of parasite eradication. Available data for goats in this area are equivocal.
**Drench efficacy**

The classification of drenches into families and an understanding of drench resistance are discussed by other contributors to this workshop. This information will not be repeated here so please refer to the other articles for details.

For many years goats were assumed to metabolise anthelmintics with the same dynamics as sheep, and goats were given the same dose rate as sheep. It is now known however, that "Comparative studies have revealed considerable differences between ruminant species regarding the pharmokinetics of anthelmintic drugs." and that "...it is necessary to evaluate the kinetic parameters separately for each species and that extrapolated data can be misleading in predicting adequate dosage regimes and withdrawal times."(4) The results of some of these studies are outlined below.

Nine month old Saanen goats maintained worm-free from birth and drenched lambs were each given 8,000 *Haemonchus contortus*, 10,000 *Ostertagia* spp. (85% *O. circumcincta*, 15% *O. trifurcata*), 15,000 *Trichostrongylus colubriformis* and 12,000 *Cooperia curticei*. Twenty three days after infection, the animals were assigned to treatment groups, treated and slaughtered five days later. Treatments were untreated control group, oxfendazole 5 mg/kg, morantel 10 mg/kg, levamisole 8 mg/kg and ivermectin 0.2 mg/kg. The results are set out in Table 5.2. The authors suspected that *Haemonchus* had a degree of resistance to oxfendazole and *Trichostrongylus colubriformis* to morantel. They summarise the results as: "Ivermectin and oxfendazole achieved similar levels of efficacy in both hosts against all four worm genera, as did levamisole and morantel against *Haemonchus contortus* and *Cooperia curticei*. Against *Ostertagia* spp. and *Trichostrongylus colubriformis* however, the latter two drugs were less effective in goats than sheep."(5)

In a similar trial using goats dosed with drench susceptible *Ostertagia circumcincta* and *Trichostrongylus* spp. worms from sheep, drench efficacies were respectively: morantel 69% and 68%, levamisole 55% and >99%, fenbendazole 98.5% and >99%, and oxfendazole >99% and >99%.(6)

Albendazole was administered to Merino sheep and Angora goats at 4.75 mg/kg and the levels of albendazole and its metabolites in plasma and abomasal fluid compared. The systemic (plasma) availability was significantly lower in goats than in sheep. The availability in abomasal fluid was similar in
TABLE 5.2: Mean percentage reduction in worm counts for a controlled slaughter trial comparing anthelmintic efficacy in sheep and goats (geometric mean of log(count+1), 5 animals per group).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Haemonchus</th>
<th>Ostertagia</th>
<th>Cooperia</th>
<th>Trich.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sheep</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4,024</td>
<td>5,140</td>
<td>2,620</td>
<td>11,760</td>
</tr>
<tr>
<td>OXF</td>
<td>93.2</td>
<td>99.6</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
</tr>
<tr>
<td>MOR</td>
<td>99.9</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>71.4</td>
</tr>
<tr>
<td>LEV</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
</tr>
<tr>
<td>IVM</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>99.8</td>
</tr>
<tr>
<td><strong>Goats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1,662</td>
<td>1,580</td>
<td>7,220</td>
<td>10,000</td>
</tr>
<tr>
<td>OXF</td>
<td>93</td>
<td>99.9</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
</tr>
<tr>
<td>MOR</td>
<td>99.9</td>
<td>96.2</td>
<td>99.4</td>
<td>55.6</td>
</tr>
<tr>
<td>LEV</td>
<td>99.2</td>
<td>81</td>
<td>&gt;99.9</td>
<td>97.8</td>
</tr>
<tr>
<td>IVM</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>&gt;99.9</td>
<td>99.6</td>
</tr>
</tbody>
</table>

OFX = oxfendazole at 5 mg/kg, MOR = morantel at 10 mg/kg, LEV = levamisole at 8 mg/kg, IVM = ivermectin at 0.2 mg/kg.

goats and sheep, but the level of albendazole sulphoxide lower in goats. Performance might be improved in goats by administering at a higher dose rate.\(^{(7)}\)

Two albendazole regimes were investigated in Angora X New Zealand feral goats in a controlled slaughter trial. Goats were naturally infected on pasture, moved to pens, ranked according to faecal egg count, restrictively randomised into three groups, treated, slaughtered after 7 days, and adult worm burdens determined. The recommended dose rate for albendazole in sheep is 3.8 mg/kg (4.75 mg/kg when efficacy against adult liver fluke is desired). Group 1 received 1 oral dose of albendazole at 3.8 mg/kg on Day 0 and again on Day 1, 24 hours later. Group 2 were dosed orally with 7.6 mg/kg of albendazole on Day 0, Group 3 were untreated controls. Both treatment regimes removed >99% Ostertagia spp. and Trichostrongylus spp.; and all Haemonchus contortus, Cooperia spp. and Chabertia ovina, although only small numbers were present in the controls. There was a 96% removal of Oesophagostomum venulosum in Group 1 and apparently complete removal in Group 2. There was no apparent difference between numbers of Trichuris in either treated group compared with the Controls.\(^{(8)}\)
These data show that benzimidazoles, levamisole and morantel all appear to have lower bioavailability in sheep than goats. It is now common to increase the dose of benzimidazoles to 1.5 to 2 times the sheep dose rate. Increasing the dose of levamisole is risky as toxic reactions may occur. Advice from the manufacturer is to use oral ivermectin in goats rather than the injectable, because it is more effective.

Incidentally, these differences extend also to the fasciolicide drugs clorsulon and closantel.\(^4\)

**Drench resistance**

The susceptibility of goats to worms and their poorly developed age resistance mean that goats on pasture were often drenched more frequently than other domestic animals.\(^{9,10}\) Some, if not all these drenches had reduced efficacy in goats. Goats have been therefore, prime hosts for the development of drench resistant worms, and this has been the case. Further, ivermectin resistant worms in New Zealand appeared first in goats. These resistant worms because of their ease of transfer, pose a threat to the sheep industry.

Drench resistant worms are common in goats throughout the world.\(^{11,12}\) Unfortunately, New Zealand has developed a reputation for distributing multiple resistant worms to the world in exported goats.\(^{12,13}\)

**Guidelines for the control of gastrointestinal nematodes in goats**

Drench strategies:

- Reduce number of drenches given.
- Do not misuse drenches.
  - weigh stock.
  - use correct dose.
  - check volume delivered by drenching equipment.
  - drench correctly.
- Monitor faecal egg counts to determine when drenching is needed.
- Adopt strategies to minimise drench resistance.

Other strategies for controlling worms in goats:

- Ensure goats receive a good diet.
• Ensure trace element intake is adequate.
• Avoid stressing goats.
  - stress increases susceptibility to worms.
• Utilise browse.
  - goats do well on browse and it keeps them away from the infective larvae near soil level.
• Keep pasture long
  - grazing goats on pasture >10 cm long resulted in low FEC and good weight gains. (1)
• Intergraze or alternately graze with other species (except sheep).
  - intergrazing effectively reduces stocking rate so reducing larval challenge.
  - because sheep and goats interchange worms no benefit is gained from intergrazing.
• Provide safer pasture through some of the following:
  - spelling
  - cropping
  - new pasture
  - grazing by other species
• Watch out for the results of research on other forage species that may reduce intake or establishment of worms.

**Lungworms**

Lungworms do not usually constitute a disease problem.

**Tapeworms**

Tapeworms are not regarded as a problem that requires treatment.

**Liver fluke (Fasciola hepatica)**

The liver fluke is discussed in Chapter 19.

**Protozoa**

Four protozoan genera, *Eimeria*, *Sarcocystis*, *Toxoplasma* and *Cryptosporidium* have been reported from goats in New Zealand. Little is
known about the significance of these organisms in goats because few outbreaks of disease have been documented, but extrapolation from other domestic animals would suggest that exposure to these parasites is common, although disease is uncommon. An extensive review of protozoa in domestic animals has been published Charleston, and much of the information here comes from that review.\textsuperscript{(14)}

**Coccidia - Eimeria spp.**

Fifteen species of coccidia have been reported from goats in New Zealand.\textsuperscript{(14)} Coccidia have simple life cycles, adults live in the intestine of the goat and produce oocysts which leave the goat in the faeces. After a period of development on the ground the oocysts become infective to susceptible goats. Disease solely attributable to coccidia is uncommon, but coccidia are likely to contribute to disease in association with other conditions. Between 1990 and 1993 inclusive, the MAF Animal Health Laboratories recorded 434 cases of coccidiosis including 73 in goats, most of which occurred in spring.\textsuperscript{(15)}

**Sarcocystis**

*Sarcocystis* spp. have two host life cycles and are very specific about the identity of their hosts. Little is known about *Sarcocystis* in goats in New Zealand except that a microscopic species (*S. capricanis*) transmitted by dogs has been reported.\textsuperscript{(14)}

**Toxoplasma**

Like *Sarcocystis*, *Toxoplasma* has a two host life cycle. The sexually reproducing stages are found only in members of the cat family, but the asexually reproducing stages can affect every mammal that has been examined and many species of birds with vary degrees of pathogenicity. As with many other mammals, does that become infected when pregnant often abort. Unlike sheep, goats may abort again at a later pregnancy. Serological evidence not surprisingly, indicates that positive titres are common and prevalence increases with age. A vaccine is available to protect ewes, this can be safely administered to goats and may be effective.\textsuperscript{(14)}

**Cryptosporidium**

*Cryptosporidium* has a single host life cycle like *Eimeria*, but is not host
specific. There may be a few species of *Cryptosporidium*, but their host ranges have not been properly determined. It is assumed that most animals, including man, become exposed to *Cryptosporidium* at a young age without significant disease occurring. Clinical disease usually occurs in young animals in the first few weeks of life and may spread rapidly, but it can also affect animals at other times, particularly if they have a compromised immune system. The usual sign is a mayonnaise-like diarrhoea, but other organisms may also be present and contribute to the condition. No effective treatment is known so supportive therapy is usually given.\(^{(14)}\)

**References**


Life cycles and development of nematode parasites of ruminants

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P O Box 84, Lincoln University, Canterbury, New Zealand

Introduction

Nematode parasites create by far the most serious production constraint affecting ruminant animals. To develop effective and sustainable control programmes against these parasites it is necessary to have a good understanding of the life cycle as it occurs both within and outside the host animal and the factors which can influence this.

With a few exceptions, nematodes have a simple direct (no intermediate host) life cycle with sexual reproduction confined to the adult parasitic stage. Each worm in the host has been acquired as an infective larva from ingestion of contaminated pasture and has developed into either a male or female adult nematode inside the body. The females lay eggs which are passed out in the faeces. These eggs develop within the faeces and, when a certain stage of development is reached, larvae which have hatched from the eggs, leave the faecal mass and migrate onto pasture where they may be consumed by the grazing ruminant.(1)

Life cycle

The life cycle of common gastrointestinal (GI) parasites of cattle is shown in Fig. 6.1 and is similar to that of GI parasites in all ruminant animals. The life cycle of the lungworm, *Dictyocaulus viviparus*, is shown in Fig. 6.2. These life cycles comprise a stage within the host and a stage outside the host. Under New Zealand's temperate weather conditions it has been calculated that more than 90% of the total parasite population is present in the life cycle phase outside the host at any one time,(2) Even under the comparatively dry Australian conditions one writer, when discussing an outbreak of

Sustainable control of internal parasites in ruminants
FIG. 6.1: The life cycle of gastrointestinal nematode parasites of sheep. (Reproduced by courtesy of MSD Agvet)

FIG. 6.2: The life cycle of a lungworm. (Reproduced by courtesy of MSD Agvet)
haemonchosis, estimated that sheep harboured only 3% of the parasite population involved in the outbreak.\textsuperscript{(3)} The proportion of the population of parasites which are on pasture will vary at different times of the year. For example the number of larvae on pasture during the dry summer months can be lower than at other times of the year because of high temperatures and desiccation. Use of irrigation or constant summer rain will provide an optimal microclimate which will help to maintain the population size during summer. Whatever the summer conditions are, it is important to realise the significance and size of this pasture reservoir of infective larvae and its effect on the epidemiology of clinical parasitism and that drenches, however efficient they may be, will be acting only on a very small proportion of the total parasite population. Epidemiology is defined here as the study of the dynamic changes which occur both within the host and within the environment. Understanding epidemiology allows us to appreciate the complexity of developing control programmes which work.

**Development of the parasite within the host**

The parasite enters the host as an L\textsubscript{3} larva (3rd larval stage) ingested along with herbage grazed by the animal (see Fig. 6.1). Once within the digestive tract these L\textsubscript{3} larvae exsheath. The stimulus to exsheath normally occurs in the section of the digestive tract anterior to the site of infection. Abomasal parasites normally exsheath in the rumen whereas small intestinal parasites exsheath in the abomasum. This process is responsive to local changes in carbon dioxide (CO\textsubscript{2}) level, temperature and pH.\textsuperscript{(1)}

Exsheathed L\textsubscript{3} larvae move to the preferred site of development for each species, which for *Ostertagia* is the abomasal glands, while others, such as *Cooperia*, become intimately associated with the deep mucosal crypts in the doudenal section of the small intestine. These L\textsubscript{3} larvae moult the outside skin and become L\textsubscript{4} larvae. Within a few days development of L\textsubscript{4} larvae proceeds with increasing size causing loss of function of abomasal glands in the case of *Ostertagia* spp., and intestinal mucosal damage in the case of *Trichostrongylus* spp. Damage to the acid producing cells of the abomasum caused by *Ostertagia* spp. can cause a rise in the pH of abomasal fluid to values which may interfere with the digestion of protein. After about 8 - 10 days the L\textsubscript{4} larvae moult to form immature adults (L\textsubscript{5}) which become sexually
mature over the next 7 - 10 days. Copulation occurs between male and female adults and the female then produces fertile eggs which are passed out in faeces of the host animal.\(^{(4)}\)

### Development of parasites within the external environment

Nematode parasite eggs are passed out in faeces, with the exception of the lungworm, *Dictyocaulus*, where the eggs hatch within the host animal and the early larval forms are passed out in the faeces (see Fig. 6.2). Each female nematode produces large numbers of eggs, contributing to a total which may be counted and expressed as eggs per gram (epg) of faeces. Eggs are small, ovoid and measure approximately 40 \(\mu\)m x 110 \(\mu\)m (1 \(\mu\)m is one millionth of a metre). They develop from the single cell stage after fertilisation and form a small embryonic larva.

Under certain conditions of temperature and moisture the eggs hatch and release the first stage larvae (referred to as L\(_1\) larvae). These actively feed on micro-organisms within the faeces and grow. After a short period of inactivity the larvae moult, shed the old cuticle and become L\(_2\) larvae which again go through a period of active growth and feeding, still within the faeces. [An exception to larval development in the faeces is the case of *Nematodirus* spp. which develop to the L\(_3\) stage within the egg, the L\(_1\) and L\(_2\) stages feeding on material within the egg, which accounts for the large size of this egg.] The L\(_2\) larvae develop into L\(_3\) larvae after a second moult, which is incomplete because L\(_3\) larvae retain the cuticle of the L\(_2\) stage as a protective covering until they enter the host. L\(_3\) larvae do not feed and are extremely resistant to desiccation because of this double skin. At low temperatures, when activity is reduced, these larvae can survive for periods in excess of 12 months. Under adequate moisture levels L\(_3\) larvae migrate from the faeces onto the surrounding pasture and other herbage or into the soil via water films.

### Environmental effects on egg hatching and on free living larvae

The three most important factors influencing egg hatching and the development and survival of nematode larvae are oxygen (O\(_2\)) concentration, moisture
and temperature. Generally worm eggs and L₁ and L₂ larvae require warmth and moisture to develop successfully. The most critical requirement however is that of moisture, as L₁ and L₂ larvae are basically aquatic animals. The conditions required by L₁ and L₂ larvae are different from those required by L₃ larvae. It is important to appreciate that only a small proportion of eggs passed in the faeces (1% to 17%) reach the infective L₃ stage, depending on the prevailing environmental conditions. It is possible that cattle parasites, because of the larger faecal mass, may have greater developmental success.

**Oxygen**

In recent years it has become apparent that oxygen is necessary for the development of eggs, as lack of oxygen inhibits hatching, subsequent larval development and larval activity. In solid cattle dung eggs develop more rapidly closer to the surface, presumably because of lack of air penetration into the centre. As faecal breakdown occurs from weather, insect or microbial action, egg development proceeds as a result of progressive aeration of the dung.

**Moisture**

Because water is essential for the development and maintenance of the free living larvae, these could be described as being aquatic at this stage of their development. The presence of a thin water film where adequate levels of both moisture and oxygen are present favours development of both eggs and larvae. Optimal levels of moisture and oxygen probably occur at different times within the decaying faecal mass, which may account for the different lengths of time over which eggs hatch and larval development occurs. In moist environments, drying out of the faecal mass is prevented and a large proportion of the eggs will develop to the infective larval stage. However in dry periods the surface of the faecal mass can desiccate providing a protective crust which prevents drying out of the interior of the faecal mass and subsequent release of the infective larvae. This situation may continue until water breaks down the crust allowing larval release. Other influences such as irrigation can enhance the ability of larvae to migrate from the faeces and increase their survival time, as well as assisting their migration, either passively or actively throughout the soil.
Temperature

Ambient temperature has a profound influence on egg hatching, larval development and the subsequent survival of the pre-parasitic stages. The influence of constant temperature on egg survival in faeces and larval survival in water for *O. ostertagi* is shown in Table 6.1. Note that these are survival temperatures and not those required for continuous development.

The most important factor arising from this information is that L3 larvae can live for a very long time in the pasture environment. The other point to note is that low temperatures do not kill eggs or larvae immediately. So the arrival of the first frosts of winter do not kill the parasites, as is sometimes thought. All it does is slows down the activity of the preparasitic stages.

TABLE 6.1: Effect of a constant temperature on egg and larval survival of *Ostertagia ostertagi*. (From Reference 12)

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Egg survival</th>
<th>L3 survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>-10 °C</td>
<td>6 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>1 °C</td>
<td>46 weeks</td>
<td>&gt;52 weeks</td>
</tr>
<tr>
<td>4 °C</td>
<td>50 weeks</td>
<td>&gt;52 weeks</td>
</tr>
<tr>
<td>20 °C</td>
<td>nd</td>
<td>42 weeks</td>
</tr>
<tr>
<td>25 °C</td>
<td>nd</td>
<td>30 weeks</td>
</tr>
<tr>
<td>30 °C</td>
<td>nd</td>
<td>18 weeks</td>
</tr>
<tr>
<td>35 °C</td>
<td>nd</td>
<td>10 weeks</td>
</tr>
<tr>
<td>40 °C</td>
<td>24 hours</td>
<td>2 days</td>
</tr>
<tr>
<td>45 °C</td>
<td>12 hours</td>
<td>8 hours</td>
</tr>
<tr>
<td>50 °C</td>
<td>4 hours</td>
<td>1 hour</td>
</tr>
</tbody>
</table>

(nd = not determined)

Laboratory studies under controlled conditions give an indication of the factors affecting development and the longevity of some of the stages but they do not reflect fluctuations, such as diurnal temperature variation, that occur in pasture. Development times of pre-parasitic stages observed in the field are often considerably longer than those predicted on the basis of laboratory
experiments. Therefore models of the population biology of the pre-parasitic stages should be based on field rather than laboratory studies.

Although optimal development occurs between 15°C and 30°C, development will take place at varying rates within the temperature range of 4°C to 35°C providing moisture is present. Eggs of the genera *Haemonchus*, *Trichostrongylus*, *Ostertagia* and *Chabertia* develop to L3 larvae most rapidly at mean monthly air temperatures of 15°C - 24°C. However even at a temperature of 0.6°C and a relative humidity of 76% some parasites reach the L3 stage in 65 days. These larvae can survive for 11 months in the external environment under suitable climatic conditions. In summer months larvae which had emerged from faeces were destroyed in 2 - 4 months as a result of higher air temperatures and lower relative humidity. In very dry summers larvae may develop successfully to the infective stage in faeces, but some do not emerge until moisture levels are optimal even though infected faeces continue to be passed by the host, so that when moisture is available, pasture contamination by larvae can rise to a very high level.

It is important to realise that eggs and larvae of most species of gastrointestinal parasites of sheep (with the exception of *Haemonchus contortus*) will tolerate cold temperatures even though their metabolic rate is reduced. For some species such as *Ostertagia* and *Trichostrongylus*, development is possible in mild winter conditions. Average air temperatures during the winter months in Canterbury, New Zealand for example are between 5.8°C and 7.6°C so that considerable egg hatching and larval development does occur during this season. One further important factor in maintaining this optimal larval environment in both the summer and winter periods is the mass of the dung. It is thought that a soft unpelleted mass of faeces would provide a more protected environment than the small pellets.

**Pasture larval levels**

Faeces on pasture are a substantial reservoir of infective larvae. The number of L3 larvae on pasture is determined by their rate of release from the faecal reservoir and by the relative growth of pasture. Levels of infective larvae on pasture must be expressed as a concentration, or as number of larvae per kilogram of pasture. This can range from 0 to 30,000 larvae per kilogram of pasture.
pasture and intakes of over 2000 larvae per day can adversely affect sheep. These values can be influenced by the rate at which pasture grows. Rapid pasture growth will tend to reduce larval concentrations because of a dilution effect. In late autumn and winter, as pasture growth slows down, the rate of release of the remaining larvae is increased as a result of faecal breakdown and greater moisture. It has been reported that larvae can reach their highest levels in winter in the United Kingdom and New Zealand for both sheep and cattle pastures. A very high proportion of these larvae successfully overwinter and contribute substantially to the larval population recorded on pasture in the following spring.

**Larval migration**

Migration of L₃ larvae from faeces can be either active or passive. Active larval migration is dependant on the available water film. This film is dependant on water being available from rain, dew or irrigation. The movement of L₃ larvae from the faeces has been found to occur in waves, coinciding with the presence of water. In the case of rain a fall in the order of 25 - 50 mm is usually required for such migration. Larvae generally are not found any further than 30 cm in a horizontal direction from the faecal mass and their concentration decreases as the distance from the faeces increases (Fig. 6.3).

Vertical migration of L₃ larvae occurs up plant material but the majority of larvae (50%) are found in the first 2 cm of the plant or in the first 1 cm of the soil (see Fig. 6.4). Increasing numbers of larvae in the upper sward component occur in conditions of high humidity and temperature but this can

**FIG. 6.3:** The migration pattern of infective nematode larvae from faeces onto pasture. (From Reference 6)
The vertical distribution of infective nematode larvae on herbage. (From Reference 6)

vary with plant species.\(^{(5, 6)}\) L₃ larvae are also capable of downward movement. It has been suggested that sunlight may also play some part in the active migration of larva.

Passive transport of L₃ larvae away from the faecal mass has been caused by rain drops creating a splash effect and this may be a decisive factor in the movement of cattle *Cooperia* and *Ostertagia* larvae. Larvae have been measured up to 90 cm horizontally and 30 cm vertically from the faecal mass after simulated rain.\(^{(5)}\) A certain amount of transmission may be performed by insects, earthworms, birds or fungi although the earthworms may be more important as a factor in the destruction of L₃ larvae.\(^{(5)}\)

**Removal of larvae**

Larvae die when climatic conditions are unfavourable and they can be removed from the pasture population by active means. One important consideration is the rate of removal of the larvae from pasture by the various classes of livestock. If larvae are not specific to the animal species or the animal has a high degree of natural resistance larvae may not reproduce or even establish. Such animals may used as ‘vacuum cleaners’ to remove larvae from pastures.

*Sustainable control of internal parasites in ruminants* 75
Dry matter requirements of animals at various stages of their growth and reproductive cycle change considerably and this will influence the number of larvae removed from the pasture at any particular time and it will influence the size of the parasite challenge to susceptible animals. This is shown in Table 6.2. It can be seen that levels of between 800 and 2000 larvae/kg of fresh herbage can result in intakes well in excess of 2000 larvae per day.

**Sources of contamination**

It has been known for many years that both mature and immature animals can act as sources of contamination for the young. In New Zealand several authors\(^{2,18,19}\) have mentioned the danger of underestimating the contribution of the ewe by ignoring the volume of faecal material (see Table 6.3) and concentrating solely on eggs per gram. A ewe with an egg count equal to only 30% of a weaned lamb's egg count will be an equivalent source of pasture contamination. Another way of looking at the problem is to calculate that 2000 ewes producing 2 kg of faeces per day with a mean worm egg count of 250 eggs per gram pass 1 billion eggs onto the pasture each day. An estimation of the daily faecal egg output of various classes of livestock can be calculated by multiplying the daily faecal output by the number of eggs per gram.

From this table it can be seen that, in the spring/summer period, a ewe with a faecal egg count of 338 epg is capable of producing of 1 million eggs in a 24 hour period. If we estimate that about 6% of these eggs will reach the L₃ larval stage, then there is potentially 60,000 infective larvae from each ewe.

**TABLE 6.2:** Theoretical relationship between light, moderate and heavy herbage contamination (larvae/kg fresh herbage) and daily larval intake in fully fed sheep in the spring (assuming pasture 20% dry matter)

<table>
<thead>
<tr>
<th>Category</th>
<th>Dry matter intake (kg/day)</th>
<th>Larval contamination (larvae/kg fresh herbage)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>200 (low)</td>
</tr>
<tr>
<td>lactating ewe</td>
<td>2.7</td>
<td>2700</td>
</tr>
<tr>
<td>12 month old sheep</td>
<td>1.6</td>
<td>1600</td>
</tr>
<tr>
<td>unweaned lambs</td>
<td>0.8</td>
<td>800</td>
</tr>
</tbody>
</table>

_Familton & McAnulty: Life cycles of nematodes_
TABLE 6.3: Faecal output (mean wet weight for each 4 month period, g/day) of sheep throughout a year.

<table>
<thead>
<tr>
<th>Period</th>
<th>Spring/Summer</th>
<th>Summer/Autumn</th>
<th>Autumn/Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean fresh faeces lambs</td>
<td>870</td>
<td>2000</td>
<td>1900</td>
</tr>
<tr>
<td>output hoggets/2 teeth</td>
<td>1700</td>
<td>1500</td>
<td>1700</td>
</tr>
<tr>
<td>(grams/day) ewes</td>
<td>2960</td>
<td>1750</td>
<td>1800</td>
</tr>
</tbody>
</table>

in a 24 hour period. The biotic potential of these parasites is quite staggering, but then - Why should we be surprised? They have been around for a long time and have resisted our efforts so far to tame them. Perhaps there is much to be gained if we understand better the free-living phase of these parasites. Then we might know what we are dealing with.

**Conclusion**

Any attempt to achieve sustainable parasite control must involve a good understanding of the epidemiology and life cycles of the parasites concerned. In the development of control programmes we must take the following points into consideration.

- Considerable development of eggs and larvae occur over the winter months (i.e. May, June and July) and these augment the larval reservoir already present on pasture which has overwintered from the previous autumn.
- Administration of anthelmintic has no effect on the parasite reservoir outside the host animal and that this is a very large component of the total parasite population.
- The temperature within the faecal mass does not equate with the ambient air temperature. During winter months the faecal environment is much more conducive to parasite development than previously thought and considerable development occurs, albeit if it is slightly delayed and possibly occurring at lower percentage development rates.
- During autumn and winter adult ewes on an all-grass grazing system make considerable contributions to the infectivity of pasture, particularly under
intensive rotational grazing systems even when the faecal egg output is considered to be low.

- Under New Zealand conditions, the highest levels of infective larvae on pasture are consistently found during the winter months and larval challenge to ewes on an all-grass diet can be as high as 30,000 larvae per day.

Despite the vast array of knowledge of the pre-parasitic stages of GI parasites of sheep, it would be a mistake to assume that we have all the answers to deal with outbreaks of infection, particularly when we are faced with control programme breakdowns. There is still a lot of basic research to be done if parasite control programmes in the future are to be based on sound epidemiological evidence. All of New Zealand may be regarded as a temperate climatic zone but it is essential to recognise that large differences in climatic factors which affect parasite development occur between districts and between the microclimatic zones which can occur within a farm. Parasite control programmes, therefore, must be based on sound understanding of the specific environmental conditions prevailing at each site.

References


Effects of nematode parasitism on ruminant animal performance

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Introduction

Gastrointestinal nematode parasitism is probably the major disease syndrome of pastoral ruminants simply because environments which favour pastoralism also favour the free living stages of helminth parasites. The resulting host-parasite association is not cost-free to the host, though the best adapted parasite is one which can maintain its life cycle with minimum disturbance to the host. Historically, this host-parasite relationship was probably established under circumstances in which the ability of the wild host to roam relatively freely - largely determined by availability of feed - limited its exposure to nematode larvae. The intensive pastoralism developed during recent centuries has changed this balance to the point at which the rate and level of exposure tests the ability of the host to adapt at minimum cost. This adaptation is recognised in the failure of the host to meet target productivity based on assessment of its genetic potential and nutrient supply.

Effects on production

Host-parasite interactions

The time course of the association between the host and a common parasite of sheep in temperate pastoral systems is illustrated in Fig. 7.1. Naive lambs were infected daily for 34 weeks with 2500 larvae of *Trichostrongylus colubriformis*. The typical rapid rise in nematode eggs in faeces during the period 2-8 weeks after commencement of infection was observed indicating a period of establishment of a mature worm population. The subsequent rise in eosinophil count is indicative of developing immunity at the height of which numbers of nematode eggs in faeces were falling rapidly. Loss of weight gain
FIG. 7.1: Typical pattern of response of naive lambs to gastrointestinal nematode infection. (From (26), reproduced by permission of Commonwealth Agricultural Bureau.)

was most closely associated with the period of rise in eosinophil count. From about 14 weeks after infection commenced numbers of eosinophils began to fall and growth rate returned to normal, despite continuing exposure to nematode larvae.

**Limiting the impact of parasitism**

The levels of exposure used in this work (viz. Fig. 7.1) were carefully chosen to produce a stable nutritional situation, that is a larval challenge which the host could withstand without catastrophic pathophysiological consequences, an extreme example of which is death of the host. As a generalisation the outcome of exposure to nematode parasite larvae, in terms of change in animal performance, is the resultant of at least five basic factors:

- the severity and composition (nematode species) of the parasite challenge,
- the effectiveness of the host immune response,
• the duration of exposure, reflecting time period for development of an effective immune response,
• the effect on metabolism of the susceptible host and
• the metabolic cost of a competent immune response under continuous challenge.

Two basic approaches have been used to quantify production loss due to parasites; firstly the use of controlled rates of infection in the laboratory in comparison with isolated and unaffected controls; secondly, the production of control animals in natural infections by regular administration of anthelmintic to a proportion of the herd or flock. Both approaches have limitations. Indoor trials still beg the questions 'What is a typical size and pattern of field infection?' and 'Was the opportunity for normal development of immunity allowed?' In natural infections, controlled by anthelmintic, larval challenge has rarely been measured due to technical difficulties. Moreover, poor trial design has often not allowed estimation of the full impact of parasitism. Two benefits of anthelmintic therapy must be recognised: firstly, the benefit to the treated animal from immediate removal of an established worm burden and secondly, the future benefit to the flock or herd from the ensuing reduction in egg production and therefore larval contamination of the environment. The importance of limiting larval intake, as opposed to removing a mature worm population from a host has been demonstrated by Coop et al. (2) who found that even a very frequent use of anthelmintic (every 17 days) which prevented establishment of mature egg-laying worms restored only 30% of the loss of growth caused by continuous exposure to larvae of Ostertagia (Teladorsagia) circumcincta (Fig. 7.2). The implications of this are that even the early larval stages of O. circumcincta cause major damage to the host. While this may not apply to the same degree with other nematode parasites which may have a less intimate association with host tissue (3rd stage larvae of O. circumcincta burrow into the gastric glands), this has yet to be tested. The typical farm situation is one in which animals are treated intermittently with anthelmintic while exposed to continuous larval intake, as simulated in this trial. Moreover, farm scale trials (3) in which lambs were allocated to clean or dirty pasture and, within both pasture types, groups of animals were run in self contained mobs which were drenched at either 3, 6 or 9 week intervals, have similarly shown the importance of removing larval challenge to – rather
FIG. 7.2: Effect of increasing intake of *O. circumcincta* larvae and frequent anthelmintic therapy on growth of lambs. (★ - control, uninfected; ▲ - 1000 larvae/day; ■ - 3000 larvae/day; ● - 5000 larvae/day; ○ - 5000 larvae/day plus anthelmintic every 21 days. From (2), reprinted by permission of Cambridge University Press.)

![Graph showing growth of lambs with different larval intakes and anthelmintic treatments.](image)

TABLE 7.1: Effect of clean or contaminated pasture and frequency of use of anthelmintic on weight gain (g/day) of lambs in the 3-4 months after weaning (n=80/group). Data from (3).

<table>
<thead>
<tr>
<th>Pasture type</th>
<th>Frequency of drench (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Trial one:</td>
<td></td>
</tr>
<tr>
<td>clean</td>
<td>151</td>
</tr>
<tr>
<td>contaminated</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial two:</td>
<td></td>
</tr>
<tr>
<td>clean</td>
<td>146</td>
</tr>
<tr>
<td>contaminated</td>
<td>104</td>
</tr>
</tbody>
</table>

84

*Sykes: Animal performance & parasitism*
than limiting worm population in - the host (Table 7.1). Brunsdon and Vlassoff\(^4\) used the approach of contaminating pasture artificially using ‘seed’ animals and were able to demonstrate 35% and 15% reductions in weight gain and wool production, respectively, in lambs as a result of pasture contamination with fewer than 200 larvae/kg fresh herbage. As a consequence of such trials and indoor trials it is possible to conclude that intakes of 2000-3000 larvae/day of the major nematode parasites (*O. circumcincta, T. colubriformis/vitrinus*) can be accommodated in weaned lambs at the cost of a 40% loss in productivity until immune competence is established. **Importantly,** such animals do not necessarily show any clinical symptoms of disease.

**Resistant sheep**

The effect of continuing larval intake in the immune-competent sheep has not been well researched and such information as does exist is conflicting. Barger and Southcott\(^5\) reported that resistant sheep, as judged by lack of egg count when infected with *T. colubriformis*, still suffered reduction in wool growth by 11 to 18% and appeared to have depressed live-weight gain. On the other hand Kimambo *et al.*\(^6\) were unable to detect an effect of infection with *T. colubriformis* on nutrient utilization or performance in ‘resistant’ lambs. Similar findings - lack of effect on feed intake, weight gain, wool production or lamb birth weight - have been observed during mid-pregnancy in sheep\(^7\) ‘resistant’ to challenge with 4000 larvae/day *O. circumcincta*, as judged, again, by lack of eggs in faeces. However, resistance is lost during late pregnancy and early lactation, and early lactational body weight loss may increase from 1-2 kg to as much as 5-6 kg, lactation yield be reduced by 20%, and wool growth and staple strength can be reduced by 20%\(^7\) by typical rates of infection. This ‘window of susceptibility’ appears to last for about 6 weeks around parturition before resistance is again established.\(^8\)

**Cattle**

Losses in cattle from nematode parasitism are even less well quantified. Evidence suggests that cattle are more resistant to parasites than sheep. However, field studies in which anthelmintics have been used to provide ‘controls’ have provided 20-65% improvements in live-weight gain\(^9, 10\) and infections picked up during summer grazing have caused reductions of
60-400g/day in growth rate when animals were subsequently housed. Type II ostertagiasis, in which inhibited fourth stage larvae simultaneously develop during late winter can cause death without previous clinical symptoms of disease.

It is more difficult to judge the effect of parasitism in lactating cattle. Generally, responses to anthelmintic, where obtained, have been found in higher yielding cows in the herd. However, most studies have examined the effect of dry cow therapy on subsequent milk production because of the problems of withholding periods for anthelmintics in milk. Such studies have shown only 1-2% improvement in performance or none at all. As with sheep the need to consider the importance of ongoing larval intake was raised by the finding of greatest response to treatment in herds in which cows were overwintered on areas previously grazed by calves subjected to minimum parasite control measures. This has not been effectively tested.

Other production costs

In production systems losses are not necessarily confined to the animal 'affected' by parasitism. Thus, the need to retain young stock on a property for a longer period than planned to meet market requirements, because of reduced growth rate caused by infection, has the effect of diverting available forage to that category of animal at the expense of another. Thus, for example, opportunity may be lost to promote weight gain in ewes prior to mating which is likely to reduce the number of lambs available for sale in the subsequent year.

Pathophysiology

Intake

A common feature of the infection of a susceptible animal with nematode parasites is reduction in feed intake and there is evidence this is centrally (brain) mediated. This reduction can range from 16-20% in chronic subclinical infections to complete inappetence if the animal is overwhelmed before resistance can develop. As a consequence efficiency of use of metabolisable energy (ME) is reduced because a larger proportion of energy intake has to be used for maintenance.
**Feed digestion**

The evidence that feed digestion is impaired is equivocal. Most studies have found no or only small (<2%) reductions in feed energy digestion\(^{20,21}\) though another study\(^{22}\) did record larger effects.

There is unanimity of view, however, that infection induces protein deficiency, not because ability to absorb protein is necessarily impaired\(^{23,24}\) but because of damage to the alimentary tract which increases (a) losses of serum proteins,\(^{25,26}\) (b) sloughing of epithelial cells and (c) mucus secretion\(^{23}\) into the alimentary tract. The alimentary tract, accounts for about 5% of total body protein and contributes 25-45% of body protein synthesis.\(^{27}\) This compares with muscle which, though making up 45% of body protein mass, accounts for only about 20% of body protein synthesis. Thus the damage which occurs to the alimentary tract as a result of infection\(^{29}\) appears to cause major stimulation of body protein synthesis and therefore ME requirement for maintenance. Indeed, evidence from guinea pigs\(^{30}\) suggests that infection in one site may stimulate protein turnover in the whole alimentary tract. Not only is protein which is lost into the tract reabsorbed with less than 100% efficiency - estimates suggest that 70%-85% is reabsorbed\(^{23,24}\) - but the additional protein synthesis has an energetic cost.\(^{31}\)

The consequence is a shift in protein synthesis away from the carcase (muscle and bone) and towards the liver and alimentary tract (Fig. 7.3). This causes a reduction in efficiency of ME utilization for growth (Fig. 7.4). We have little information on changes in specific amino acid metabolism though these are anticipated both as a consequence of change in gastrointestinal secretions and the immune response, both of which are considered likely to increase requirement for sulphur-amino acids.\(^{26}\)

**Mineral metabolism**

Bone growth is reduced in infection and prolonged infection can result in osteoporosis.\(^{32,33}\) A general effect is a matrix osteoporosis probably as a consequence of diversion of amino acids away from bone and muscle to the alimentary tract. In addition, however, absorption of phosphorus is impaired in infection of the proximal small intestine,\(^{34}\) resulting in hypophosphataemia and bone mineral osteoporosis,\(^{32}\) and as a consequence slower skeletal growth.
FIG. 7.3: Effect of infection by nematode parasites on the distribution of protein synthesis in the body. (□ - controls fed *ad libitum*; ■ - infected animals; □ - controls restricted to the feed intake of infected animals. Adapted from the data of (26) and (37).)

<table>
<thead>
<tr>
<th>Tissue/Junction</th>
<th>Controls</th>
<th>Infected</th>
<th>Restricted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body</td>
<td>100</td>
<td>110</td>
<td>90</td>
</tr>
<tr>
<td>Liver</td>
<td>90</td>
<td>110</td>
<td>80</td>
</tr>
<tr>
<td>Stomach &amp; small intestine</td>
<td>70</td>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>Caecum &amp; large intestine</td>
<td>80</td>
<td>110</td>
<td>70</td>
</tr>
<tr>
<td>Muscle &amp; bone</td>
<td>60</td>
<td>80</td>
<td>50</td>
</tr>
</tbody>
</table>

FIG. 7.4: Reduction in energy retention and efficiency of energy use due to parasitism may occur as a result of reduction in efficiency of use of metabolisable energy (A), reduction in food intake (C) or a combination of the two (B).

Evidence for effects on trace element metabolism is less clear, though copper absorption from therapeutic copper oxide wire particles is reduced in animals in which abomasal pH has been elevated by infection in that organ. Infection
with haematophagic parasites, such as *Haemonchus contortus* will result in anaemia\(^{36}\) but the evidence for effect on trace element metabolism or effect of trace element status on the pathogenesis of infection, though suspected on the basis of clinical experience, is still anecdotal and needs to be clearly established.

**References**


*Sustainable control of internal parasites in ruminants* 89


Sykes: Animal performance & parasitism
The diagnosis of gastrointestinal nematode parasitism in ruminants and investigating anthelmintic resistance

P B McKenna

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Introduction

The general effects that gastrointestinal nematode infections have on the productivity of grazing ruminants are widely recognised and on most farms steps are taken to control them. Anthelmintic treatment is the most commonly employed control procedure and currently New Zealand sheep and cattle farmers are spending about NZ$59 million annually on drenches.\(^{(1,2)}\)

In temperate climate countries such as New Zealand, grazing ruminants are rarely free of worm infection but their effects on stock health and productivity may vary widely. At one extreme animals may die and represent a total economic loss. At the other extreme the effects may be so slight that they can not be detected. Between these there may be a gradation of production penalties involving reductions in weight gain, milk production and wool growth.\(^{(3,4}\text{ and see Chapter 7})\)

The degree of damage inflicted by gastrointestinal nematode burdens is influenced to a large extent by the numbers and species of parasites present although this may be modified by several host factors including age, immunity, general health and nutrition. The diagnosis of gastrointestinal parasitism, therefore, is essentially concerned with identifying and measuring the levels of parasitic infection and then interpreting these in relation to the history and management of the stock and the presence or absence of such clinical signs as illthrift, diarrhoea and anaemia. However, because the subclinical effects of parasitic infection may be equal to or even of greater importance than clinical disease,\(^{(5,6)}\) it is probably fair to say that deciding when treatment to
remove worm burdens is warranted is considerably easier than deciding when it is not.

There are a number of laboratory tests available to assist veterinary practitioners in the diagnosis of gastro-intestinal parasitism in ruminants. All have their limitations and none should be considered as capable of providing a definitive diagnosis on their own. Rather such tests should be looked on merely as aids to help in the achievement of this objective.

Aids to the diagnosis of gastrointestinal nematode parasitism

**Worm counts**

Postmortem worm counts are an obvious means of determining the numbers and identities of gastrointestinal worm burdens in grazing ruminants. However, because the level and composition of infection may vary considerably between individuals, worm counts need to be performed on several animals in order to obtain meaningful information on the parasite status of the flock or herd as a whole.(7) In cattle, and probably deer also,(8, 9, 10) such counts should be accompanied by digestion or prolonged saline/water soaking of the abomasal mucosa,(11, 12) particularly in animals beyond their first year of life. These procedures are not only required to provide an indication of the numbers of early fourth stage *Ostertagia* larvae present - important for the differential diagnosis of Type I and Type II ostertagiosis - but also to provide an accurate measure of burdens of *Trichostrongylus axei*, many of which remain adhering to the mucosa following washing.(15) In addition, differentiation of *Ostertagia* burdens into adult, late fourth and early fourth stage larvae may enable estimates of larval intake to be made while examination of the condition and degree of development of adult female worms may permit assessment of the animals acquired resistance to infection.(14) In sheep, the routine use of abomasal digest procedures is not necessary as most of the abomasal parasites in these hosts are recovered during washing, especially where some autolysis of the mucosa has occurred.(15) A similar situation is likely to apply to goats also.
Faecal egg counts

The faecal egg count (FEC) technique, is the most widely used of a number of ante-mortem aids available for the diagnosis of gastrointestinal parasitism in ruminants. In many respects faecal egg counting is an ideal procedure for determining the worm burdens of groups of animals. It is comparatively cheap and easily performed enabling a large number of samples to be processed in a relatively short space of time. As a result, it has the potential to provide a better parasite profile of groups of animals than does the worm count procedure.

The rationale behind the use of FEC is based on the assumption that there is a good relationship between the number of worm eggs in faeces and the number of worms in the host. Although this has generally been shown to be true of mixed gastrointestinal nematode burdens of sheep and goat, FECs are usually considered to be of less diagnostic value in cattle. In Ostertagia infections in calves, for example, FECs are frequently depicted as following a stereotypical course and, due to the effects of host immunity on worm ovulation, to have little diagnostic value except when they deviate from the expected pattern. While much has been made of this stereotypical decrease in Ostertagia egg production and the limitations it imposes on the interpretation of FECs in cattle, some believe that its importance has been greatly overstated. It has been pointed out, for instance, that Ostertagia infections rarely occur on their own and that egg production in Cooperia and Trichostrongylus may not be affected by host immunity to the same degree. Consequently, in mixed infections, FECs may still provide useful guidelines regarding herd parasite status even though they may not necessarily be directly representative of the primary genus involved. Some support for this point of view may be provided by an examination of trial data in New Zealand which tends to indicate that, for their first 6-8 months of life, differences in the degree of parasite control achieved in groups of July/September born dairy calves may be reflected by their mean FECs. Undoubtedly FECs in older cattle are frequently unreliable with high worm burdens often being associated with low egg counts. Nevertheless, even in these hosts FECs may, in some instances, still have some diagnostic value. High egg counts in older cattle, for example, may indicate a breakdown in host immunity and a possible outbreak of parasitic disease.
Less is known about the relationship between FECs and worm counts in deer than cattle. Usually FECs in deer are low,$^{(8, 26)}$ probably because, unlike lungworm infection, gastrointestinal parasitism is rarely a problem in these hosts.$^{(27 \text{ and see Chapter } 4)}$

In sheep and goats a good correlation between egg and worm counts, particularly in animals in their first year of life,$^{(16, 18)}$ has led to their widespread adoption in New Zealand for a variety of diagnostic and other purposes including monitoring the effectiveness of worm control programmes and as aids to drench decision-making. For these and for other objectives, faecal samples are usually collected from 10 to 15 representative members of a flock and egg counts performed on each sample.$^{(28)}$ In some cases, these individual counts may then be summed and divided by the number of samples examined to provide an arithmetic mean count. In cases where such group mean counts only are required, a quicker and cheaper procedure may be to utilise a composite faecal egg count technique. Using this procedure, individual faecal samples from a group of animals are pooled and a single egg count carried out to provide a mean egg count for the group. Although such composite counts have been little used in New Zealand, they are currently being employed for various purposes by some laboratories in Australia.$^{(29, 30)}$

The composite FEC technique may not be suitable for all of the purposes that traditional FECs are currently used for. Information regarding mean egg counts only is, for example, unlikely to be appropriate for use in faecal egg count reduction (FECR) tests where information about individual animal counts may be of considerable relevance to their correct interpretation. Group mean counts may not always be as good as individual counts in helping to identify the causes of scouring or illthrift either, particularly if *Nematodirus* is heavily involved. *Nematodirus* is a poor egg producer and information regarding mean egg count levels for this parasite may, therefore, be of less relevance than that relating to the numbers or proportions of animals passing these eggs.$^{(31)}$

Where group mean counts, and accordingly composite FECs, may be more usefully employed are in the areas of parasite monitoring, in determining if parasite infections are of sufficient magnitude for anthelmintic resistance testing purposes and where FEC levels are being used as aids to drench decision-
making. In the latter case, this is especially likely to be true in those instances where drenching is being based on a mean FEC 'trigger-level' concept.

Regardless of what counting procedure is adopted, an obvious apparent deficiency of FECs is that they provide little information on the identity of the worm genera represented. This problem can, of course, be readily overcome by the use of faecal larval cultures in conjunction with FECs. However, since treatment to remove mixed gastrointestinal nematode infections in grazing ruminants usually involves the use of broad-spectrum anthelmintics, the utilisation of larval cultures for routine diagnostic purposes may be of limited value.

**Biochemical and other aids**

Perceived limitations in the reliability of FECs, particularly as an aid for the diagnosis of ostertagiosis in older cattle, has resulted in a search for alternative laboratory tests. Amongst these are such clinical biochemical procedures as plasma pepsinogens, serum gastrin, serum albumin and serum fructosamine determinations, measurements of abomasal pH\(^{(32, 33, 34, 35, 36, 37, 38)}\) and, more recently, immunodiagnostic methods like faecal antigen assays.\(^{(39, 40)}\) Like FECs all of these tests are aimed at providing an indirect measure of parasitism but it is probably fair to say that none have so far completely fulfilled their original promises as quantitative diagnostic aids.\(^{(23)}\) As well, many are primarily directed at providing an indication of abomasal worm burdens and, because of this, tend to have greater applicability to the diagnosis of gastrointestinal parasitism in cattle than other ruminants since the most important worm species are more inclined to be restricted to this organ in cattle.\(^{(18, 41)}\) A possible exception to this generalisation may be the use of serum fructosamine concentrations for the diagnosis of both abomasal and small intestinal parasitism in sheep,\(^{(38)}\) although the value of this assay in field infections remains to be proved.

The use of pepsinogen determinations as an aid to the diagnosis of bovine ostertagiosis is the most well established of these procedures. In New Zealand, a plasma pepsinogen level of about 2.6 iu/l in calves has been found to be indicative of total abomasal worm burdens of above 30,000.\(^{(19, 24)}\) Summarising British findings, Armour\(^{(42)}\) concluded that plasma pepsinogen levels in excess of 3 iu/l are usually associated with severe clinical ostertagiasis in calves in that country and that levels of between 2 and 3 iu/l may be present in an
outbreak or after recovery. Regardless of what level is accepted as being ‘significant’ in cattle, however, plasma pepsinogens should be interpreted in relation to age and clinical condition of the animals and the quality of nutrition available. In addition, the use of serum gastrin and serum albumin levels in conjunction with plasma pepsinogens may also enhance the diagnostic reliability of this procedure. Together with increased pepsinogen levels, serum albumin levels of $<30$ g/l or group mean gastrin levels of $>1000$ pg/ml have, for instance, been suggested as useful diagnostic indicators of clinical parasitism with group mean gastrin concentrations of $400$ pg/ml being indicative of subclinical cases.

The detection of anthelmintic resistance

While the previously discussed laboratory aids are primarily concerned with determining whether or not parasite burdens warrant anthelmintic treatment, tests for the detection of anthelmintic resistance are more concerned with identifying which anthelmintics are still likely to be effective against them.

There are a number of in vitro and in vivo procedures available for the detection of anthelmintic resistance. However, apart from the FECR test and a recently introduced commercially available larval development assay (DrenchRite™), many of these procedures remain more appropriate for research and experimental purposes rather than as tools for evaluating anthelmintic performance in the field.

**DrenchRite™ larval development assay**

The DrenchRite™ assay was developed at CSIRO’s McMaster Laboratory (Australia) and has now been made available commercially by Horizon Technology Pty Limited. The obvious advantage of this test over that of the FECR procedure is that it involves only a single collection of faecal samples and can be conducted on any occasion (providing the mean faecal egg count is greater than $100$ eggs/g). It does not require the treatment of animals before testing, their sorting into treatment groups or the collection of both pre- and post-treatment samples. However, while the DrenchRite™ assay greatly reduces the time and complexity of the field component of the test, it vastly increases the laboratory time and expertise required to perform it and it is unlikely, therefore, to be any cheaper than the FECR test.
The assay works by exposing worm eggs isolated from sheep faeces to a range of concentrations of different anthelmintics on a single microtitre plate and then determining the point where 50% of them are blocked from developing to the third larval stage. For benzimidazole, levamisole and benzimidazole-levamisole combinations, this point can then be used to provide estimates of the likely efficacy of these drenches. However, such efficacies can be determined only for *Haemonchus contortus*, *Ostertagia (Teladorsagia) circumcincta* and *Trichostrongylus colubriformis*. The assay cannot be used for the detection of resistance in other gastrointestinal parasites commonly present in New Zealand sheep such as *Cooperia*, *Oesophagostomum/Chabertia, Nematodirus* or other species of *Trichostrongylus*, nor to quantify the efficacy of the milbemycin/avermectins against any nematode genus. Although a number of these latter genera may be considered to be of comparatively minor importance, *Nematodirus*, a parasite commonly associated with benzimidazole resistance in New Zealand sheep,\(^{(45)}\) certainly can not. Moreover, the regular presence of strongylid worm eggs other than *Haemonchus, Ostertagia* and *Trichostrongylus* in faecal samples in sheep in New Zealand\(^{(46)}\) is not only likely to complicate considerably interpretation of the assay but also, as a result of their consequent reduced proportionate representation, possibly compromise the reliability of the test for these latter genera as well.

**Faecal egg count reduction test**

Like the larval development assay, the FECR test is primarily aimed at providing an indirect measure of anthelmintic efficacy against adult worms in the host. It is capable of detecting resistance to any anthelmintic type in all gastrointestinal nematode genera in virtually all grazing ruminants. In this test, the post-treatment egg counts of a group of anthelmintic-treated animals are compared with those that were recorded at the time of treatment or with those of an untreated control group sampled at the same time after treatment. In this test, a less than 95% reduction in FEC is usually taken as an indication of the presence of resistance in sheep nematodes\(^{(47)}\) and a similar FECR is likely to be relevant to those in other hosts.

An important consideration in the correct interpretation of the FECR test, and one that has been the subject of some confusion, is the appropriate interval
between anthelmintic administration and post-treatment sampling. In New Zealand, the current recommendation is for post-treatment samples to be taken 5-10 days after administration of anthelmintic. Some authors have suggested that a 10 to 14 or even a 21 day post-treatment sampling interval may be more appropriate. The rationale for these latter proposals is based on the possibility that a temporary suppression of egg production of 10 or more days duration may occur in worms surviving anthelmintic treatment. If correct, this could mean that adoption of a 5-10 day post-treatment sampling interval might result in falsely-high FECR values with some cases of resistance being overlooked.

Evidence relating to the phenomenon of anthelmintic treatment and the suppression of egg production in gastrointestinal nematodes of sheep and cattle has been reviewed recently. The results of this review suggest that if a temporary suppression of egg production does occur in sheep nematodes following anthelmintic treatment, then such effects are unlikely to be of much practical significance and that little benefit would be derived from extending the currently recommended 5-10 day post-treatment sampling interval in the FECR test to 10-14 days. Indeed, other evidence now indicates that any such extension is likely to carry with it the very real possibility of producing false positive results, particularly where the testing of anthelmintics with limited effectiveness against developing immature stages is involved.

In cattle, the relationship between post-treatment sampling interval and the reliability of the FECR test was less readily obvious than it was in sheep. Almost all of the cattle FECR cases reviewed involved infections of Cooperia spp. and largely entailed the testing of milbemycin/avermectin-type anthelmintics with residual activities of >99% against this parasite which persist for 7 to 14 days. Because resistance to persistent anthelmintics may be expressed either as a diminished ability to remove worms present at the time of treatment or as a reduction in residual activity, the interval between drench administration and post-treatment sampling is obviously less critical for FECR testing purposes than that which may be required for non-persistent anthelmintics. Indeed, there is no reason in such cases why the post-treatment interval could not be safely extended to one which more closely approximates to that which combines both the parasite's minimum pre-patent period and the duration of the anthelmintic's persistent activity against it. Thus, within
this aggregated interval, it is largely immaterial whether or not those eggs in
the faeces of treated animals originated from surviving adult worms that were
present at the time of treatment or from infective larvae acquired since then.
In either case, post-treatment egg counts should normally be low during this
period and the failure to reduce these to levels that are at least 95% less than
those that were present at the time of treatment would provide evidence of
anthelmintic resistance.

In the aforementioned study,\(^{(53)}\) it was found that the % FECR at 5-8 days
post-treatment exceeded that recorded at 11-14 days in 10 of 12 cattle cases
reviewed. On average, this difference was 21.7% over all 12 cases. The results
of this analysis also showed that resistance to milbemycin/avermectin-type
anthelmintics would have been overlooked on three out of eight occasions if
the shorter post-treatment interval had been used. These results suggest,
therefore, that when testing for resistance to these types of anthelmintics in
cattle, adoption of the longer post-treatment interval might be advisable.
Certainly little is likely to be lost by this practice. If this approach is adopted,
however, it should only be used for those anthelmintics with a known persistent
effect against gastrointestinal nematode genera in this host. It also needs to
be recognised that, even for these anthelmintics, the period of protection
afforded by them may vary according to both the formulation and the parasite
involved.\(^{(57)}\) Moreover, because of this and because of differences in the
occurrences of the various gastrointestinal nematode genera which may
contribute to faecal egg counts in cattle during FECR testing, the use of larval
cultures which would enable egg count reductions to be calculated for each
individual genus, may also be required.

Like most diagnostic techniques the FECR test has its limitations and its
inability to detect reliably low levels of anthelmintic resistance in particular, is
well known.\(^{(48,58)}\) However the results of recent studies in sheep\(^{(46,59)}\) indicate
that the associated use of larval cultures could considerably enhance both the
sensitivity and the diagnostic reliability of the procedure. In summary, the
findings of these studies suggest that larval cultures should always be
performed on pre-treatment samples, thereby enabling the numbers and
identities of those worm genera that are adequately represented for testing
purposes to be determined. Whether such cultures will then also be required
to be subsequently undertaken on post-treatment samples will depend firstly,
on the numbers of genera identified as being present at the time of anthelmintic
treatment and secondly, on the results of the undifferentiated FECR. If, for
example, only a single nematode genus is represented at the time of treatment,
then post-treatment cultures will not be necessary since any undifferentiated
FECR results will apply only to that parasite. Similarly, if a 100% reduction in
total strongylid worm egg counts is recorded, then it can be safely assumed
that all of those parasites adequately represented at the time of treatment are
drench-susceptible. If, on the other hand, more than one genus is found to be
represented at the time of anthelmintic treatment and the undifferentiated
FECR is less than 100%, then post-treatment cultures may be used to reveal
either the occurrence of low fecundity resistant genera that might otherwise
be obscured by the reductions in the egg counts of other nematode genera in
cases of apparent drench susceptibility (i.e. those with FECRs of ≥95%) \(^{(59)}\) or,
where the undifferentiated FECR indicates the presence of resistance (i.e. those
with FECRs of <95%), enable the resistant worm genera to be clearly
distinguished from those that are not. \(^{(60)}\)

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*Sustainable control of internal parasites in ruminants* 105


The use and optimisation of anthelmintics

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Chemical classification
The anthelmintics may be classified by chemical structure and such categorisation is useful to the clinician since it also provides groupings with common mode of action, general spectra of activity and within which parasites often develop side resistance. Chemical structure also confers physicochemical properties on the molecules upon which generalisations regarding absorption, distribution, metabolism and elimination may be made. It should, however, be appreciated that in the competitive market which exists subtle differences in structure and thus physicochemistry may provide advantages or disadvantages in terms of spectra of activity, residence time (persistent activity) and residue profile (meat and milk withdrawal periods).

The chemical groupings are given in Table 9.1 together with common routes of administration which are influenced not only by the active compound but also by the formulation (excipient) in which it is provided. General structural formulae of groups of anthelmintics are given in Fig. 9.1 from which it may be appreciated that the anthelmintic groups are likely to interact with different parasite receptors and consequently exert their antiparasitic action by different means.

Avermectins/milbemycins
Mode of action
Avermectins are probably absorbed by many parasite species through the cuticle and such absorption may vary with the cuticular structure of the parasite and the lipophilicity and three dimensional structure of the avermectin. It is
FIG. 9.1: General structure formulae of anthelmintics.

- Avermectins ($R_1 = \text{disaccharide}$)
- Milbemycins
- Benzimidazole (carbamate)
- Tetrahydropyrimidine (morantel)
- Salicylanilide
- Benzoenedisulphonamide (clorsulon)
- Probenzimidazole
- Benzimidazole (thiazole)
- Imidazothiazole (levamisole)
- Organophosphate (trichlorphon)
- Nitrophenol (nitroxynil)
- Pyrazinoisoquinoline
also likely that for blood sucking nematode and particularly arthropod parasites ingestion of the avermectins plays a large part in the way they reach their target sites for antiparasitic action.\(^{(1)}\)

Avermectins are known to induce presynaptic gamma aminobutyric acid (GABA) release or to function as GABA agonists in some parasites.\(^{(2)}\) Gamma aminobutyric acid acts as a neurotransmitter substance and avermectins may interfere with interneuronal transmission within the parasite. It is now, however, accepted that a more likely mechanism for the activity of avermectins and milbemycins at pharmacological concentrations is by increasing the parasite neuronal membrane permeability to chloride ions. This action is thought to be mediated by a glutamate gated mechanism potentiated by the avermectins and milbemycins.\(^{(3,4)}\)

**TABLE 9.1:** Classes of anthelmintics based on chemical structure.

<table>
<thead>
<tr>
<th>Class</th>
<th>Route of administration</th>
<th>Representative drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avermectin</td>
<td>PO, SC, T, B</td>
<td>Ivermectin, Abamectin, Doramectin</td>
</tr>
<tr>
<td>Milbemycin</td>
<td>PO, SC, T</td>
<td>Moxidectin</td>
</tr>
<tr>
<td>Probenzimidazoles</td>
<td>PO, SC</td>
<td>Febantel, Netobimin</td>
</tr>
<tr>
<td>Benzimidazole (thiazoles)</td>
<td>PO, SC</td>
<td>Thiabendazole, Cambendazole</td>
</tr>
<tr>
<td>Benzimidazole (carbamates)</td>
<td>PO, IR, B</td>
<td>Albendazole (oxide), Fenbendazole, Mebendazole, Oxfendazole, Parbendazole, Triclabendazole</td>
</tr>
<tr>
<td>Imidazothiazole</td>
<td>PO, SC, T</td>
<td>Levamisole</td>
</tr>
<tr>
<td>Tetrahydropyrimidine</td>
<td>PO, B</td>
<td>Morantel</td>
</tr>
<tr>
<td>Organophosphate</td>
<td>PO</td>
<td>Trichlorphon</td>
</tr>
<tr>
<td>Salicylanilide</td>
<td>PO</td>
<td>Closantel, Oxyclusanide, Radoxanide, Niclosamide</td>
</tr>
<tr>
<td>Nitrophenolic compounds</td>
<td>SC</td>
<td>Nitroxynil</td>
</tr>
<tr>
<td>Benzoenedisulphonamide</td>
<td>SC</td>
<td>Clorsulon</td>
</tr>
<tr>
<td>Pyrazinoisoquinoline</td>
<td>PO</td>
<td>Praziquantel</td>
</tr>
<tr>
<td>PO - per os</td>
<td>B - bolus (controlled release device)</td>
<td></td>
</tr>
<tr>
<td>SC - subcutaneous</td>
<td>IR - intraruminal</td>
<td></td>
</tr>
<tr>
<td>T - transcuticular</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sustainable control of internal parasites in ruminants*
These anthelmintics have specific activity on parasites and not on their mammalian hosts since mammals lack the glutamate-gated chloride channels on which they act. Furthermore the avermectins and milbemycins do not penetrate the central nervous system well in mammals and mammals possess active transport systems which remove avermectins and milbemycins from the central nervous system. It is likely that in those animals susceptible to avermectin/milbemycin toxicity (neonates, collie dogs, some Murray Grey cattle) the blood brain barrier including the active transport systems may be deficient.

**Pharmacokinetics**

The avermectins and milbemycins are characterised by long persistence in the body and large volumes of distribution. They have high lipophilicity which means that they distribute well into body compartments, especially liver and fat and are eliminated slowly from these compartments. Furthermore, the pharmacokinetics can be dramatically altered by the formulations in which the active compounds are presented. This is particularly true for ivermectin, abamectin and doramectin when given by the subcutaneous route whereby the absorption from the administration sites may be slowed depending on the excipient and thus the persistence of the anthelmintic effect may be extended. The persistent effect attributed to moxidectin is associated with the active molecule and not the formulation since moxidectin is given as an aqueous formulation by the subcutaneous route whereby it distributes into and slowly redistributes from the fat compartment.\(^{(5)}\) Structural adaption of the avermectin skeleton has led to the development of eprinomectin. This is an avermectin with physicochemical characteristics which permit its absorption as a transcuticular preparation and unique partitioning characteristics which provide effective concentrations in the loci of important parasites (gastrointestinal tract and lungs) but very low concentrations in milk.\(^{(6,7)}\) Eprinomectin has therefore been registered in some markets for the pour-on treatment of dairy cattle.

Formulation and pharmacokinetic characteristics of the endectocides confer on them variable prophylaxis against nematode parasites in cattle. Abamectin has persistent activity against most gastrointestinal nematodes for 7 days and against *Dictyocaulus viviparus* for 14 days. Ivermectin and doramectin
have respectively 7 and 21 days persistence against *Cooperia* spp., 21 and 28 days against *Ostertagia* spp. and both have at least 28 days persistence against *D. viviparus*. Moxidectin is highly lipid soluble and has a long residence time conferring activity against *Ostertagia* spp. for 35 days and *D. viviparus* for 42 days. Parasite control programmes on set stocked pasture have utilised the subcutaneous administration of ivermectin at 3, 8 and 13 week intervals, doramectin at 0 and 8 weeks and in some countries moxidectin at 0 and 10 weeks and abamectin at 0 and 6 weeks after turnout. These strategies use knowledge of the epidemiology and prepatent periods of the common target pathogens together with the persistent prophylaxis of the drugs to utilise their activity to best advantage. Those strategies utilising a treatment at the time of turnout (0 weeks) are more convenient since they avoid one gathering period but are a compromise since they are treating animals without a parasite burden and which will not be contaminating pasture for a three week period (prepatent period) following turnout.

In sheep ivermectin has persistence of about 10 days against most gastrointestinal nematodes if given by the subcutaneous route and moxidectin given orally will prevent reinfection by *Ostertagia* (*Teladorsagia*) *circumcincta* and *Haemonchus contortus* for about 5 weeks.

**Spectra of activity**

The avermectins and milbemycins have been classified as endectocides because of their broad spectrum nematocidal and arthropod activity. They have no activity against trematodes or cestodes which may lack the glutamate-gated chloride channels upon which they act in nematodes. The different available compounds also have different nematocidal spectra such that some members have greater potency than others against particular species. (5,8) Those which have been commercialised for sheep all have good activity against important gastrointestinal and lung nematodes, at 200 µg/kg. Ivermectin is effective against *Oestrus ovis* and against the scab mite *Psoroptes ovis* if given on two occasions with a 7 day intertreatment interval.

The effect of feed intake on the pharmacokinetics and efficacy of ivermectin was investigated by Ali and Hennessy(9) in sheep. These workers found that reducing feed intake improved the availability and extended the residence time of orally administered ivermectin. These pharmacokinetic changes caused
an improvement in ivermectin efficacy against ivermectin resistant *H. contortus* from 53% to 97%. These results have led to the recommendation that food intake be reduced for 24 hours prior to and 12 hours after administration of ivermectin.

**Pro-benzimidazoles and benzimidazoles**

*Mode of action*

The probenzimidazoles are metabolically hydrolysed or reduced and cyclized into benzimidazole carbamates and consequently owe their activity to these moieties. Furthermore the sulphide benzimidazoles are oxidised into sulphoxides and ultimately sulphones. The parent thiazolyl and carbamate benzimidazoles and the sulphoxide metabolites are all thought to have anthelmintic activity and differences in efficacy of the compounds probably reflect differences in their bioavailability and pharmacokinetics. Benzimidazoles are thought to act in parasites by binding to tubulin molecules and thus inhibiting the formation of microtubules. Microtubules are then no longer able to transport secretory granules or secrete enzymes within the cell cytoplasm and this eventually results in cell lysis. Parasite gut cells appear to be particularly sensitive to benzimidazoles and destruction of parasite gut may result in malabsorption of nutrients by the parasites and contribute to parasite death.

Mammalian cells appear to be much less sensitive to the effects of benzimidazoles and this may be associated with different protofilament make-up of their microtubules. Furthermore it is likely that benzimidazoles do not achieve such high concentrations within mammalian cells as they do in parasite cells. The mode of action of the benzimidazoles is of particular clinical significance since it is dependent on time of exposure as well as concentration and those benzimidazoles to which the parasites are exposed for the longest period at effective concentrations have greatest efficacy. The parasite locus and pharmacokinetic characteristics of the drugs are thus critical.

*Pharmacokinetics*

The benzimidazoles are extremely insoluble in water and this feature precludes their administration parenterally. They are all generally administered orally.
(or intraruminally) as suspensions with the exception of the prodrug netobimin which is sufficiently soluble for subcutaneous administration in cattle. A recently introduced formulation of oxfendazole is available in some markets for transcuticular delivery. It is likely that the excipients in which the oxfendazole is delivered are critical to its cutaneous penetration. The relatively more water soluble benzimidazoles such as thiabendazole and cambendazole dissolve sufficiently well in the rumen fluid following oral administration to be rapidly absorbed and subsequently excreted. The slower dissolution of the less soluble sulphide and sulphoxide benzimidazoles limits their rate of absorption and consequently extends their residence times within the body. At extremes of insolubility benzimidazoles would be retained in the gut and excreted directly in faeces having gut residence times equivalent to and limited by gut transit time. It is now accepted that much of the activity of the benzimidazoles on gastrointestinal parasites is associated with redistribution of drug from the vascular compartment across the gut epithelium.

Thiabendazole may be detected in plasma of sheep for 15-20 hours after oral administration of a therapeutic dose whereas fenbendazole and oxfendazole can be detected for 120-180 hours and it is likely that gut nematodes will be exposed for periods equivalent to the residence times of the drugs. The absorptive processes influenced by drug solubility and gut anatomy and transit time clearly influence efficacy. However, metabolic processes are equally important and the greater oxidative metabolic capacity of cattle and goats result in more rapid sulphoxidation and sulphonation (inactivation) of benzimidazoles in these species compared to sheep and probably largely accounts for the higher dosage recommendations for most benzimidazoles in cattle and goats.

**Spectra of activity**

In sheep the commonly used benzimidazoles all have broad spectrum nematocidal activity with the exception of triclabendazole which is highly active against liver fluke only. Most members of the group have excellent activity against adult and developing larval stages of the gastrointestinal nematodes including *Nematodirus* spp., lungworms and tapeworms. However, the dosages of thiabendazole and mebendazole may have to be increased for inhibited gastrointestinal larvae, lungworms and tapeworms and activity
against these parasites may be poor. Thiabendazole and oxibendazole have poorer activity against lungworms and inhibited larvae in cattle, in which species thiabendazole is more rapidly metabolised to an inactive metabolite 5-hydroxy thiabendazole than in sheep.\(^{(12)}\)

The normal dosage rate for single administration of the sulphide benzimidazoles in sheep is 5 mg/kg and in cattle is 7.5 mg/kg reflecting the more rapid metabolism in cattle. Albendazole and its prodrug netobimin have extended spectrum of activity to include adult stages of the liver fluke, but must be given at an increased dose rate for optimal efficacy against this parasite (7.5 mg/kg ABZ and 20 mg/kg NTB in sheep). Triclabendazole has excellent activity against all developing and adult stages of liver fluke and is given at 10 mg/kg in sheep and 12 mg/kg in cattle. In goats the benzimidazoles have similar spectrum of activity to that described for sheep although generally the dosages should be equivalent to those used in cattle (in milligrams per kilogram live weight).

Imidazothiazole

Levamisole is the L-enantiomer (isomer) of tetramisole and is now largely preferred to the racaemic compound (tetramisole) since the other enantiomer which comprises 50% of the racemate is conferred with similar mammalian toxicity but little if any nematocidal activity. Levamisole (and in some markets tetramisole) is now the only imidathiazole used commercially.

Mode of action

Levamisole acts as a cholinergic agonist at the neuromuscular junctions in nematode parasites. These junctions have been characterised as nicotinic, resembling most closely the vertebrate nicotinic ganglionic receptors. Levamisole has been shown to open and subsequently block acetylcholine receptor mediated cation channels. Furthermore it has been demonstrated that receptor desensitization may occur at high concentrations of levamisole and it has been suggested that increasing the dosage of levamisole may not be therapeutically advantageous.\(^{(13)}\) This is fortunate since levamisole also acts as a nicotinic agonist in mammalian species and consequently has a rather narrow therapeutic index. As well as its antinematodal action levamisole is known to act as an immunomodulator and has been used in combination
with clostridial antigens in order to treat ewes during the periparturient period while simultaneously administering the prelambing clostridial vaccination.

**Pharmacokinetics**

Levamisole is rapidly and extensively absorbed following subcutaneous administration and is adequately absorbed following oral administration in sheep. Higher peak plasma concentrations are achieved following subcutaneous administration and although this may have some therapeutic advantage for non-gut dwelling nematodes (e.g. lungworm) it does also increase the potential for toxic adverse reactions, particularly if treating small lambs with disparate weights and where weighing is not practicable. In cattle, preparations of levamisole are available for transcuticular administration and such preparations deliver therapeutically adequate drug concentrations for gastrointestinal nematodes. Levamisole does not have any long residual activity and where animals are continually exposed to parasite challenge it may be necessary to repeat treatments at around the pre-patent period (approximately 3 weeks or less if Nematodirus battus is prevalent).

**Spectrum of activity**

Levamisole has excellent nematocidal activity and is highly efficacious against gastrointestinal trichostrongyles including Ostertagia spp., Cooperia spp., Nematodirus spp. and Trichostrongylus spp. and against lungworm. It is effective against inhibited stages of O. circumcincta in sheep but has poor activity against inhibited O. ostertagi in cattle. It has no useful trematocidal or cestodicidal activity. Because it can be administered parenterally (subcutaneous or topically in cattle) its use may avoid potential respiratory distress associated with oral treatment of animals with lungworm.

**Tetrahydropyrimidine**

Morantel is the only tetrahydropyrimidine commonly used in cattle and sheep although the related analogue pyrantel is also used in horses.

**Mode of action**

Morantel is thought to act as a cholinergic agonist in nematode and cestode neuromuscular systems, thus causing paralysis and parasite expulsion. The
commonly used tartrate salt displays differential host:parasite toxicity since it is largely unabsorbed from the gastrointestinal tract and is only administered orally.

**Pharmacokinetics**

Morantel salts (tartrate, fumarate, citrate) have different pharmacokinetic properties which principally relate to their extent of absorption.

Morantel tartrate is available as a sustained release device for cattle and morantel citrate as a drench for sheep. The tartrate salt is highly polar and consequently very poorly absorbed from the gastrointestinal tract. The majority of an administered dose passes through the gastrointestinal tract and is excreted unchanged in the faeces. The sustained release bolus for cattle comprises a sandwich of two ethylene vinyl acetate sheets with a layer of morantel tartrate between. The morantel is released through holes punched in the laminate. The whole device is rolled up into a cylinder for delivery and opens up upon entering the aqueous phase of the reticulo-rumen. Morantel release reaches steady state (zero-order kinetics) after 10 days from the time of delivery and concentrations of approximately $1.0 \mu g/ml$ are achieved in abomasal and ileal fluid throughout the 90-100 day life of the bolus.\(^{14}\)

The other salts of morantel are thought to be more extensively absorbed following oral administration and it has been recorded that peak plasma concentrations of morantel are achieved within six hours of administration. Absorbed morantel undergoes some hepatic metabolism and only 17% of the administered dose is excreted unchanged in faeces.\(^{15}\)

**Spectrum of activity**

Morantel is highly effective against *Haemonchus* spp. and *Coopera* spp. in cattle and sheep and adult and developing immature *O. circumcincta* in sheep. It is less effective against developing larvae of *O. ostertagi* in cattle and is not recommended for inhibited *Ostertagia* spp. It is effective against adult *O. ostertagi* in cattle. Morantel tartrate has useful activity against *D. viviparus* larvae as they are ingested but because of its poor absorption is not effective against pulmonary stages of lungworm.
Organophosphates
Many organophosphate compounds have been produced for their anthelmintic and insecticidal activity, they all have the same general structure as that of trichlorphon (Fig. 9.1) although the methyl groups may be substituted with ethyl or amino and the oxon group may be replaced by a sulphur. The parent thio compounds are often less active than the oxon (or inactive) forms and are generally metabolically converted to the oxon from in the host or target parasite.

Mode of action
The organophosphates exert their anthelmintic action by inhibiting the enzyme acetyl cholinesterase which is responsible for the degradation of the neurotransmitter acetyl choline. An initial bond is formed between the organophosphate and a serine group on the acetylcholinesterase. This bond is relatively weak and this intermediate reaction can be dephosphorylated if a nucleophilic competitor reagent (e.g. pralidoxime) is administered. However, if the bonds between the phosphate and its methyl, ethyl or amino groups are cleaved then the phosphorous atom becomes relatively negative in change and is rendered insensitive to nucleophilic attack i.e. it has ‘aged’ and cholinesterase activity will only reappear if new enzyme is synthesised.

Acute toxicity in host animal species is also associated with acetylcholinesterase inhibition. This results in muscarinic stimulation in the autonomic nervous system, nicotinic stimulation at the neuromuscular junctions and central cholinergic stimulation. Clinically increased secretions, bronchoconstriction, increased intestinal motility and miosis (pupil constriction) are seen and at higher exposure involuntary muscle fasciculations. Chronic toxicity is also recognised and is associated with inhibition of an enzyme called neurotoxic esterase which is associated with nerve cell axons. This causes functional and structural changes in neurones which appear as demyelination.

Pharmacokinetics
The organophosphorous compounds are generally quickly absorbed following oral administration and are metabolised by phosphatases which hydrolyse the molecules and which occur in the liver. Phosphatases are species specific and this has been demonstrated using paraoxon which is metabolised twice
as rapidly in sheep sera than goat sera and ten times as rapidly in rabbit than sheep sera.\(^{(16)}\) Some organophosphates were prepared in vinyl resin pellets (the volatile agent dichlorvos) from which absorption was slowed. Organophosphorus metabolites are excreted in urine.

**Spectrum of activity**

Organophosphates generally have greater activity against abomasal parasites such as *H. contortus* than against large intestinal parasites although trichlorphon was used for *Oesophagostomum* spp. in cattle.

**Salicylanilides**

**Mode of action**

The salicylanilides share the structural characteristics associated with the chemical bonding of salicylic acid and aniline. They also share a common mode of action. Salicylanilides inhibit several enzymes within trematodes, however the mechanism by which they are thought to owe their trematocidal activity is by uncoupling oxidative phosphorylation within the parasite and preventing energy storage as NADH.\(^{(17)}\) Oxidative phosphorylation occurs within mammalian cells as well as parasites and toxicity in mammals is probably associated with the same mechanism which may account for the relatively narrow therapeutic index of these drugs.

**Pharmacokinetics**

Salicylanilides are absorbed following oral administration and become highly plasma protein bound (more than 99%). This may partially account for their long elimination kinetics which reflects the plasma albumin turnover rate and accounts for their good activity against blood ingesting parasites such as *H. contortus* and mature *F. hepatica*. The long elimination half lives of rafoxanide (16.6 days) and closantel (14.5 days) confer upon these drugs persistent activity against *H. contortus* which allows their use in strategies with extended interdosing intervals. The salicylanilides are not extensively metabolised although a glucuronide metabolite of oxyclozanide has been identified.\(^{(18)}\)
**Spectra of activity**

The salicylanilides have a rather narrow spectrum with particular activity largely confined to blood ingesting parasites including adult *F. hepatica* and *H. contortus*. Some members of the group have activity against some arthropods (including *Oestrus ovis*) and against cestodes. Niclosamide is used exclusively in sheep for its activity against *Moniezia expansa*.

**Nitrophenolic compounds**

Nitroxynil is the only nitrophenolic compound marketed globally. It is used exclusively for fluke infections in cattle and sheep.

**Mode of action**

Nitroxynil is thought to uncouple oxidative phosphorylation since it stimulates oxygen uptake by intact fluke at concentrations which correlate well with lethal concentrations.\(^{(19)}\)

It causes stunting of flukes, which survive treatment and inhibits oogenesis and spermatogenesis in fluke. Morphologically nitroxynil causes vacuolation of parenchymal cells and denuding of gut columnar epithelium in parasites.\(^{(20)}\) Nitroxynil is reasonably well tolerated but may cause transient depression in milk yield in dairy cattle and this may be associated with uncoupling of oxidative phosphorylation in mammalian cells.\(^{(21)}\)

**Pharmacokinetics**

Nitroxynil must be administered parenterally (subcutaneously) in ruminants since the nitro group is reduced by rumen microorganisms and thus the compound is inactivated if given orally. Following subcutaneous administration it is thought to become strongly protein bound in plasma and has a long elimination half life of approximately 8 days. Tissue concentrations remain higher than plasma concentrations some time after a single administration of 10 mg/kg.\(^{(22)}\)

**Spectra of activity**

Nitroxynil is highly effective against mature *F. hepatica* but efficacy decreases proportionally against successively less mature stages.\(^{(23)}\) It is also highly
effective against adult *Fasciola gigantica* and the haematophageous nematodes *Haemonchus* spp., *Oesophagostomum* spp. and *Bunostomum* spp. in sheep and cattle.\(^{(24)}\)

**Benzoenedisulphonamide**

Clorsulon is a sulphonamide derivative only marketed as a combination drug together with ivermectin.

**Mode of action**

Clorsulon is bound in blood to erythrocytes, together with which it is ingested by haematophageous parasites. It is thought to act on parasite energy metabolism as a competitive inhibitor of 3-phosphoglycerate kinase and inhibits the oxidation of glucose to acetate and propionate. By blocking glycolysis it inhibits ATP formation.\(^{(25)}\)

**Pharmacokinetics**

Clorsulon is extensively absorbed following subcutaneous administration which is the recommended route for the marketed products. It has a terminal elimination half-life of 30 h determined following subcutaneous administration.

**Spectrum of activity**

Clorsulon is used specifically for its activity against *F. hepatica*. It is highly effective against adult *F. hepatica* in cattle and has 90% efficacy against 6-8 week old stages. At very high dosage levels (15 mg/kg) it has been shown to have 97% efficacy against 4-week old stages of *F. hepatica*.\(^{(26)}\)

**Pyrazinoisoquinoline**

Praziquantel is the only member of this group currently used in ruminants.

**Mode of action**

Its exact mechanism of action is unknown but it does affect muscular activity in cestodes and causes vacuolation and disruption of the tegument of the parasite.
Pharmacokinetics

Praziquantel is rapidly absorbed following oral and parenteral administration but undergoes first pass metabolism in the liver resulting in rapid and almost complete metabolism of the parent compound. Metabolites are principally excreted in urine.

Spectrum of activity

Praziquantel has excellent cestodicidal activity and is used for this purpose in many species. It is also a highly effective schistosomicide and has good activity against most trematodes with the unfortunate exception of F. hepatica.

Change in efficacy by manipulation of administration and or delivery systems

Formulations

Avermectins and milbemycins

The injectable preparations of avermectins owe much of their persistent activity to depot administration formulations from which drug is slowly absorbed. Ivermectin is formulated in propylene glycol (60% v/v) and glycerol (40% v/v) and doramectin in sesame oil (90% v/v) and ethyl oleate (10% v/v). The commercial moxidectin preparation is essentially aqueous (in benzyl alcohol and the surfactant polysorbate 80) and owes persistence to redistribution from tissue ‘depot’ sites (vide supra). All these formulations have excellent tissue site tolerance. Ivermectin, abamectin, doramectin, eprinomectin and moxidectin are all now available as pour-on preparations which are generally administered at rather higher doses than the subcutaneous preparations in order to achieve persistent and high efficacy. The pour-on preparations may achieve some ectoparasiticidal activity by distribution from the site of administration in sebum but are likely to owe most of their endo- and ectoparasiticidal activity to absorption from the site of administration, distribution in blood and further distribution in tissues to the parasite loci.

Ivermectin may now be delivered to cattle and sheep in controlled release devices (CRD). The cattle CRD consists of a semipermeable barrel containing ivermectin in wax, which softens at body temperature. This is separated
from an expandable osmotic tablet, consisting of a polymer salt mixture, by a
solid partition wax. Part of the barrel is contained within a sintered iron
density element which confers sufficient specific gravity to ensure that the
device is retained in the reticulo-rumen. Ivermectin is able to exit the barrel
through delivery ports which control the rate of exit and prevent entry of
foreign material into the bolus. Within the reticulo-rumen water is drawn
into the polymer salt which expands and drives ivermectin from the barrel.
The cattle ivermectin CRD delivers ivermectin in sufficient concentrations (12
mg per day) to control parasite infection for 135 days.

A CRD is now available for sheep in some markets. This consists of a
polypropylene cylinder containing a core of stacked tablets in which ivermectin
is formulated in a sucrose fatty acid ester and lactose base. The formulation
expands and forms a gel when exposed to aqueous rumen fluid and is designed
to deliver 0.8 mg/day (weaner sheep) or 1.6 mg/day (adult sheep) over a
100 day period. The CRD is delivered as a cylinder from which wings extrude
laterally when in the rumen thus ensuring retention.\cite{27,28}

**Benzimidazoles**

Benzimidazoles are normally administered orally since their insolubility limits
absorption from parenteral sites of administration. For cattle and sheep, drench
preparations have been commonly used and CRD are available which provide
convenience of administration and where release of active drug is sustained
greater efficacy (per mg drug administered) *vide supra.*

Weighted CRD for cattle have been designed to release a therapeutic dose of
drug at time intervals approximately equivalent to the prepatent period of the
common parasitic nematodes. These devices use the predictable and constant
corrosive properties of an alloy retaining core to confer delivery of tablets of
ofxendazole on five or six occasions throughout the grazing period. A cattle
CRD for sustained delivery of fenbendazole is also available in some markets.
The bolus consists of ten tablets of fenbendazole weighted with steel ‘shot’
and surrounded by two concentric cylindrical sleeves of alloy. The sleeves
are wrapped in plastic rings. The exposed end surfaces of the alloy corrode
when immersed in the reticulo-rumen and thus release fenbendazole
(equivalent to 0.2-0.4 mg/kg) over 130 days. Several bolus preparations
containing albendazole are also available for sheep. These use the Laby
design whereby wings extrude from the barrel of the bolus when it reaches the rumen and they deliver albendazole in a sustained fashion over an 80-105 day period.

Recently a pour-on benzimidazole product has been licensed for use in New Zealand. This product delivers oxfendazole and claims a unique prolonged action, relative to oral drench products. It is likely that other benzimidazole products may become available for topical administration to cattle as transcutaneous delivery technology improves. This may prove more difficult in sheep than cattle since the epidermis in sheep differs in structure and where wool and wool follicles may provide a more significant barrier to penetration.

**Morantel**

Morantel (tartrate) is available in a CRD in Europe. The device consists of a laminated ethylene vinyl acetate sheet containing 11.8 g of morantel tartrate. The bolus is administered rolled in a cylinder and has a retaining tape which releases in the aqueous phase of the reticulo-rumen. It is thus retained by geometry and releases morantel tartrate through holes in the laminate over a 90 day period.

**Levamisole**

Levamisole is available as drench, injectable and pour-on preparations thus providing alternative convenient delivery routes. Although a CRD and in-water delivery system have been investigated for ruminants none is widely available.

**Manipulation of delivery**

Delivery of anthelmintics may be manipulated by changing the route of administration or altering the formulation in which the active drug is administered and these have been described above. Delivery may also be altered in more subtle but equally clinically significant ways. The site of subcutaneous administration may be changed and technique of delivery in the buccal cavity of oral formulations may be altered, also the dose volumes may be adjusted. Furthermore delivery in relation to the time of feeding is of critical importance to the bioavailability of many drugs.
In sheep the bioavailability of levamisole is less after oral than subcutaneous administration but there is no difference in bioavailability if levamisole is given subcutaneously in the thoracic, neck or gluteal regions. Bioavailability is however increased if the subcutaneous dose is divided between five sites in the gluteal region than if injected into a single site. This may be of some pharmacokinetic interest but does not offer a practicable alternative to single site subcutaneous administration.

Dose volumes (delivering the same amount of drug in mg/kg body weight) do not per se alter bioavailability of orally administered benzimidazoles however dose volume may affect delivery technique and where drug is deposited within the buccal cavity bioavailability is reduced compared to delivery over the animal's tongue, i.e. into the pharynx. Delivery into the buccal cavity probably causes stimulation of the oesophageal groove reflex and thus bypass of the reticulo-rumen and deposition of drug directly into the abomasum from which it is more rapidly absorbed and consequently is more rapidly excreted.

The time of drenching with several anthelmintic classes relative to feeding has been shown to significantly affect bioavailability in ruminants. Benzimidazoles and ivermectin associate strongly with digesta particles. They subsequently dissociate and are absorbed as the particulate matter passes down the digestive tract. Food restriction in ruminants slows the rate of digesta flow from the rumen and thus extends the period of absorption of associated anthelmintic drugs and increases their bioavailability.

Other factors such as age, sex and whether the animals are parasitised or not may also affect bioavailability however, the normal efficacy studies required for registration take these factors into consideration and marketed products would be expected to have acceptable efficacy in the various husbandry and management situations in which they are used.

Potentiation of anthelmintics by metabolic inhibition

Potentiation of the benzimidazole oxfendazole by co-administration with parbendazole was first demonstrated in 1985 by Hennessy and co-workers who attributed the effect to decreased hepatic metabolism and biliary secretion of oxfendazole and increased extra-biliary secretion and thus exposure of
parasites in the gastrointestinal tract. In man the clinical efficacy of mebendazole and albendazole in the treatment of echinococcosis were improved by co-administration with cimetidine which inhibits the metabolic inactivation of the benzimidazole.\(^{(35,36)}\)

The metabolism of the sulphide benzimidazoles (e.g. fenbendazole) has been shown to involve sulphoxidation by flavine-monooxygenase and cytochrome P450 enzyme systems and sulphonation and hydroxylation by the cytochrome P450 system. The flavine inhibitor methimazole and the cytochrome P450 inhibitor metyrapone have been shown to inhibit the oxidative metabolism of netobimin and albendazole sulphoxide thus improving the pharmacokinetic profile and efficacy of the active moieties of these anthelmintics in sheep and cattle.\(^{(37,38)}\)

The effect of the cytochrome P450 inhibitor piperonyl butoxide has also been demonstrated on the pharmacokinetics and clinical efficacy of fenbendazole. The combination produced threefold greater relative bioavailability for fenbendazole and fenbendazole sulphoxide moieties and improved efficacy against benzimidazole resistant \textit{O.circumcinta} from 7.9\% to 97.8\%.\(^{(39)}\) The use of metabolic inhibitors is clearly an extremely effective way of improving the efficacy of benzimidazole drugs. No such combinations have been registered and issues associated with tissue residues in food animals and cost benefit analysis must be considered prior to their clinical development.

Other methods of delivery and delivery vehicles could be used to improve the efficacy of anthelmintics or make delivery more convenient. Sustained release implants have been investigated for delivery of avermectins\(^{(40)}\) and liposomes, matrices and alginites for the delivery of benzimidazoles\(^{(41)}\) and in the absence of novel anthelmintic molecules these strategies deserve further investigation.

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*Sustainable control of internal parasites in ruminants* 127


Anthelmintic resistance

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Introduction

The relative cheapness, high levels of safety, efficacy and wide spectrum of activity of anthelmintics have resulted in farmers throughout the world coming to rely almost entirely on their use to control worm parasites in grazing livestock. Unfortunately, for the sheep industry at least, this situation is rapidly changing.

High levels of resistance (exceeding 50% of farms) towards two of the three major groups of anthelmintics (i.e. the benzimidazoles and levamisole/morantel) is now commonplace throughout the sheep raising countries of the world.\(^1\) The third, latest and possibly the last broad-spectrum group of anthelmintics, the macrocyclic lactones (avermectins and milbemycins), can not be expected to ‘hold the line’ against the evolution of resistance.

Since the first report of resistance to ivermectin in South Africa in 1987,\(^2\) there have been a spate of similar findings in other sheep producing countries, including New Zealand.\(^3\) However, surveys had not detected resistance to this drug class until recent large-scale investigations in the South American countries of Argentina, Brazil and Uruguay.\(^4\) Resistance to ivermectin was reported in all three countries and although the level was not high, it was superimposed on very high levels of resistance to the benzimidazoles, levamisole/morantel and also to the combination of both these drug classes. Thus, the stage is set for the rapid development of resistance to the macrocyclic lactone anthelmintics in parasites of sheep in southern Latin America as farmers now have to rely on this class of drugs to control worms in their flocks. This is likely to be a rapid process, evidenced by more than 70% of sheep farms in the neighbouring country of Paraguay having ivermectin resistant parasites.\(^5\) Unfortunately, the situation has been reached in Paraguay where
farmers have virtually exhausted all chemotherapeutic options to control worms in their flocks and now face the situation of having to drastically modify their management practices, or to abandon sheep farming altogether. Although the situation is not the same elsewhere in the world, there would be some regions in sheep and goat producing countries that are not far behind, and the rest moving down the track at a variable, but inexorable rate of progress.

Whilst anthelmintics are under serious threat, it is totally unrealistic to imagine parasite control schemes in the future without them being an integral component. What is certain, however, is that farmers need to move away from mindless drenching. In this respect, veterinary parasitologists, sheep advisers and extension workers in Australia can justifiably feel well satisfied with their collective efforts in the development, promotion and servicing of a battery of worm control programmes tailored for various sheep producing regions in that country. By any benchmark, these have been highly successful ‘research-extension packages’, as illustrated by the exceptional levels of acceptance by producers. The aim of all of these programmes is to maintain high levels of animal production, prevent clinical disease and reduce the frequency of anthelmintic treatment in order to minimize selection for resistance. However, although there has been success in formulating, ‘selling’ and documenting the acceptance of strategic worm control programmes in Australia, there has been no evidence that these programmes have been effective in slowing the development of resistance. Recommendations for strategic parasite control have also been in place for several years in New Zealand. The same principles apply as in the Australian programmes and likewise, although the frequency of drenching sheep has diminished there is no clear evidence that the ‘resistance wave’ has been halted.

**Operational factors associated with anthelmintic resistance**

It has been shown repeatedly that the development of resistance is an inevitable consequence following the use of any chemotherapeutic agent. No drug can be expected to be 100% effective against 100% of the target pest organisms, 100% of the time. So it is with nematode parasites, livestock and the use of anthelmintic. Thus the small numbers of surviving worms, which are the genetically resistant portion of the population, have an increased opportunity
to contribute to the next generation. Much has been written about the various factors associated with development of anthelmintic resistance. Briefly, these include:

**Drench frequency** The most obvious factor and the one most clearly associated with resistance is the frequent use of anthelmintics. In situations where suppressive anthelmintic treatment (4-6 weeks) have been practised, high levels of resistance invariably occur within a short period of time.

**Under-dosing** Whether deliberate or unintentional (e.g. use of faulty or improperly calibrated drench guns) underdosing is widespread and common and must be a major contributor to selection for resistance.

**Continuous use from the same drug class** The practice of continuous use of anthelmintics from the same class, irrespective of whether different brands or formulations were used, has resulted in high levels of resistance to the specific class of anthelmintics with little or no reversion towards susceptibility even after many years following drug withdrawal.

**Parasites species involved** Drench failure in regions where highly pathogenic parasite species e.g. *Haemonchus contortus* are endemic is obvious to research worker and the farmer alike, with clinical episodes due to drug resistant worms. In the more temperate regions, where *Trichostrongylus* and *Ostertagia* spp. assume dominance and are responsible for enormous subclinical production losses, resistance is not normally detected until specifically investigated.

**Animal management practices** There is reasonable basis in the statement that drench resistance is essentially a problem of small ruminants in the Southern Hemisphere. Producers in Australia, New Zealand, South Africa, and the countries in southern Latin America, which have the greatest resistance problems in their flocks, largely practice continuous grazing on permanent pastures. This is in contrast to the diversified systems of agriculture in the Northern Hemisphere. Theoretically farmers in the Northern Hemisphere have more flexibility to capitalise on the greater availability of ‘worm-safe’ grazing afforded by new pasture leys, stubbles, aftermath, root crops, alternation with cattle, etc., and thus have a reduced need to drench sheep. In reality this is often not the case. Farmers often manage sheep as discrete units within their overall farming operations, fail to capitalise on the above opportunities and drenching of sheep can often be as frequent as that practised in Australasia.
However, one factor which may account for the lower levels of resistance in countries of the Northern Hemisphere, is that treatment is generally given at times when the climate is favourable for the survival of the free-living stages on pasture. Therefore, a greater proportion of the total parasite population escapes exposure to anthelmintic treatment, and thus selection for resistance is reduced.

The impact of sheep management practices, more relevant to Australia and New Zealand, on the development of resistance will be considered in more detail below.

**Significance of resistance**

The level of anthelmintic resistance means different things to different people. A reduction in the faecal egg count of 95% or less after treatment is the criterion generally recognised by research workers and veterinary diagnosticians for declaring the presence of resistance. Notwithstanding the debate regarding the correlation of faecal egg counts and worm burdens, a 95% reduction in faecal egg count (and even as low as say 70%) would certainly prevent any immediate threat of clinical parasitism to the producer. However, this provides a warning that resistance genes have reached a high level in the parasite population. If control practices are not changed, then resistance levels can be expected to escalate rapidly with failures likely to occur soon.

The question that needs to be answered as far as farmers are concerned is - ‘What does drench resistance mean to me?’ This was specifically investigated in Australia, where productivity was compared in young sheep exposed to moderate parasite infections for which drenches with varying levels of efficacy (100%, 85% and 65%) were used. The results are sobering. The greatest difference was seen between the highly effective treatment and the least effective, which translated into a reduction of approximately Aus$4.50/head in wool production, but there was also a substantial difference (Aus$1.25/head) between the middle and least effective treatment.

In Australia at least, it is considered by the experts in the field of anthelmintic resistance detection and management, that producers generally do not recognise the significance of resistance in their flocks. Despite the evidence
that the overwhelming losses due to parasites are sub-clinical, which have been recently estimated to be in the order of Aus$150 million annually to sheep farmers in Australia,(12) they simply consider that worms are a problem only when signs of clinical parasitism are apparent. It would seem to be not unreasonable to assume that the same attitudes would prevail amongst New Zealand sheep farmers.

**Detection of resistance**

A whole range of *in vitro* techniques have been developed for the detection of anthelmintic resistance, but up until recently the procedure of choice for field survey investigation is the faecal egg count reduction test (FECRT). There are some shortcomings to this procedure, but it allows for all anthelmintics to be tested at the same time and does not require sophisticated equipment or highly trained staff.

A new innovation to the methods of anthelmintic resistance detection, which may well supersede the FECRT, is the recently commercialised ‘DrenchRite™’ assay. This *in vitro* assay can be used to detect resistance to benzimidazoles, levamisole, benzimidazole/levamisole combination and the macrocyclic lactone anthelmintics in the major nematodes of sheep, *Haemonchus contortus*, *Trichostrongylus* and *Ostertagia* spp. In this assay, nematode eggs are placed into the wells of a microtitre plate and hatched larvae develop to the infective stage in the presence of anthelmintic. The concentration of anthelmintic required to block development is related to an anticipated *in vivo* efficacy. The advantage of ‘DrenchRite™’ is that it eliminates the need for farm visits (farmers can be easily instructed in how to collect samples) and does not require the availability of a large number of animals. However it does require a high level of technical expertise in the laboratory.

**Management of resistance**

A. **Eliminating resistance - the chances of success**

There is some evidence to suggest that if resistance genes are not high in the parasite populations, then the withdrawal of the drug (group) can lead to susceptibility which can be rapid even in field situations.(13) However, re-introduction of the offending drug results in an equally rapid return to resistance. Theoretically, it would seem that the forces that drive these processes
would depend on how far along the track towards complete (homozygous) resistance the parasite population had travelled. Once this stage is reached, then susceptibility takes a long time, or may never, return.\(^{14}\) It also seems that the introduction of one drug can hasten the reversion process (i.e. counter-select) to the original.\(^{15}\) In practice however, it would be difficult to manage the competing forces of counter-selection against drug A and the emergence of resistance to drug B if it was used for an extended time.

Novel attempts to restore anthelmintic efficacy have been reported by veterinary parasitologists in South Africa. Firstly, an attempt was made to reintroduce anthelmintic susceptibility genes into a field population of *H. contortus*, which had developed high level multiple resistance following intensive anthelmintic use, by dosing sheep with susceptible larvae of the same species of parasite.\(^{16}\) Although the intentions are theoretically sound, the practical management of this procedure would be hazardous in the extreme, because to achieve this objective requires no anthelmintic intervention otherwise it becomes self-defeating. There would be little comfort to the farmer to see his flocks decimated by this parasite, albeit with much less resistant worms! Secondly, quite drastic efforts were made in South Africa to eliminate the first reported field case of ivermectin resistance in sheep parasites.\(^{17}\) Again, *H. contortus* was the problem parasite and eradication was achieved by a combination of suppressive drenching with alternative anthelmintics, overnight housing, pasture replacement, alternate grazing with cattle, slashing and burning of pasture. Eradication was achieved, but this is an entirely unrealistic procedure for management of resistance at large.

**B. Learning how to live with the problem**

Apart from those sheep management systems which either through location (e.g. semi-arid, mountainous regions) or choice of operation (e.g. wether grazing) have no apparent worm problem thus little drenching is carried out, it would be rare indeed to find a sheep farm in Australia or New Zealand that did not have anthelmintic resistant parasite populations present. It also seems clear that for all practical purposes, resistance cannot be eliminated. Therefore, what needs to be aimed for is the management of existing anthelmintic resistance in such a way as to ensure hopefully that no rapid escalation in the extent or spectrum occurs. The following measures are considered to be the ways to achieve this:
Strategic drenching Strategic drenching forms the basis of the regional control programmes in Australia and the current Ministry of Agriculture and Fisheries recommendations in New Zealand for the control of nematode parasites of sheep. Essentially, strategic drenching are treatments given at critical times of the year in relation to the epidemiology of parasite infection, often in association with some form of animal management. The aim is to maximise the effect, and thus reduce in number, of treatments required to achieve effective control. However, it is difficult to estimate whether these programmes actually delay the development of resistance. In fact, certain aspects of strategic drenching may actually increase the possibility of resistance development. These include the drenching of weaners onto 'clean' paddocks and for Australia at least, double summer drenching in the uniform and winter rainfall regions. The logical explanation for this is that only a small percentage of the parasite population is on pasture and any survivors of the anthelmintic treatment will make a much greater contribution to succeeding parasite generations. However, the total population size will, for the short-term at least, be relatively small. The main determinants as to whether strategic drenching is a good or a bad thing from the resistance standpoint are:

- the efficacy of the anthelmintic treatment
- the 'cleanliness' of the pastures to which the stock are moved
- the gene frequency for resistance in both the remaining parasite population after treatment in the host and on pasture
- the prevailing weather conditions following the drench and/or move

The outcome, in terms of degree of resistance, will be determined by the relative importance of these factors in the interactions amongst them. The effect that this has on the development of resistance needs to be balanced by the control that is achieved by such treatments and the increased frequency of treatment and accompanying selection for resistance, that is required if these practices are not adopted.

Narrow spectrum treatments The most important example of narrow spectrum treatments is the use of closantel to control *H. contortus* at specific times of the year to prevent contamination of pasture in spring and early summer in the summer rainfall regions of Australia. This has the benefit of reducing the number of broad spectrum treatments that are necessary to control
the other important and less fecund species, particularly *Trichostrongylus* and *Ostertagia* spp., thus reducing the selection pressure for resistance.

**Pasture management** It is beyond question that greater efficiency of parasite control can be achieved if drenching is combined with some form of grazing management, whereby treated animals are moved to pastures of lower infectivity. As discussed for strategic drenching above, these procedures have the potential to select more rapidly for anthelmintic resistance. Only for control systems that avoid the use of anthelmintics altogether is there any certainty of avoiding selection for resistance. Although it is natural to be highly sceptical about the practicality and possibilities of worm control in sheep by grazing management alone, it has been shown to be possible.\(^{18}\) Young Merino sheep, given just a single drench at weaning, and then alternated with cattle on three occasions without any additional drenches over a 12 month period, showed similar weight gains and wool production to weaners that were set-stocked but drenched every fortnight. In other words, one drench and three pasture moves were as good as 26 drenches! This concept has not been investigated any further and it would seem obvious that there is an urgent need to follow this up further because the tremendous potential benefits both in terms of animal productivity as well as anthelmintic resistance management.

**Monitoring** Important benefits can be gained by the monitoring the changes in parasite burdens by means of faecal egg counts. The young, most susceptible portion of the flock (weaners) are of course the most important, but should not be the only class to be followed. Regular sampling of adult, non-breeding stock will certainly present different patterns calling for different action. To achieve success in the adoption by farmers of worm control programmes, they must have relevance to reasonably large regions and be applicable on a year-to-year basis. However, refinements should be aimed for with time, and monitoring of faecal egg counts allows for the detection in subtle differences between locations and years. Not only will this provide assurance to the farmer that the worm control programme is working effectively, but also will indicate when specified drenches can be eliminated for the whole, or part of, the flock. Effective monitoring is a key requirement in managing anthelmintic resistance.

**Preserving anthelmintic efficiency - the combination recommendation** Formulated combinations of benzimidazoles and levamisole have been available
for several years and are useful when the individual components are no longer effective. However, this at best can only be relied upon as a short-term measure as multiple resistance to the combination product is either at a high background level, or will rapidly occur because of previous use of these two drug groups. Computer predictions have shown that the use of cocktails of anthelmintics, in which all drugs have high levels of efficacy, are the most powerful means of maintaining long-term drug efficacy.\(^{(19)}\) The question of rationality and reality of course determines the likelihood of this actually occurring. Even if the happy situation did arise and several chemically unrelated, highly effective anthelmintics became available, then the commercial considerations of obtaining between-company agreement to pool their chemical resources and at the same time keep the cost of such a hybrid product at a level affordable to the majority of farmers, would be extremely difficult to achieve.

**Capsules** Albendazole controlled release capsules are another option for controlling benzimidazole-resistant *Trichostrongylus* and *Ostertagia* spp. in sheep. They exert their effect by preventing the establishment of ingested infective larvae, but not on established infections. To remove these adult worms, a therapeutic dose of an effective short-acting anthelmintic needs to be given at the time as the capsules are administered. Although the use of these capsules extends the life of the benzimidazoles, field evidence has clearly indicated that this will only be for a short time if they are used exclusively.\(^{(20)}\)

**Quarantine treatments** Although the free-living stages of worm parasites provide the only means by which animals become infected, they are not important for dispersal. Except in extreme conditions of rainfall run-off, worm larvae do not migrate more than a few centimetres. The only way in which resistant worm populations can be effectively dispersed is by movement of their hosts. This is an important distinction from insecticide resistance. First, it is likely to have a bearing on the non-uniform distribution of anthelmintic resistance compared with insecticide resistance. Second, and more important, it highlights the fact that the individual farmer is responsible for their own resistance problem, whether they create it themselves or import it with purchased stock. Effective treatments of purchased sheep are important. In Australia, the persistent macrocyclic lactones, in combination with levamisole, is a commonly recommended quarantine anthelmintic treatment strategy.\(^{(11)}\) Farmers should also be aware of the much greater likelihood of importing
resistance onto their farms with the purchase of goats. Sheep and goats share
the same parasite species and resistance has developed much more rapidly
and at a much higher level in goats. This is due to the great susceptibility of
goats to worms, necessitating frequent drenching. The problem is exacerbated
by rapid drug metabolism in goats leading to lowered efficacy. Thus the ‘deadly’
combination of anthelmintic overuse and under-dosing is an unfortunate fact
of life in intensively reared goats.

Conclusion

The development of resistance has proved to be an inevitable evolutionary
consequence in our efforts to combat pest organisms by chemotherapy. This
is testimony not only to the genetic diversity of the target organisms but also
the habitual misuse of any new chemical compound by mankind. Squandering
such valuable resources is inefficient, expensive and unsustainable.

Resistance in nematode parasites to anthelmintic drugs has followed this well-
beaten path and we now find ourselves in a position, reached some two decades
ago in the control of insect pests, of widespread drug failure. It has progressed
from largely academic interest to a major threat to the sheep and goat industries
in many countries of the world. There seems to be a degree of mesmeric
fascination as to what happens next. Some believe that the international
pharmaceutical industry will come to the rescue, but the high risks, high
costs and the relatively low returns makes this unlikely. In addition to the
resistance problem, marketing and social imperatives, such as reducing
chemical residues in the environment, will increasingly come to bear on the
ways in which anthelmintics are used in the future. To meet what now has
become fashionably termed ‘ecologically sustainable’ objectives, a greater
sophistication in the ways in which anthelmintics are used is essential. Ad
hoc drenching practices need to be abandoned for more judicious use of
anthelmintics, coupled with supplementary control measures. At present these
are mainly associated with various grazing management options and selecting
for worm resistance in breeding programmes, but in the future will hopefully
include worm vaccines and biological control.

The task of achieving sustainable nematode parasite control in grazing livestock
not only rests with the farmers but also with the veterinary chemical industry,
research and extension workers. Consumer education is also important, because these changes will inevitably be associated with an increase in commodity price. However, on the basis of precedent with the success of various integrated pest management schemes in insect pests, there are grounds for optimism that effective parasite control programmes which slow the development of anthelmintic resistance will be achieved in the future.

References


Long-acting and controlled-release anthelmintics

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Introduction

In the last few years, new formulations of some broad-spectrum anthelmintic classes have appeared on the Australian and New Zealand markets for use in sheep. Their common feature is the maintenance of effective plasma concentrations for extended periods, which offers protection against reinfection after administration and enhanced efficacy against resistant worms. These desirable outcomes have been achieved in two ways. First, in the Captec controlled-release device, by means of a rumen capsule that releases its payload of anthelmintic at a constant rate over a period of 90 or 100 days, and secondly, by pharmacological variants of the macrocyclic lactone (ML) class of anthelmintics that have an extended biological half-life when compared with the original ivermectin molecule, particularly when administered as a subcutaneous injection. In this paper, controlled-release and long-acting drugs will be referred to collectively as persistent anthelmintics.

These developments have led to a proliferation of claims and counter-claims by manufacturers regarding both the efficacy and sustainability of the use of such formulations. Many sheep producers are understandably confused by this conflict, particularly as it impinges on selection for drench resistance. In an environment where the ML drenches are often the only fully effective broad-spectrum group available, and with increasing reports of resistance by worms to this class of drenches, producers are concerned that they do not exacerbate their resistance problems by inappropriate use of these persistent formulations.
Do they work?

There is no doubt at all about the ability of persistent anthelmintics to add a new dimension to on-farm worm control. As well as killing worms resident in the sheep at the time of administration, which they will do at least as well as the more traditional formulations, persistent anthelmintics provide protection from re-infection for periods ranging from one to four weeks (depending on parasite species) for injectable moxidectin to around 14 weeks for albendazole or ivermectin capsules. This extended protection period has two major consequences. First, the treated sheep are allowed to express their full production potential without the constraint of parasitism for at least this period. Secondly, the epidemiological effect of this prevention of pasture contamination with worm eggs during, and for three weeks after, the protection period can be profound. Following a traditional drench, egg counts fall to close to zero for about three weeks, which represents the time taken for larvae picked up from pasture after the drench to reach maturity and produce eggs. A persistent drench with a four-week protection period extends this 'egg-free' time to seven weeks, while a 14-week capsule extends it to 17 weeks. The pasture is thus not being contaminated with worm eggs for periods that are long enough for significant mortality to occur among the existing free-living stages.

A good example of the consequences of control of pasture contamination by a persistent anthelmintic was provided by the narrow-spectrum compound closantel in Australia in the 1980s. Sheep farmers in the summer rainfall regions usually controlled Barber's Pole worm (Haemonchus contortus) by monthly drenching until closantel became available in 1983. This compound, with its excellent activity against Haemonchus and mature liver fluke, binds strongly to plasma proteins and provides a high level of protection against reinfection with Haemonchus for four to five weeks after treatment. By adopting a strategic control programme involving three closantel treatments annually at two-monthly intervals beginning in spring, outstanding control and even eradication of Haemonchus has been achieved on some farms. Admittedly, the climatic requirements for development of the free-living stages of Haemonchus mean that it need only be controlled during the summer, and to that extent, is easier to control than Trichostrongylus or Ostertagia. Nevertheless, outstanding control of all species has been achieved with the albendazole capsule in Australia and New Zealand, in unpublished trials.
with the ivermectin capsule in both countries, or with moxidectin injection in New Zealand.\(^9\)

**Why do they work?**

Controlled-release capsule formulations of drugs previously used as traditional single-dose anthelmintics, such as albendazole or ivermectin, have a daily release rate of around one tenth of the single-dose rate. For long-acting but single-dose compounds, such as moxidectin or closantel, the dynamics are more complicated in that these compounds are preferentially distributed within a body compartment that maintains an extended, though declining, plasma concentration of the drug over time. This compartment is plasma protein in the case of closantel, and probably body fat for moxidectin. How can these low concentrations of drug achieve efficacies superior to those of more transient concentrations an order of magnitude higher?

In order to reach and then kill the parasite, the drug must bind to receptors on both host and parasite. A prolonged association between drug and receptor is much more effective in promoting this binding than is a shorter association at a higher concentration. In the case of the benzimidazole (BZ) drugs, and probably the MLs as well, one mechanism of drug resistance in the worms is selection of worms whose receptors bind less strongly to the drug.\(^8\) Prolonging the presence of the drug promotes binding to a much greater extent than does increasing the dose rate for a shorter time, thus accounting for the superior efficacy of controlled-release formulations of BZs against BZ-resistant worms.\(^2\) Less is known about the efficacy of controlled-release ivermectin against ML-resistant worms, but it is probable that similar arguments would apply. Certainly, increasing the duration of ivermectin presence increases its efficacy,\(^1\) and longer-acting MLs like moxidectin are more effective against ML-resistant worms than shorter-acting drugs such as ivermectin.

**Persistent anthelmintics and drench resistance**

Because the use of persistent drugs for worm control is relatively new, many of the issues surrounding their use are unfamiliar to farmers and provide fertile ground for extravagant claims by those who are, for various reasons, strongly opposed to, or strongly in favour of, the use of one or both kinds of
persistent drug delivery. Superimposed on this uncertainty is farmer suspicion of the cost of these delivery systems, which can be an order of magnitude greater than for one dose of a traditional drench. This issue is by far the easiest to deal with, as it can be settled by experiments and on-farm trials. Clearly, the economics of persistent drench use depends critically on current prices for wool and meat, but as a general guide, results of several field trials over the last ten years indicate that even at today's depressed commodity prices, productivity gains from treated sheep will easily exceed the cost of using persistent drenches, leaving the improved worm control and cleaner pastures as a bonus.

Because of the relative paucity of factual information, debate about the impact of persistent drugs on drench resistance tends to be far more heated than debate about their economics. There is a profound shortage of factual information for the simple reason that drench resistance under field conditions takes between 5 and 10 years to evolve, and these formulations have not yet been in widespread use for sufficient time for all the facts to emerge. What follows is therefore speculative, but illuminated by observations on what has happened in Australia with closantel, and by judicious exploration with computer models. Its only claim to be taken more seriously than some other contributions on the subject is that it comes from a reasonably well informed, sceptical observer with no particular axe to grind!

'Screening' for resistance by persistent drugs

Opponents of the use of these drugs point out that with a traditional drench, only the small fraction of the total parasite population that happens to be in the sheep on the day of drenching is exposed to the drug. The larger number of free-living stages on pasture escape selection. They contrast this with a persistent drug, where not only is the parasitic population on the day of dosing selected, but also all infective larvae picked up from pasture during the delivery period of the capsule or protection period of the long-acting drug. They argue that the much greater population of worms screened by the persistent drug must result in more intense selection for resistance.

This is a persuasive argument, and one to which I originally subscribed. There are two mitigating facts that I believe reduce its force. First, it is wrong to
imagine that traditional drenches do not screen a larger worm population than is present in the sheep on the day of dosing. The worms present in a sheep on any given day were acquired over a more prolonged period, typically of two or three months, depending on when the sheep was last dosed. Thus far then, a persistent drench is no different from a traditional drench. Secondly, an infective larva picked up during the protection period that happens to be resistant to the drug is not guaranteed similar luck in surmounting all the other obstacles in its path before it passes on its useful resistance genes to future generations. It still has to establish (which only some 1% to 65% will achieve, depending on previous experience by the host), to survive the host's further immune responses, to find a mate, and for its eggs to be deposited in the right place at the right time and develop into infective larvae that are lucky enough to be picked up by a susceptible sheep. In addition, it has to withstand the continued presence of the drug for the remainder of the protection period while it undertakes these drug-sensitive activities. On balance then, while I agree that persistent drugs will screen a greater proportion of the worm population for resistance, I do not think that the difference between their screening activity and that of traditional drenches is as great as it first appears.

'Tail' selection

Some proponents of the controlled-release capsule point with alarm at the exponentially declining drug concentrations during the protection period of long-acting drugs like closantel or moxidectin, and contrast this 'tail' with the perfectly rectangular profile of drug release from the Captec capsule. They correctly argue that the declining tail of long-acting drugs will progressively allow less-resistant larvae to establish and reproduce, and most seriously disadvantage the fully susceptible larvae. The claim is that long-acting drugs are therefore more likely to select for resistance than their more fortunate cousins safely ensconced in their well-behaved capsule, which is either still running and killing all larvae, or completely finished and killing none, but not selecting in either mode.

Again, I believe that this case is overstated, if only from the viewpoint that even a perfectly functioning capsule also has a tail - not in drug concentration but in duration of drug/worm contact. Clearly, a less-resistant worm picked
up on day 95 of a 100 day capsule release period is more likely to survive than the same worm picked up on day 50 or day 1, and as discussed previously, duration of drug-worm contact has been shown to be extremely important in determining efficacy. Furthermore, computer simulation studies\(^6\) indicate that resistant larvae acquired during the protection period are disadvantaged in the contribution they can make to the resistance of future generations of worms when compared with resistant worms that survive the initial kill of either a persistent or short-acting drench. As pointed out above, they still have to establish, grow to maturity, mate and survive - a process that also delays by at least three weeks any contribution they might make to resistance development.

**The closantel analogy**

At the time of its launch in the early 1980s, dire predictions were made about the propensity of closantel to select for resistance, on the basis of its persistence and its 4-week long tail. Fourteen years later, after virtually every sheep producer in the northern half of the Australian high-rainfall zone has used it every year, with no rotations or alternatives, What has happened? Briefly, for the vast majority of users, the experience has been one of fourteen years of outstanding *Haemonchus* control to the extent that outbreaks of haemonchosis are a distant and receding memory. Certainly, resistance has developed on probably a couple of hundred farms across the country, and this number will undoubtedly increase, but the aggregate economic benefits that have accrued to farmers from its use are enormous. It is not known why resistance to closantel has taken so long to develop. One possibility is that it was usually administered with a broad-spectrum drench, which would have killed most of the closantel-resistant survivors of closantel alone. Another is relevant to all persistent drugs; because of their persistence and thus higher efficacy, they leave fewer survivors.

**BZ capsules and BZ-resistant worms**

The first commercial application of the Captec anthelmintic capsule was with albendazole as an active ingredient, and this occurred at a time when BZ resistance was already widespread from use of these drugs as traditional drenches. There are therefore some particular issues and uncertainties relating to the use of BZ capsules and resistance that have been discussed more fully
elsewhere.\(^{(2)}\) Briefly, it is advisable to field-test a BZ capsule before using it on a farm where BZ resistance is known or suspected, and to administer it with a 'priming dose' of an unrelated effective broad-spectrum drench if given to sheep with a significant existing worm burden. This is because it has been found that the BZ capsule is more effective against resistant incoming larvae than it is against resident adult worms, and its activity against resistant larvae can really only be determined by trial and error on any given farm.

**Conclusion**

Persistent anthelmintics, whether released at a constant daily rate from intraruminal capsules or of the long-acting drench type can achieve significantly better worm control and productivity in grazing sheep production systems. These benefits come at a cost, however. The higher monetary cost and its resulting production benefits are readily calculated or demonstrated, and are therefore not controversial. Much less is known of the cost of the increased risk of drench resistance that may be provoked by these formulations. In my view, which is supported by experience with closantel and by computer models, \(^{(8,9)}\) these risks have probably been overstated, but I suspect it is not possible to get substantially better worm control at no cost at all through increased selection for resistance. Finally, I see little point in discriminating between the two delivery systems on the basis of whether or not they have a 'tail'. As far as I can see they both do.

**References**


Introduction

Until relatively recently it was thought that no effective natural immunity was generated by infections with ruminant nematodes; that worms living in the gut were effectively outside the body and could neither initiate nor be affected by the immune system. Repeated reinfections also were clearly apparent in livestock. That viewpoint has changed as the knowledge of immunity to nematode infections has accumulated, along with the discovery of new ways of producing vaccines, both of which now tempt us with the possibility of future control by vaccination.

From an evolutionary perspective it is the intention of a parasite to survive in the hostile host environment long enough to generate offspring for the next generation. With typical prepatent periods of 21 days for many gut parasites of ruminants, a long period of coexistence with the host is necessary to achieve this.

Parasites are typically host specific and cause chronic infections (infestations) with a high morbidity. The complexity of the life cycle of these organisms relative to other pathogens, along with the great variety of antigens (substances that stimulate the immune system) present during each developmental stage, mean that the immune response is very complicated.

Natural immunity in sheep

The response of the immune system to infectious agents can be divided into innate (or non-specific) and acquired (or specific) immunity. The former mechanism is important for the initial exposure to parasites and thus is important in young lambs, but in a temperate environment such as New Zealand where ingestion of infective larvae occurs more or less throughout the year, acquired immunity is most important.
**Innate immunity**

Innate immunity can be envisaged as being comprised of four types of defensive barriers: anatomic (such as the gut endothelial wall and mucus), physiologic (such as intestinal motility), phagocytic (ingestion and killing) and inflammatory (allowing leakage of serum proteins and phagocytes). These mechanisms are similar with repeated infections. The acquired immune response (see later) is dependent on aspects of innate immunity such as phagocytic activity that enable parasite antigen to be presented to certain critical immune cells.

**Acquired immunity**

Acquired immunity reflects the ability to specifically recognise and selectively eliminate parasites and displays four attributes: antigenic specificity, diversity, memory and self/non-self recognition. What that means in terms of gut parasite infections is that immunity develops against a wide range of antigens from specific worm species, independently of each other, even if some non-specific immune factors produced by one species of helminth may interfere with the establishment or maintenance of another. While immunological memory exists, leading to protection after cessation of infection, it is neither as solid nor long-term as with other infective agents. In general, sheep need to graze the infective larvae of gut parasites, and therefore be exposed to the different developmental stages for up to 12 weeks to engender resistance. However, this process is not apparent in young lambs which need to be 6-8 months of age to allow the development of acquired immunity.

Acquired immunity is commonly divided into humoral (antibody or immunoglobulin-Ig based) or cellular mediated mechanisms. Both mechanisms are tightly interwoven in parasitic infections, as indicated in Fig. 12.1.

**Humoral immunity**

There is still some uncertainty over the role of serum antibodies in the expulsion of gut parasites. Even though negative phenotypic correlations of up to 0.63 (worm burdens) and 0.62 (faecal eggs) have been described between serum antibody levels (especially IgG) and host resistance in older lambs of various breeds, it is possible that the associations are indirect and not causal. Other
FIGURE 12.1: Interaction between humoral and cellular immunity. APC - antigen presenting cells, B - B lymphocyte, T - T lymphocyte, Ig - immunoglobulin.

Factors may be more important. Strong evidence exists that levels of IgA from lymph draining the abomasum indicate protection against *Ostertagia (Teladorsagia) circumcincta*,(6) but this is not often correlated with blood levels of IgA. Levels of serum IgE measured by ELISA have been associated with resistance to *Ostertagia ostertagi* in cattle,(7) but not constantly in sheep infected with *T. colubriformis* when measured by percutaneous anaphylaxis assay (RG McFarlane, unpublished data). Humoral immunity either measured in the peripheral blood or locally is important only after sufficient stimulation by parasite antigens and is generally less important in young lambs.

**Cellular immunity**

The importance of mononuclear lymph cells (lymphocytes and monocytes) in mechanisms of immunity was initially shown in laboratory animal models,(8) but later also in sheep(9) where lymphocytes derived from sites infected with gut parasites conferred resistance when transferred to parasite-naive recipients. It appears that lymphocytes have a major role in the amplification

*Sustainable control of internal parasites in ruminants* 151
(multiplication of sensitized clones) and regulation (secretion of cytokines) of the immune response. In general, it is believed that a particular type of helper T (thymus derived) cell population is important for helminth infections (T helper 2 cell) in mice, man and probably livestock. These cells secrete cell regulators (e.g. interleukin 3 or IL-3, IL-4, IL-5, IL-9 and IL-10), which promote IgG, IgA and IgE production from plasma cells, mast cell hyperplasia and the increased production and release of eosinophils in the blood. The development of a systemic eosinophilia is associated with parasitic burdens such as *T. colubriformis*, but not *Haemonchus contortus*. Local hypersensitivity reactions in the gut are frequently associated with the immune expulsion of gut parasites. Mucosal mast cells (MMC) appear in animals made resistant by repeated infections, which upon being triggered by parasite antigen that activates bound IgE, release vasoactive substances (histamine, leukotrienes, prostaglandin E₂) that cause an inflammatory response allowing egress of plasma antibodies into the gut lumen as well as acting directly on parasites *in situ*. This response is similar to an immediate hypersensitivity response. Studies have shown that a number of these effector mechanisms act in concert and that if they are antagonised individually then overall host immunity is not massively impaired. However, the function of helper T cells (CD4) does appear to be critical in mature animals.

The resultant immune response may interfere with worm development by: rejection of incoming larvae, retardation of larval development, rejection of adult worms, and interference with worm fecundity. Note that parasite species differ in certain aspects of immunity. *Nematodirus battus* stimulates a particularly rapid response to primary infection leading to a high degree of protection. In general, blood sucking helminths such as *H. contortus* are more affected by systemic immunity as compared with mucosal browsers such as *T. colubriformis* which are especially affected by local immunity. The rate of ingestion and developmental time (>7 days necessary for *T. colubriformis*) of infective larvae may influence the type of immune response and subsequent protection level. That is, some particular immune responses may need a certain threshold of infection to trigger them and persistent exposure to parasites may be necessary to maintain a protective immune response.

There is widespread DNA and protein variability in outbred sexually reproducing populations of parasites and they have evolved systems to help...
them evade the host's immune system. For example, adult worms of *T. colubriformis*, *H. contortus* and *O. circumcincta* secrete enzymes (cysteine proteases) that can cleave and inactivate blood clotting factors and antibody, and disable lymphocytes.\(^{(17)}\)

**Interactions between alternative hosts and nematodes**

Interactions between gut parasites of sheep can occur as a result of cross immunity, or physiological factors such as competition between established nematode species. Thus, existing infections with *O. circumcincta* interfere with the establishment of *H. contortus* in the same site\(^{(18)}\) and *T. vitrinus* situated downstream in the small intestine\(^{(19)}\). Clinically this protective effect may be more than offset by the increased pathogenicity of concurrent mixed infections. However, it could also account for some differences in the seasonal prevalence found in these species. Resistance to infection with heterologous nematodes (*H. contortus* or *T. colubriformis*) in flocks selected for genetic resistance (see details later), was not as great as for the homologous infection against which the selection was based.\(^{(12)}\)

It has been frequently noted that goats are more susceptible to gut parasites than sheep are. This fact has been associated with a paucity of mucosal mast cells and lower concentrations of sheep mast cell proteinase (SMCP) in does, as compared with ewes.\(^{(20)}\)

As with sheep, acquired immunity to ostertagiosis in cattle develops slowly after prolonged or repeated infections, and is more pronounced in degree and faster in adults. Sequential infections of *O. ostertagi* induce serum IgG, IgM and IgA antibody responses to infective larvae (L₃) antigens in calves, with secondary (amnestic) responses. It is believed that this parasite induces an immediate hypersensitivity response in the abomasal mucosa with increased production of IgE, leukotrienes and prostaglandins which are particularly elevated in Type I infections.\(^{(7)}\) Limited information is available on the nature of the antigens of *Ostertagia ostertagi*, many of which are cross-reactive with other gut parasites of cattle such as *Cooperia oncophora*.\(^{(21)}\)

*Sustainable control of internal parasites in ruminants*
Influence of genetic and physiological factors

A feature of ruminant immunity to gut nematodes is the large between-animal variation in response (see Chapter 13). Resistance differences between sheep breeds or within a breed undoubtedly have significant genetic components. The former may be due to innate or acquired differences but the latter appears to be largely a difference in acquired immunity. Attempts to find linkage between resistance and certain genes have been variable. Resistance to the *Trichostrongylus* selection flocks in Australia and New Zealand and the *Haemonchus* selection flock in Australia have an immunological basis. High responder animals have greater parasite recognition (enhanced cellular and humoral responses) and effector responses (elevated MMC and eosinophil numbers and release of mediators) than low responder animals.

Physiological status has a marked influence on host immunity. Male sheep have been shown to be more susceptible than females to experimental infections with *T. colubriformis*, *H. contortus*, and *O. columbianum*. The reasons are unknown. A temporary loss of acquired immunity to gut parasites around the time of parturition and during lactation has been described in ewes but also in other species such as cattle. This leads to increased worm burdens and excretion of faecal eggs. Ewes may be particularly susceptible to recrudescence of *O. circumcincta* infections late in pregnancy and lactating ewes are more susceptible to the establishment of *T. colubriformis*. Causes may include a change in hormonal status, stress, and under supply of nutrients such as protein (see Chapter 15). The resistance of young growing lambs is dependent on adequate dietary protein.

Vaccines

Until very recently the prospect of using vaccines to protect against helminth infections seemed very remote with rare exceptions. Early attempts to develop vaccines against gut parasites in ruminants utilized the approach successful in developing an irradiated larvae vaccine against *Dictyocaulis viviparus*, the lungworm of cattle, and *Ancylostoma caninum*, a hookworm of dogs. Although some reasonable protection was afforded against *O. circumcincta* with high doses of vaccine, the logistical problems of generating such large numbers of larvae that were needed for the procedure (10^4-10^5), and attendant
Table 12.1: Experimental vaccines used in protection studies. (Adapted from 30)

<table>
<thead>
<tr>
<th>Nematode</th>
<th>Component</th>
<th>Recombinant Ag</th>
<th>Vaccine protection %</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. colubriformis</td>
<td>• tropomyosin, L₃</td>
<td>+</td>
<td>43-51 worms (guinea pig)</td>
</tr>
<tr>
<td></td>
<td>• exsheathing fluid, L₃</td>
<td>-</td>
<td>&lt;50 worms, (guinea pig)</td>
</tr>
<tr>
<td></td>
<td>• excretory/secretory fluid, adult</td>
<td>+</td>
<td>&lt;50 worms, 30-60 FEC (sheep)</td>
</tr>
<tr>
<td></td>
<td>• secretory fluid (AChE)</td>
<td></td>
<td>31 worms, 0 FEC (sheep)</td>
</tr>
<tr>
<td>H. contortus</td>
<td>• exsheathing fluid, L₃</td>
<td>-</td>
<td>60 worms, 46-66 FEC (sheep)</td>
</tr>
<tr>
<td></td>
<td>• tropomyosin, L₃</td>
<td>-</td>
<td>54 worms, 46 FEC (sheep)</td>
</tr>
<tr>
<td></td>
<td>• gut H11, adult</td>
<td>+</td>
<td>78-95 worms, 78-99 FEC (sheep)</td>
</tr>
<tr>
<td></td>
<td>• intestine H-gal-GP, adult</td>
<td>+</td>
<td>54-93 worms, 58-97 FEC (sheep)</td>
</tr>
<tr>
<td>O. circumcincta</td>
<td>• excretory/secretory, L₃</td>
<td>-</td>
<td>58 worms, &lt;50 FEC (sheep)</td>
</tr>
<tr>
<td>O. radiatum</td>
<td>• excretory/secretory, L₃</td>
<td>-</td>
<td>99 worms, 75 FEC (calves)</td>
</tr>
</tbody>
</table>

FEC = faecal egg count

Concerns of distributing a refrigerated product discouraged further development. Modern methods of molecular fractionation, and more recently recombinant DNA methods, have allowed the production of highly specific vaccine preparations.

Experimental vaccines have been made from structural or excreted/secreted products of the adult parasite or infective larvae. Immunogenic fractions have been identified by reacting fragments of the parasite with immune serum from resistant animals. Some authors have termed these 'conventional' vaccines as compared to 'hidden' or 'concealed' vaccines that are made up from internal antigens of the parasite that are not usually recognised by the host’s immune system, under natural infection. Hence, conventional vaccines might be used to mimic natural infection and hidden vaccines provoke immunity to previously unrecognised (by the immune system) parasite antigens.

To date the most efficacious vaccines for H. contortus have been of the concealed variety, derived from part of the parasite gut, and now...
recognised to be peptidase enzymes. The H-gal-GP vaccine derived from parasite intestine\(^\text{29}\) affects worm establishment (especially females) and faecal egg output. These vaccines are injected systemically and it is believed that protection arises from increased levels of circulating antibody that binds to the parasite gut cells, following ingestion of blood by the abomasal nematode. Since the antigens of these types of vaccines are from the interior of the parasite, there is little chance of a memory response (boosting effect) due to natural infection. Parasites such as \textit{T. colubriformis} and \textit{O. circumcincta} which browse on the mucous membrane may not be so affected by such a vaccine, although it has been noted that these worms also ingest some (albeit smaller amounts) host antibody. So far no cross protection has been found between parasite species, for example against \textit{Nematodirus battus} or \textit{Ostertagia circumcincta} following \textit{H. contortus} vaccination with H-gal-GP.\(^\text{29}\)

A number of structural and excreted/secreted products from \textit{L}_3 or adult parasite stages have been used as vaccines. A major challenge remains as to the best way to apply them to the immune system so as to mimic natural infection and without inducing immune tolerance. This may necessitate a particulate oral formulation, possibly with enteric vectors and/or adjuvants.

As mentioned previously with natural infection, certain classes of animals (young, pregnant and lactating) are more susceptible to gut parasite infections, and it might be anticipated that their response to vaccination would be diminished.

Ultimately the question must be asked - What level of vaccine protection needs to be reached to have a substantive effect on parasite control? Total freedom from gut parasites may not be possible or indeed desirable (in order to keep restimulating host immunity), but recent computer simulations indicate that a protection level of 80% would be a very useful adjunct to current control practices.\(^\text{31}\)

In conclusion, the recent and exciting development of vaccines against ruminant nematodes means that field trials will soon be conducted. Refinement will hopefully lead to vaccines effective against several of the economically important worm species in New Zealand and which can be integrated into the current control measures. However, an improved knowledge of vaccine function will be necessary to optimise their usage in certain classes of livestock.
References


*Sustainable control of internal parasites in ruminants* 157


The selection of sheep for natural resistance to internal parasites

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Introduction

Selection for sheep that are resistant to nematode parasite establishment has been the subject of research in New Zealand and Australia for over twenty years. The objective of this research has been to provide an alternative to anthelmintics for internal parasite control. In practice few would envision the complete cessation of anthelmintic use, rather the rationale has been to reduce farmers reliance on chemicals as their sole form of parasite control. Breeding for host resistance is only one of several potential methods to reduce this dependence. This review will focus primarily on New Zealand host resistance research and its subsequent application in dual purpose sheep breeds.

Host resistance to internal parasite infection (i.e. the animal’s ability to prevent the establishment and growth of internal parasites) is largely thought to result from the animal developing an acquired immunity to the infection. The young lamb is highly susceptible to infection and only after exposure to infective nematode parasite larvae will it gradually develop an immunity. Individuals differ in their ability to develop resistance to internal parasite infection, both in the rate at which immunity develops and the final level of immunity (Fig. 13.1). The first and possibly most important point at which acquired immunity prevents the establishment of internal parasite infection is immediately after ingestion of worms at the infective L₃ stage of development. Establishment
rates decline from around 50% of ingested larvae in susceptible animals to less than 1% when they are resistant. Sufficient New Zealand information exists on development of host resistance to make modelling the process possible on a flock basis.\(^{(1)}\)

**FIG. 13.1:** Schematic diagram showing the difference between a resistant, normal and susceptible lamb in the development of immunity to internal parasite infection. From (2).

![Schematic diagram showing the difference between a resistant, normal and susceptible lamb in the development of immunity to internal parasite infection. From (2).](image)

### Previous research results

**Heritability**

Initially, New Zealand genetic research on host resistance concentrated on methods to measure host resistance to internal parasite infection, including the estimation of the heritability for traits such as strongyle faecal egg count (FEC), dagginess, and faecal consistency in lambs.\(^{(3,4,5,6)}\) Of the traits studied, FEC has become widely used as an estimate of host resistance due to its relative simplicity and ease of measurement. However, it has limitations, because of low repeatability and the inability for the counting to be automated. Based on 9 published estimates, the \(h^2\) of log transformed FEC has a weighted mean of \(0.23 \pm 0.02\).\(^{(7)}\) More recently, nematode antibody levels have been evaluated as indirect predictors of host resistance to internal parasites and found to also provide useful information.\(^{(8)}\) A modified test and sampling regime has subsequently been commercialised by AgVax and is marketed as the ‘Blood Antibody Host Resistance Test’.\(^{(9)}\)
**Breed differences**

An alternative to selection within breeds is to use existing genetic differences between breeds or strains. Unfortunately, information on the host resistance to internal parasite infection in existing or recently imported New Zealand breeds is sparse. Watson *et al.*\(^6\) showed that small but significant differences existed between different Romney strains. Several independent reports have suggested that the Perendale breed is significantly more resistant to internal parasite infection than either the Romney or Coopworth breeds\(^{10, 11}\) or the Dorset Breed.\(^{12}\) More recently, New Zealand results have also suggested that Texel crosses may be more resistant to infection.\(^{8, 13, 33}\) Finally, a small pilot study has suggested that the Wiltshire breed may have a higher host resistance, fewer dags and lower susceptibility to flystrike than either Romney or Merino breeds.\(^{14}\) However, the value of these observations to the New Zealand sheep industry is difficult to ascertain, as breed choice by commercial sheep farmers is determined by many factors other than susceptibility to internal parasite infection. In the medium term, genetic selection based on the considerable variability within breeds will have greater industry impact than any recommendation on breed substitution.

**Correlated traits**

Results from New Zealand lines of sheep selected for reduced FEC as lambs suggest that the trait is accompanied by reduced worm burdens of virtually all our most important ovine nematode species\(^{15}\) as well as reduced faecal egg counts in older animals.\(^{16}\) Until recently genetic correlations between FEC and production traits were poorly estimated. Available evidence suggested that its genetic relationship with wool production was antagonistic in the Romney breed under conditions where animals were exposed to moderate larval challenge levels.\(^{5, 17}\) More recently these results have been independently verified in Romney flocks selected for production traits\(^ {18, 19}\) and in Romney and Perendale flocks selected on the basis of FEC.\(^ {20}\) As any commercial genetic selection by ram breeders would be based on a combination of production and host resistance traits, it was important that genetic relationships be accurately defined. In order to do this an extensive series of trials on commercial Romney, Perendale and Coopworth ram breeding flocks were undertaken in partnership with the breeders involved commencing in...
1990. In total more than 30,000 progeny of 882 sires were measured for host resistance to internal parasites and production traits. These results when combined with results from other smaller studies suggested that a significant unfavourable genetic correlation does exist between FEC and hogget fleece weight with an estimate of 0.13 ± 0.05, but the correlation with live weight is smaller and non significant. For this reason most New Zealand researchers agree that selection for improvement of production and host resistance should be on the basis of a combined index in order to make efficient progress. Unfortunately the genetic antagonism with productivity has received the unwarranted perception by many that it presents an insurmountable impediment to the selection of host resistance by the industry. However, it should be viewed in its proper context. For example, the magnitude of the genetic antagonism is a third to a half of that between lean and fat weight in sheep, and this has not impeded successful industry adoption of a lean growth index by New Zealand ram breeders.

**Effect of environment on genotype ranking**

A valuable additional benefit of the research on breeders properties was that it also allowed robust estimates of the magnitude of genotype by environment interactions (GxE) for host resistance to nematode parasites and production traits. A fundamental assumption in most animal improvement schemes is that the true breeding value of an individual, measured at a particular time and location, would be identical if it were measured in another environment. In the case of the host resistance traits, it was already known that there was large variation in parasite species and larval challenge between farms due to geographical location and management practices and it was feared that this could also influence individual genetic ranking. The results suggested that GxE effects were highly significant for many traits including those related to host resistance, but they were minor relative to the amount of genetic variation that was independent of environment. This was consistent with evidence from an earlier small scale study involving 26 sires and two locations. This means that breeders and commercial sheep farmers can select rams based on host resistance breeding value confident that they should perform acceptably on their property.
**Dags**

Many farmers and breeders believe that the daggy animals in their flock indicates those genetically susceptible to parasites and that the two traits are the identical. Research results suggest that this is not the case. The situation is more complex and it is better to consider host resistance to nematode parasites and dagginess as two separate traits, each with their own economic benefits.

Dagginess causes economic loss via increased crutching of animals, increased susceptibility to flystrike, and downgrading of wool and slaughtered lambs. The potential losses have increased since the introduction and spread of the Australian green blowfly (Lucilia cuprina) to New Zealand, and increasingly strict requirements on meat and wool insecticide residue levels have also restricted chemical treatment options. It has long been known that high levels of parasite challenge in the flock are often associated with increased dagginess. Unfortunately, dagginess can be caused by many other factors, including the type of feed, making it an unreliable indicator of parasite status in a flock.

A summary of 6 published New Zealand studies (CA Morris, pers. com.) suggests that the mean heritability of the dagginess was 0.24 ± 0.02 with a repeatability of 0.44. This suggests that selection for reduced dagginess is possible and that using repeated measures of the trait will provide additional progress. The mean genetic correlation between FEC and dagginess when animals are grazed in the same environment was -0.14 ± 0.11 which suggests that selecting for lower FEC will result in a moderate increase in dagginess if parasite challenge levels remain unchanged i.e. exactly opposite to what many farmers would expect! These results are supported by correlated responses in the Wallaceville and Ruakura Romney selection lines, where the low FEC lines have increased dagginess relative to the high FEC lines when grazed together under the same larval challenge. As a possible explanation for this phenomenon Bisset et al. suggested that in some cases selecting for low FEC may have boosted the hypersensitivity reaction of the immune system to larval parasite challenge. This type of host response could be expected to result in increased gastrointestinal motility and passage rate in the more resistant animals while decreasing water absorption. Correlations between dag score and faecal consistency support this hypothesis as does a wide variety of immunological evidence.
In practice the situation is even more complex because grazing a flock of resistant animals by themselves has been shown to result in markedly lower pasture parasite larval challenge. In theory this might be expected to reduce dagginess, although the sum of these effects is difficult to predict and more work is required. Experiments are currently underway to examine this situation more comprehensively (D Leathwick, pers com.). However, it should be stressed that the genetic relationship appears to be weak even when animals are exposed to the same level of pasture challenge. Therefore both traits can be improved simultaneously with little loss of progress in either trait.

Given these facts, it is suggested that in the interim breeders should use independent culling levels i.e. select on an index of production and host resistance traits such as the WormFECT™ desired gains index (see later) with additional phenotypic culling of daggy animals. In the longer term index selection would be more efficient once appropriate methods of incorporating this trait can be devised.

**Productivity under challenge and resilience**

A possible alternative to selecting for increased host resistance, is to select for animals which require less drenching to maintain acceptable productivity. This trait has sometimes been referred to as resilience but is more correctly productivity under challenge. This trait has been has been investigated by New Zealand workers and this work has been recently reviewed. The term resilience was originally coined by Riffkin and Dobson to describe the ability of the host to withstand the pathogenic effects of internal parasite infection rather than limit the infection itself. In its broadest sense measurement of resilience includes all clinical symptoms, including reductions in live-weight gain, wool growth, prolificacy, survival and increases in scouring and dagginess due to internal parasite infection. Its measurement also implies that individuals or their relations are exposed to contrasting environments, one parasite free and another with a known level of larval challenge in order for the difference in production in the two environments to be estimated. However, this makes resilience extremely difficult to measure and only one study has been undertaken. Their results suggested resilience had a low heritability and was positively correlated to resistance. This appears to be consistent with
results obtained in some overseas studies under conditions of severe natural challenge, particularly as it affects survival.\(^{(29, 30)}\)

In practice ram breeders want animals to perform at a high level no matter what the level of parasite challenge. The search for a simple solution led to the New Zealand evaluation of a variety of ‘production under challenge’ criteria including the number of individual drenches required to maintain productivity based on visual criteria (scouring, live weight and dagginess) or determined by live-weight gain during challenge.\(^{(4, 31, 32)}\) Traits derived from these criteria have been shown to be low to moderately heritable (0.10 to 0.19) with some indications that the heritability may be related to the level of internal parasite challenge. In addition they were favourably correlated to dag score, autumn live weight and hogget fleece weight, but showed no significant correlation with host resistance. The value of these criteria is still uncertain and further study is continuing. In the meantime however, there is no recommendation for farmers to use this approach. Phenotypic selection would be unlikely to give satisfactory genetic progress due to the low heritability and in addition it would tend to have a bias towards early born lambs, singles rather than twins and lambs born from ewes in their second or third parity unless correction was made for these effects. The selective drenching procedure required also necessitates regular flock inspection and complicates the calculation of breeding values for productivity traits. There is therefore general agreement that at present it is more sensible to select animals on the basis of an index of productive traits in an environment of moderate internal parasite challenge and host resistance measurements coupled with appropriate economic weightings of each trait in the breeding objective.\(^{(30)}\) This is the approach used by Nemesis and WormFECT\(^{\text{TM}}\). However, in defence of productivity under challenge criteria, they are probably more closely related to Nemesis and WormFECT\(^{\text{TM}}\) selection indices then either for productivity selection under conditions of frequent anthelmintic treatment or selection solely for host resistance, and indeed research results have already shown a promising reduction in drenching frequency in experimental selection lines.\(^{(53)}\)

**Selection for host resistance in commercial flocks**

The majority of the commercially available techniques for measurement of host resistance are described in detail in the WormFECT\(^{\text{TM}}\) breeders manual.\(^{(2)}\)
Briefly, three protocols are presently recommended: the 'standard' of two field challenge regime, where lambs are drenched at weaning, grazed on contaminated pasture until FEC levels rise to 800 epg, and then are individually sampled with strongyle (FEC1) and *Nematodirus* (NEM1) faecal egg count measured. The animals are then drenched and subjected to a second challenge and FEC2 and NEM2 recorded (Fig. 13.2). Typically the first challenge is terminated in mid to late summer, while the second challenge is terminated in autumn. An additional recommended practice is to undertake a drench check 7-10 days after drenching to ensure that the anthelmintic has been administered correctly and is effective. In the brief protocol, animals are subjected to the same protocol as the 'standard’, but are sampled at the end of the second challenge, with two samples collected on different days i.e. FEC2, NEM2, FEC2b, and NEM2b. The third protocol exposes the animals to a natural field challenge of parasite larvae, with a serum sample collected between 7 and 9 months of age that is analysed for host antibody levels to *T. colubriformis* L₃ excretory/secretory products (ELFC2). This last measurement is commonly known as the AgVax ‘blood antibody host resistance’ measurement.

**FIG. 13.2:** Summary of the standard host resistance to internal parasite challenge protocol. From (2).

Regardless of the protocol used, breeding values (BV) for host resistance are expressed in terms of a FEC BV% and calculated for host resistance in lambs during the summer (FEC1), autumn (FEC2) and in adult ewes (AFEC). Faecal egg count is log transformed prior to analysis and breeding values are obtained by back transformation and expression as a percentage difference from the average flock breeding value. The presentation method is to aid interpretation.
by breeders. For example a FEC2 BV% of -20 means that an animal has a breeding value for FEC as a lamb in autumn 20% below the average of the flock. In this case negative BV% are better.

Currently, estimation of WormFECT™ breeding values for production and resistance traits are undertaken using a multiple trait, repeated measure, animal model BLUP evaluation. This allows across sex and year evaluations, with associated estimates of genetic trends for individual ram breeders. Where breeders have genetic links between their flocks then across flock analyses and genetic trends can also be provided.

**Benefits of selecting for host resistance: desired gains index**

There has been much scientific discussion regarding the financial return from selecting for host resistance to internal parasite establishment. The approach WormFECT™ has taken is that benefits of host resistance to internal parasites are indirect, resulting from reduced pasture contamination,\(^{22}\) and the approach is similar to that outlined by Woolaston.\(^{34}\) Preliminary estimates of the benefits (relative economic value of resistance) have been obtained using epidemiological models available under likely New Zealand conditions.\(^{35}\) The results suggest that including host resistance traits in the breeding objective will provide significant benefits with a substantial proportion resulting from reduced ewe contamination in spring. When these economic values are combined with the genetic estimates discussed previously into a selection index the optimal solution can be determined. The predicted genetic gains from using these indexes are considerably easier to comprehend than the genetic parameters themselves. In fact the initial predictions suggest that the overall economic benefit of including host resistance may be up to 20% greater than the current NZABT Animalplan index and that even if the benefits of host resistance were only half that expected, including selection for host resistance in the selection index would still provide greater returns than the existing index. Because there is no estimate of the accuracy of these epidemiological estimates, a desired gains index, which will produce similar responses, is being used in the interim while experiments to validate key parameters of the model are undertaken.
TABLE 13.1: Estimates of the changes that would occur using a desired gains index to increase host resistance, while also improving production, relative to the present Animalplan dual purpose objective. It assumes that both male and female lambs are measured for host resistance using the standard protocol and that all animals in all years are challenged similarly i.e. it does not include the additional gains in productive traits and observed FEC values due to alterations in the epidemiological feedback loop of the parasite lifecycle. From (32).

<table>
<thead>
<tr>
<th>Trait</th>
<th>Units</th>
<th>Animalplan index (A)</th>
<th>Desired gains index (B)</th>
<th>B/A %</th>
</tr>
</thead>
<tbody>
<tr>
<td>LW8</td>
<td>kg</td>
<td>+0.408</td>
<td>+0.307</td>
<td>75</td>
</tr>
<tr>
<td>FW12</td>
<td>kg</td>
<td>+0.039</td>
<td>+0.028</td>
<td>72</td>
</tr>
<tr>
<td>NLB</td>
<td>LB/EM</td>
<td>+0.012</td>
<td>+0.012</td>
<td>94</td>
</tr>
<tr>
<td>FEC2</td>
<td>%</td>
<td>+1.8</td>
<td>-3.8</td>
<td>-</td>
</tr>
<tr>
<td>Adult ewe FEC</td>
<td>%</td>
<td>0</td>
<td>-4.0</td>
<td>-</td>
</tr>
</tbody>
</table>

The results from the WormFECTM desired gains index with a standard two challenge protocol are shown in Table 1. Economic progress for autumn live weight (LW8), fleece weight (FW12) and prolificacy (NLB) will be about 80% of what is presently is presently achieved using the NZABT Animalplan dual purpose index, but instead of FEC slowly increasing it will decrease by about one third the potential rate (i.e. if all selection pressure was placed solely on reducing FEC). This reduction in internal parasite susceptibility will bring benefits from a lower loss in growth and wool production due to reduced challenge from internal parasite larvae on pasture, and/or reduced drenching costs. We expect that these benefits will more than compensate the reduced genetic progress in production traits, when anthelmintics are used sparingly to delay the emergence of anthelmintic resistance (i.e. lambs 3-5 times in the first year of life, with ewes not drenched in normal circumstances).

Industry adoption of selection for host resistance

As a consequence of research into breeding for host resistance to nematode parasites, two commercial stud sheep breeders in New Zealand approached Ruakura and Wallaceville personnel, in 1987 suggesting that they wanted to include breeding for reduced FEC in their long-term breeding objectives. (36, 37)
The data collected from one of these flocks was subsequently utilised by the Animalplan, or the New Zealand Animal Breeding Trust as it is now known, to establish FEC as a 'trait under development'. This process commenced in 1989.

At this stage the genetic correlations of FEC with production traits were inadequately defined so in 1990 the extensive series of trials on commercial ram breeding flocks described previously was undertaken in partnership with the breeders involved. The results have since permitted the estimation of genetic parameters involving FEC, host antibody levels to nematode parasites, and the production traits to a precision suitable for the inclusion of these traits as an indicator of host resistance to nematode parasites in dual purpose sheep breeding indices. Near the completion of this work it was realised that selection for host resistance by breeders needed a single body to provide advice on challenge protocols, arrange faecal egg counting and antibody estimation, calculate of breeding values and also provided general advice on breeding matters. This resulted in the setting up of WormFECTM in late 1994 including the production of a breeding manual for this trait. Subsequently, the initial industry penetration by WormFECTM was estimated by McEwan et al. to be close to 15,000 animals evaluated annually, the majority ram lambs that are retained through winter and subsequently sold. This equated to approximately 10% of annual dual purpose ram sales. Since that report this penetration level has been maintained.

On reflection a major factor in the rapid industry uptake of this technology was that genetic parameters had been derived from work conducted on the ram breeders properties. This made the breeders familiar with the technology during the development and evaluation phase and ensured that the measurement protocols were sufficiently flexible and practical for industry adoption. Another factor has been the availability of advanced genetic analyses not only for host resistance but also production traits as part of the desired gains index development. Currently, issues limiting further penetration of the industry are the lack of robust relative economic values for host resistance and the cost of measurement. In the longer term cost of measurement will decline in importance as across flock and year breeding values will enable commercial sheep farmers to accurately determine the benefits of genetic improvement on their property. This is expected to lead to greater ram price differentiation on the basis of breeding values than currently exists. Similarly,
considerable research is underway to derive accurate economic values for host resistance and the first phase of this work is hoped to be complete by June 1998.

**Time scale**

Selection for host resistance to internal parasites is subject to the same restrictions as any sheep genetic selection programme. The salient facts are the selection pressure applied and the variability and heritability of the trait. Based on the current industry structure it takes around 8 years for the benefits of selection in the stud flock to be fully expressed in the commercial tier, with around one half those benefits available after 3-4 years. Given that using the desired gains index in the ram breeding flock will decrease FEC by 4% per year (Table 13.1), then approximately 20 years will be required before the commercial animals reach an interim target of a 50% reduction in FEC under conditions of constant challenge. In practice the actual reduction will be greater than this due to the feedback effect reducing pasture larval contamination levels as well. However, it demonstrates that the ram breeder has to anticipate industry trends far into the future. This is a difficult exercise given the problems of predicting the rate of anthelmintic resistance emergence, consumer concerns regarding residues in foods, and how these impact on the future economic value of host resistance. An additional complicating factor in any analysis is risk. Most ram breeders and their clients are risk adverse and so place additional value on any procedure that reduces risk over and above the future economic benefits.

Potential new aids to selection may reduce this time frame and make it less expensive and more predictable. Some breeders have been including FEC in the selection programmes for nearly a decade and estimated genetic trends indicate that they have made significant progress while concurrently increasing their flocks' productive abilities. As the level of flock resistance increases the economic value of further change will decrease. In the longer term the optimum solution may be the stabilisation of host resistance at a new and higher level.
Potential new aids to selection

*Phenotypic markers*

Phenotypic markers are measurements that are both heritable and genetically related to the breeding objective. These are often called selection criteria or predictor traits to distinguish them from the actual breeding objective. A good phenotypic marker has several of the following advantages: it can be measured in young animals, is easy and cheap to measure, highly repeatable, and heritable and has a high genetic correlation with the breeding objective. Common examples currently used in New Zealand animal breeding are selecting on: live weight to improve carcass weight, hogget fleece weight to improve adult ewe fleece weight and ultrasound fat and muscle depth measurements to increase carcass lean and decrease carcass fat content. All the currently used measures of host resistance fall into this category, because both FEC and AgVax antibody level are indirect measures of the actual trait being selected for namely the number of eggs shed by the animal. In practice FEC and the number of eggs shed by the animal are considered equivalent.

The value of a phenotypic marker depends on the following equation:

\[ Q = r_g \cdot \frac{h_{pm}}{h_{bo}} \]

where \( Q \) is the relative efficiency, \( r_g \) is the genetic correlation and \( h_{pm} \) and \( h_{bo} \) are the square root of the heritability of the phenotypic marker and breeding objective respectively. Good phenotypic markers have a high heritability relative to the breeding objective and a high genetic correlation. Possible phenotypic markers for host resistance to nematode parasite infection has recently been reviewed by. They examined published and unpublished material for a variety of potential phenotypic markers of host resistance to nematode parasites including: mucosal granulocyte numbers, blood eosinophil levels, mucosal mast cell numbers and their products, circulating antibody levels and T cell subset analysis. While variations in all of these traits have been reported as being associated with host resistance, only a small fraction meet the majority of the criteria required for a suitable phenotypic marker. The most intensively studied phenotypic criteria have been antibody assays similar to the AgVax blood antibody host resistance test. These have the advantage that samples can be easily collected and stored, the measurements

*Sustainable control of internal parasites in ruminants*
can be automated and measurements are highly repeatable over the preferred 6-9 month of age sampling period. They also have moderate to high heritability levels and moderate genetic correlation with FEC. It is hoped that the current antibody test can be improved and made more specific. Development of entirely new markers will depend on advances in our understanding of the immunological basis of host resistance.

**Genetic markers of resistance**

Substantial work is currently underway to investigate the molecular genetic basis of host resistance to internal parasites in an attempt to identify quantitative trait loci (QTL). These are genes which have a major effect on the trait of interest. Large QTL effects are often called major genes. No practical applications of this technology for host resistance traits are yet available for sheep breeders and it will be at least several years before this technology can be applied in flocks selecting for resistance. However, based on the results of these techniques in human medicine, there is considerable optimism that the approach will repay the research investment in the longer term. The following describes work underway, results to date and how ram breeders may use the results of this technology.

Three approaches are currently being used to identify major genes affecting host resistance to internal parasites namely ‘mixed inheritance model’ analysis, ‘candidate genes’ and ‘genomic scanning’. Each method has its strengths and weaknesses and in practice a combination of all three procedures is commonly used.

(a) *Mixed inheritance model analysis*

The first method, examines existing pedigree structures and individual performance in an attempt to identify if there are major genes segregating (i.e. whether an offspring inherits the QTL or not) in the population. The procedure undertakes this by disentangling major gene effects from both non genetic effects, and the effects of the many genes with small effects on the trait. These techniques are currently undergoing rapid development, and while computationally demanding are beginning to show promise in identifying major genes for disease resistance in farmed species. Kerr *et al.*\(^{(39)}\) have identified a major gene for tick resistance in cattle and more recently McEwan
et al.\textsuperscript{(40)} have identified what appears to be a recessive gene for low strongyle faecal egg count in Romney, Coopworth, and Perendale flocks. The magnitude of the effect is equivalent to the homozygous recessive animals shedding around 30\% of the eggs of the other genotypes. In addition a dominant gene for low \textit{Nematodirus} faecal egg counts has also been detected in Coopworths. These results need to be independently verified by molecular techniques, but they are of a magnitude that suggests that identification and characterisation of these loci may result in useful novel methods of internal parasite control. An important aspect of this work is that in order for these QTLs to be identified, host resistance traits need to be recorded in large numbers of animals. This means that the data being collected by Nemesis in Australia and WormFECT\textsuperscript{TM} in New Zealand will be invaluable for future studies using these methods.

(b) Candidate genes

The second method of identifying major genes involves a candidate gene approach where individual loci (i.e. the gene) thought to affect the trait are examined in order to detect variation in the DNA sequence (i.e. polymorphisms or commonly called alleles). Subsequently the association between the number of copies of the specific polymorphism that an animal carries and its host resistance are then examined. Using this approach Gulland \textit{et al.}\textsuperscript{(29)} have detected an association between the ADA locus located on chromosome 13 and host resistance to both FEC and survival in Soay sheep. Similarly other workers\textsuperscript{(41, 42, 43)} have detected an association between an allele located in the ovine major histocompatibility complex (MHC) located on sheep chromosome 20. This region contains many genes integral to the operation of the immune system, particularly those which present foreign material to cells which mount a subsequent immune response. This method has been successful and may only require a small investment when good candidate genes are known. However, it does not provide a general method to identify which important genes are involved.

(c) Genomic scan

The third method uses a technique called a genomic scan and has only become possible since a map of the sheep genome detailing the location of highly polymorphic ‘marker’ loci\textsuperscript{(44)} has become available. This technique commonly
generates large half sib pedigrees from sires thought to be segregating for the trait of interest. The advantage of the technique is that it can systematically exclude regions of the genome as well as identify quantitative trait loci. Internationally, at least 4 genomic scan experiments are searching for host resistance QTLs to internal parasites in sheep. One of these is being undertaken in New Zealand and preliminary results for certain regions of the genome have now been published.\(^{(45, 46)}\) While the regions published to date have identified no useful loci, the authors note that apparent segregation has been detected in other regions. The disadvantage of this technique is that the actual locus involved is not identified.

(d) Use of genetic markers

After QTL's have been detected further work will usually be required before the results can be used by ram breeders. Initially, the QTL region may not be well localised i.e. spanning a large section of a chromosome. To more closely localise the region of interest additional polymorphic markers may need to be developed within the region and the results verified in the commercial population to be selected. If this work is successful, marker assisted selection (MAS) may become a viable addition to existing genetic tools, where closely bracketing marker loci are available and sufficiently polymorphic, without the need for identifying the actual gene involved.\(^{(47)}\)

The economic benefits of MAS will depend on several factors including the value of the trait, ease and age of measurement, the inheritance pattern of the QTL identified, the nature of the bracketing loci available and the breeding structure. Selection for host resistance to internal parasites is a good candidate for this selection technique, because existing methods involve exposing the animal to disease with consequent production losses and stock management difficulties. In addition faecal samples are labour intensive to collect, highly variable and expensive to analyse.

Conclusion

Selection for host resistance to internal parasites is now widely practised by New Zealand ram breeders as part of their overall genetic improvement strategy. The quantitative genetics of the trait as far as it impacts on its commercial implementation are now well researched. However, research into quantifying
the economic value of the trait and alternative selection predictors is still required and in progress. Similarly, a large amount of research is needed to understand the immunological basis of host resistance. This work may also provide alternative internal parasite control strategies.

The preliminary results obtained from molecular genetic work suggests that new aids for selection for host resistance to nematode parasites may emerge in the near future. It is expected that these aids will enhance the rate of genetic progress and reduce production losses and ethical concerns associated with current challenge techniques. However, for these aids to be utilised effectively they will need careful integration into existing performance recording schemes and require well designed breeding structures if their potential is to be fully realised. Most likely this structure will be some variation of an extended nucleus breeding scheme. That these breeding structures exist in the future presupposes that robust estimates of the economic value of host resistance to nematode parasites have also been derived. Without this foundation, industry uptake is expected to be slow and sporadic. One of the primary reasons why WormFECT™ was initiated by AgResearch was to support and develop performance recording for host resistance to internal parasites prior to the availability of marker assisted selection.

Summary

Selection for host resistance to internal nematode parasites is possible and practical systems involving natural parasite challenge have been devised for industry use. Selection on the basis of a desired gains index, comprising both resistance and production traits, has been available to commercial ram breeders in New Zealand via WormFECT™ since 1994. Currently, more than 50 recorded flocks use the system. A similar service, called Nemesis, is available in Australia. Genetic research is now directed at identifying genetic markers linked to genes with large effects on host resistance to internal parasites. Initial results suggest that these genes exist, but it will be some time before their commercial use becomes practical. The nature of nematode parasite infection, with its lifecycle involving both larval stages on pasture and reproductive stage in the animal, results in a feedback loop. This means that evaluation of the benefits of selection for host resistance is difficult, because estimates of...
amplification effects via feedback loop and individual versus flock benefits are required. Based on experimental results to date, it is expected that the majority of the benefit of selecting for host resistance will be indirect, via reduced pasture contamination. This reduced contamination should benefit all of the animals in the flock, not just the resistant individual.

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Effects of diet on gastrointestinal nematode infection in ruminants

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Introduction

Infection with gastrointestinal (GI) helminth parasites results in significant production losses in grazing ruminants, particularly in young and in periparturient sheep, goats and cattle. Current control relies largely on chemotherapy in combination with grazing management. However, due to the increasing prevalence of nematodes resistant to drugs and increased concern about pesticide residues in the food chain and general environment, reliance on anthelmintics is becoming precarious. For this reason, non-chemical parasite control strategies including the use of vaccines, resistant host genotypes, biological control and/or nematode growth regulators are being sought. Better integration of existing and new anthelmintics with grazing management can also be expected.\(^\text{1, 2}\)

Another important factor which has long been considered to influence the host/parasite relationship and the impact of GI nematode infections is host nutrition. Improved nutrition of sheep has been known to reduce production losses and mortality rates associated with parasitism for almost a century. Improvements in nutrition were considered as a key control measures for trichostrongylosis,\(^\text{3}\) and Whitlock and colleagues\(^\text{4}\) suggested that haemonchosis in sheep is ‘fundamentally a nutritional disturbance’. Hunter\(^\text{5}\) suggested diet supplementation as a method to prevent the establishment of helminths or as a cure for diseases caused by helminths.

In discussing the effects of diet on GI parasitism, a good understanding of the pathophysiological consequences of GI nematode infections for the ruminant host is important. The effects of GI parasites on host pathophysiology are summarised in Chapter 7, with further details to be found in recent...
reviews. The present review will discuss the important established interactions between ruminant nutritional status and GI nematode parasitism. There are effects of nutrition on the ability of an animal to prevent establishment and/or subsequent development of a worm infection, as well as effects of diet on the metabolic consequences of parasitism for the host. The ability of the host to maintain a relatively undepressed level of production during a parasite challenge is referred to as 'resilience'. The ability of an animal to prevent establishment and maintenance of a parasite population in the GI tract is referred to here as 'resistance'. Effects of host nutrition on resilience and resistance will be reviewed here, with an emphasis on energy and protein nutrition. Areas of inadequate understanding of how host nutritional status affects responses to GI parasitism will be identified.

**Host nutrition and resilience to parasitism**

*Studies with young housed ruminants*

It is perhaps not coincidental that the young lamb, which has the highest requirement for metabolisable protein (MP) relative to metabolisable energy (ME), also has the least resistance and resilience to GI parasites. Bown and colleagues attempted to distinguish between the effects of supplementary protein versus energy in lambs trickle infected with *Trichostrongylus colubriformis* and given a diet of chopped ryegrass/white clover hay (12% CP). Protein was given as casein (50 g/day infused into the abomasum) while energy was given as glucose (per abomasum). Infected control lambs deposited body energy and protein at 53% and 27% of the rate in uninfected sheep. Infusion with casein enabled infected sheep to maintain the rate of energy and protein deposition of uninfected controls (109% and 122% respectively), but glucose infusion produced relative rates of deposition of only 90% and 60% respectively. This experiment confirmed that GI nematode infections induce a protein rather than an energy deficiency, and suggested that complete resilience may be achieved with protein but not with energy supplementation.

Young sheep trickle infected with *Haemonchus contortus* and given a low protein concentrate-based diet (dietary CP 9%) suffered more pronounced pathophysiological consequences, including effects on live-weight gain (LWG) than sheep supplemented with soyabean meal (17% CP in total diet; see
references 13 and 14). Both diets supplied adequate ME and the low- and high protein diets provided 100% and 175% of the predicted MP requirements, respectively.\(^{14}\)

In some of our own studies\(^{15}\) we observed a 43% lower rate of LWG in young Merino sheep trickle infected for 20 weeks with \textit{T. colubriformis}, compared with uninfected controls (basal diet low quality chopped oaten hay containing 7% CP). In sheep supplemented with 50 or 100 g/day fish meal (providing 33 or 65 g additional CP), infection reduced LWG by only 18% and 11%, respectively. Evidence for a change in protein demand with parasitism also comes from recent diet selection studies. Sheep which were trickle infected with \textit{T. colubriformis} selected a diet with increased protein concentration,\(^{16}\) although this did not appear to meet the increase in protein requirement.

The rate of LWG of young goats infected with \textit{T. colubriformis} was not affected by supplementation of a hay diet with 2% urea alone, but was increased when urea and cottonseed meal were given.\(^{17}\) This suggests that although rumen degradable protein supply from the basal diet was not limiting, that either total microbial protein synthesis or synthesis of a specific amino acid was inadequate.

Few studies have examined the effects of mineral status on resilience to GI parasitism. The impairment in phosphorus (P) absorption in animals infected with intestinal nematodes suggests, theoretically, that dietary supplementation with P will be of little benefit.\(^{7}\) Nevertheless, a 40% increase in cumulative LWG in young sheep infected with \textit{Trichostrongylus vitrinus} for 13 weeks has been achieved by increasing the P content of the diet from a low 1.9 to a more normal 2.8 g/kg DM.\(^{18}\)

**Studies with grazing sheep**

Few studies have critically assessed the complex interactions between host nutrition and GI parasitism with grazing ruminants. Recent Australian and New Zealand work suggests that grazing of different forage species may result in different parasitological outcomes. The question as to whether this is due to nutritional attributes of the plant and/or attributes which changed the larval intake of the grazing animal are not yet well established. For example, the effects of parasitism on carcass weight gain in lambs grazing chicory were
insignificant, while in lambs grazing cocksfoot, tall fescue, lucerne or ryegrass, carcass gain was reduced by 30 to 80%.\(^{(19)}\) Differences in larval populations maintained on different plant species may have contributed to this result and there is clear evidence for variation between plant species in their ability to provide an environment conducive to larval survival and migration, and therefore variation in infectivity of swards comprising different plant species.\(^{(20)}\)

In a series of recent studies we assessed the interactions of dietary supplementation and degree of nematode control on production responses in young grazing Merino sheep, and on nematode population dynamics. In the first study,\(^{(21)}\) supplementary feeding with sunflower meal appeared to be more effective than treatment with a 100-day albendazole controlled-release capsule in reducing production losses attributable to nematode infections. In a further study,\(^{(22)}\) young Merino sheep were exposed to natural as well as artificial infection (6000 \(T\).colubriformis and 2000 \(H\). contortus every fortnight). The animals received small amounts of supplements based on fish meal (38% CP), sunflower meal (24% CP) or oat grain (8% CP) for 14 or 28 weeks. Unsupplemented control groups which were infected or kept essentially parasite-free were included also. Again, supplementation overcame the impact of nematodes on LWG, and supplementation with fish meal was particularly effective.\(^{(22)}\) These studies demonstrate that the resilience of young grazing sheep can be enhanced by appropriate supplementation, which is in agreement with results from pen studies.

Currently, dietary supplementation is more expensive than treatment with anthelmintics. Cost-benefit analyses for a whole pastoral production system will require further applied research to minimise costs of effective supplementation. In many low cost grazing systems reliant on low quality forages, maximising the production of microbial protein using urea and/or local by-products containing cheap rumen degradable protein must be an important strategy. However, the evidence suggests that the greatest responses have been achieved with protein supplements which avoid the inefficiencies of rumen fermentation (so-called bypass protein). This may point to a need for improvements in the supply of specific limiting amino acids.

Consumption of high quality fresh pasture with a high CP content normally results in the loss of considerable amounts (30-40%) of dietary protein upon...
passage through the rumen. The extra protein which has been shown to overcome the effects of *T. colubriformis* on performance of young sheep (see reference 12) could be provided from fresh pasture if the net loss of protein to the animal could be avoided. Condensed tannins reduce protein losses in the rumen and increase duodenal protein supply by forming insoluble protein complexes in the rumen.\(^{(11)}\) Pasture species with a useful tannin content may reduce the negative effects of GI parasitism on the host.\(^{(23, 24)}\) For example, parasitism reduced LWG by 49% in sheep grazing lucerne or ryegrass/clover, but by only 37% in sheep grazing forages containing tannins such as Maku lotus or sulla. Worm burdens tended to be lower in sheep grazing the tannin-rich forages.\(^{(23)}\) Further research is required to assess whether these results are due to changes in host resilience or resistance due to increased protein supply, or due to direct effects of tannins on the parasite, or due to differences in larval distribution and availability on plants.

**Host nutrition and resistance to parasitism**

Sheep may not develop full resistance to GI parasites until 8-24 months of age. There is large inter-animal variation in the rate of development of resistance, both within the same breed and between breeds, which appears to have a strong genetic basis. In addition, there are strong age effects and, as will be examined later, nutritional effects. The acquired immune response is an important component of host resistance to GI parasites. However, acquired immunity is complex and poorly understood (see Chapter 12). Different components of an acquired immune response appear to target different phases of parasite development within the host, starting with the prevention of establishment of incoming infective larvae or an arrested development of these larvae and/or stunting as adults. Fecundity of female worms may also be reduced and the final manifestation of acquired immunity is the rejection of established worms. Most work on the influence of diet on the development of immunity or resistance has been done with young susceptible sheep. Studies with other young ruminants or with periparturient ruminants are uncommon. Both will be reviewed here.
Studies with young ruminants

Nutritional status, and particularly dietary protein supply, affects the rate of acquisition of resistance to GI parasites in young ruminants, as well as other species. Generally speaking, the evidence is for an effect of dietary protein supply on the ability of the host to acquire immunity during challenge, rather than in providing a greater innate or initial immunity. In sheep infected with *H. contortus* and given low or high protein diets (9 vs 17% CP) faecal egg counts (FEC) from week 5 of infection onwards averaged 27,000 and 9000 eggs per gram despite similar feed intake. Sheep given the low protein diet carried almost three times as many worms at the end of the experiment.\(^{(13)}\) On the other hand, a related study using the same infection protocol and the same diets resulted in similar worm burdens after 10 weeks, irrespective of dietary protein concentration.\(^{(14)}\)

In sheep given pasture hay and trickle-infected with *T. colubriformis*, infusion with casein or glucose did not affect daily faecal egg excretion or worm burden compared with control sheep after 6 weeks of infection.\(^{(12)}\) However, worm burden was 50% lower after 12 weeks in sheep infused with protein, compared to control sheep or sheep infused with glucose.\(^{(12)}\) Similarly, casein infusion also accelerated the development of immunity by young sheep to *Ostertagia (Teladorsagia) circumcincta*.\(^{(25)}\) While supplementation of young sheep on a hay diet with small amounts of fish meal had no effect on the number of *T. colubriformis* after 5 or 10 weeks of infection, it enhanced the subsequent rate of worm expulsion. This was associated with elevated levels of circulating eosinophils and intestinal mast cell protease concentrations.\(^{(15)}\) Young sheep (2-6 months) given a low protein diet (11% CP; based on lucerne hay and concentrate) showed lower resistance to parasites than sheep given a high protein diet (20% CP; with concentrate containing soyabean meal and meat/bone meal), but diet had no effect in older sheep (7-12 months; see reference 26).

The results from the studies discussed above all suggest that in young sheep, nematode establishment was not affected appreciably by diet. In contrast, the rate of parasite eradication was enhanced to varying degrees in the ‘better fed’ animals. However, studies with grazing animals are more conflicting. Protein supplementation reduced FEC by over 50% in two studies with young
grazing sheep which were not or only minimally treated with anthelmintic.\textsuperscript{(21, 22)} However, worm burden was only assessed in the former study but found not to be affected by supplementation.\textsuperscript{(21)} Further studies with grazing animals are clearly required. Similarly, there is little information for young cattle and goats and the limited results are equivocal, so that further work is required in this area (see reference 11).

Few studies have examined the effects of mineral status of the host on development of resistance to GI parasitism. More work in this area is needed. Increasing the P content of the diet from 1.9 to 2.8 g/kg DM reduced the worm burden of young sheep which were trickle infected with \textit{T. vitrinus}, from 11,000 to 1300 after 14 weeks.\textsuperscript{(18)} Only a small number of studies have focussed on interactions between trace minerals and resistance to nematodes, and the information available is inconclusive. Copper has been known to have anthelmintic properties for many decades, and dosing of young sheep with copper oxide wire particles considerably reduced establishment of a subsequent challenge dose of two abomasal parasites, while it had no effect on establishment of an intestinal parasite.\textsuperscript{(27)} Cobalt deficiency in young sheep infected with \textit{O. circumcincta} appears to lead to higher FEC and higher plasma pepsinogen concentrations than in cobalt sufficient animals.\textsuperscript{(28)}

\textbf{Studies with periparturient ewes}

The reason for loss of resistance to GI parasites in ewes around lambing is poorly understood. Poor nutrition, stress or lack of antigenic stimulation have been suggested (see Chapter 15). The most favoured hypothesis has been an impairment of immune status triggered by immunosuppressive hormones such as prolactin, corticosteroids, progesterone or oestrogens, but the evidence is not compelling. Past anecdotal evidence has suggested that nutritional stress in the periparturient ewe may also play a role in the temporary loss of resistance to nematodes. The requirement for MP relative to ME is high in the periparturient period. Donaldson and colleagues\textsuperscript{(29, 30)} recently reported on a series of studies with parasitised ewes in late pregnancy which were fed at different levels in terms of ME and MP supply. Details of this work are reported in Chapter 15, but results suggest that MP supply may play an important role in the periparturient loss of resistance of ewes to GI nematodes also. Given the importance of the periparturient ewe as a source of parasite
contamination for the parasite-naive lamb, this area clearly deserves further consideration.

Conclusions and suggestions for further research

Nutritional status of the immunologically naive ruminant host has a significant bearing on the severity of parasitism. Resilience to these infections is enhanced by increases in metabolisable nutrient supply, particularly MP. Increased resilience aids the animal by allowing it to develop resistance with a significant reduction in its potentially debilitating pathological consequences. Evidence for an increased rate of development of resistance by improvements in nutrient supply (particularly MP) to the host is also presented. This appears to operate through an increased rate of eradication of parasites once the infection is established, as the establishment and consolidation phase of nematode infections do not appear to be affected significantly by nutritional status, at least in the young host. Effects of nutrition on resilience and resistance of the host also appear to operate in the periparturient ewe. The precise regulatory mechanisms involved are still largely unclear and this requires urgent investigation. The implications of these interactions for animal productivity and the relative importance of changes in resilience and resistance are, as yet, poorly described. Nevertheless, it appears that the effects of nutritional status on resilience are of greater significance for the productivity of the young parasitised ruminant than effects on resistance. The long-term systems implications of improvements in nutritional status of the grazing host for parasite epidemiology and control programmes also need to be assessed.

References


The effect of dietary protein on the establishment and maturation of nematode populations in adult sheep

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Introduction

Parasite control programmes have in the past tended to focus on the infected animal, the effectiveness of a control measure being observed directly as an improvement in the productivity of the animal. For several decades anthelmintic drenches were the main-stay of such programmes but in view of continued reporting of drench resistance\(^{(1,2)}\) and growing concern over chemical residues in animal products,\(^{(3)}\) alternative approaches must now be sought. To this end, the less direct approach of targeting the source of the infection may be appropriate.

In late pregnancy and early lactation the mature ewe experiences a temporary loss of immunity to nematodes.\(^{(4)}\) The consequence of this is a periparturient rise in faecal egg count (PPR). Research has shown that as a result of this rise in faecal egg output, the periparturient ewe is responsible for much of the larval contamination of pasture, to which naive lambs are subsequently exposed.\(^{(5,6)}\)

The precise cause of the PPR remains unclear. It has been ascribed to endocrine immunosuppression, lack of antigenic stimulation, stress and undernutrition, but to date, attempts to identify the cause have been equivocal and further research is required.\(^{(7)}\) Nutrition has been implicated but not investigated systematically.\(^{(8)}\) As outlined in Chapter 15 there is strong evidence that, in the growing animal, the development and maintenance of immunity to gastrointestinal parasitism is affected by nutrition and in particular protein supply.\(^{(9)}\) The nutrient requirements of the ewe in terms of metabolisable energy (ME) and metabolisable protein (MP) are maximal during the

Sustainable control of internal parasites in ruminants 193
periparturient period and if immunity in the adult sheep is nutrition dependent, the periparturient period would be the period of greatest susceptibility to nutrition-induced breakdown.

This chapter describes a series of trials undertaken at the Lincoln University Research Farm which were designed to investigate the effect of nutrition on nematode populations in adult sheep.

**Trial 1: The effect of energy supply**

The adequacy of the nutrient supply to the pregnant ewe can be assessed by monitoring changes in live weight and body condition of the animal. With this in mind, our initial study of the interaction between nutrition and the periparturient breakdown in resistance to infection examined the effect of such changes on the parasite status of ewes in the latter stages of pregnancy. Two groups of twin-bearing Coopworth ewes were housed indoors and fed at either above (High plane) or below (Low plane) their ME requirements. Diets consisted of a barley based concentrate ration and chaffed lucerne hay. The ewes were trickle infected daily with 4,000 *Ostertagia (Teladorsagia) circumcincta* larvae to mimic larval challenge experienced by ewes grazing under field conditions. Throughout the trial live weight, body condition score and faecal egg concentrations were recorded. The ewes were slaughtered at parturition for determination of worm burden.

Differential feeding of the two groups resulted in a greater loss of body condition in Low plane ewes than High plane ewes, -0.36 compared with -0.04 of a condition score point, while mean live-weight gain was greater in High plane than in Low plane ewes, viz. +15.5 kg and +6.0 kg respectively. Ewes on the low plane of nutrition had a significantly higher faecal egg concentration than ewes on the high plane from seven days before lambing. Egg concentrations increased rapidly in the Low plane ewes and peaked at approximately 350 eggs per gram (epg) of faeces by parturition. In the High plane group faecal egg concentrations remained below 50 epg throughout the trial period. Worm burdens at parturition were also higher in ewes on the low plane of nutrition, viz. 18,900 compared with 5,800 in ewes on the high plane of nutrition, but these differences were not statistically significant.

Donaldson: Dietary protein effects on parasitism in sheep
Despite the relatively high energy intake of the High plane ewes, sufficient to achieve a 15.5 kg live-weight gain, and significant differences in faecal egg concentrations, worm burdens indicated that breakdown in resistance had occurred in both groups of ewes. This raised some doubt as to the importance of energy supply in maintaining resistance to infection around this time.

**Trial 2: The effect of energy supply and larval challenge**

Results from Trial 1 were somewhat equivocal, indicating that energy supply per se was unlikely to be responsible for the periparturient breakdown of resistance. It has been suggested that the periparturient breakdown is related to the larval challenge which may be experienced by pregnant ewes under intensive rotational winter grazing regimens.\(^{(11)}\) Larval intake under field conditions is difficult to determine with any degree of accuracy and estimates based on pasture larval data and fresh pasture intake of grazing stock vary widely. Based on a fresh matter intake of 24 kg of pasture/day and the pasture larval data of Vlassoff,\(^{(12)}\) daily larval intake can be calculated to range from 1,000 larvae/day to upwards of 200,000 larvae/day. With the potential for such variation in larval challenge to exist, Trial 2 was designed specifically to establish whether larval intake *per se*, rather than host nutritional status, could be responsible for the breakdown in resistance.

Four groups of twin-bearing Coopworth ewes were housed indoors from nine weeks before lambing. One group was fed in excess of their ME requirements and infected daily with 10,000 *O. circumcincta* larvae (Group H10). The remaining three groups were fed below their recommended ME requirement and infected daily with either 5,000, 10,000 or 20,000 larvae (Groups L5, L10 and L20, respectively). Live weight, body condition score and faecal egg concentrations were recorded from the onset of housing until parturition. At parturition all ewes were slaughtered for determination of worm burden.

The ewes fed in excess of ME requirement gained 12.3 kg live weight while those fed below requirement gained only 5.0 kg. Despite these differences between groups there was little corresponding effect on the parasite status of the ewes. Faecal egg concentrations in all four groups rose sharply in the week before lambing. At parturition ewes on the high plane of nutrition had the lowest faecal egg concentration, 710 epg, but this was not statistically
significant. As the level of infection increased from 5,000 to 20,000 larvae/day there was a trend for increasing egg concentrations, viz. 900, 1,300 and 1,430 epg for groups L5, L10 and L20 respectively, but again this was not significant. Similarly, in terms of worm burdens at parturition there were no significant differences in worm numbers resulting from either ME supply or level of infection.

These findings demonstrated, within a wide range of larval challenge, the relative unimportance of larval intake on the periparturient breakdown and again questioned the role of dietary energy in maintaining resistance.

**Trial 3: Energy supply vs protein supply**

A third trial was designed to assess the relative importance of ME and MP supply in terms of maintaining the ewe’s resistance to parasitic infection. In addition, it was hypothesised that if the breakdown in resistance was related to nutrition then animals facing greatest nutritional demands, viz. multiparous ewes, would experience a PPR of greater magnitude than ewes bearing single lambs.

Nine weeks before lambing, adult Coopworth ewes were housed indoors and offered diets which varied in their ME and MP content. Four groups were established using combinations of ‘basal’ or ‘supplemented’ ME and MP rations. Basal rations provided adequate energy and protein to ewes in late pregnancy and lactation, according to the most recent UK feeding standards. Supplemented rations provided ME and MP in excess of these recommendations. Rations consisted of chaffed lucerne hay and pelleted barley grain at hay:grain ratios of 7:3 or 3:7 for basal or supplemented ME supply and 0 or 7.5% fishmeal, for basal or supplemented MP supply. The four groups were therefore: Group 1 - basal energy/basal protein, Group 2 - basal energy/supplemented protein, Group 3 - supplemented energy/basal protein and Group 4 - supplemented energy/supplemented protein. Each group contained equal numbers of single- and twin-bearing ewes.

The ewes were trickle infected daily with 10,000 *O. circumcincta* and 7,000 *Trichostrongylus colubriformis* larvae. During the course of the infection period, ewe live weight, body condition score and faecal nematode egg concentration were recorded. Dosing ceased at parturition but faecal egg
concentrations were monitored until three weeks after lambing, at which time the ewes were slaughtered for determination of worm burden.

Twin-bearing ewes gained on average 5.2 kg more live weight than single bearing ewes. Energy supplementation increased live-weight gain by 6.0 kg compared with the basal energy diets, while ewes on the protein supplemented diets gained 2.4 kg more live weight than ewes on the basal protein diets. Body condition score decreased by 0.7 and 0.2 condition score points in basal and supplemented energy ewes, respectively, and by 0.6 compared with 0.2 score points, in basal and supplemented protein ewes, respectively. There was no significant effect of pregnancy status on condition score change.

Protein supplementation had a significant effect on faecal egg concentration from 21 days before lambing and throughout the remainder of the trial. Three weeks after parturition ewes in the supplemented protein groups had an average faecal egg concentration of 145 epg compared with 1,610 epg in the basal protein ewes. Energy supplementation had only a short term effect on faecal egg concentration in the week before lambing but by three weeks after lambing there was no difference in egg output between groups. Twin-bearing ewes had slightly higher faecal egg counts than single-bearing ewes.

Ewes on the protein supplemented diets harboured significantly lower numbers of parasitic worms than those on the basal protein ration, viz. 1,540 worms compared with 12,020. Similarly single-bearing ewes had significantly lower burdens than twin-bearing ewes, viz. 2,300 compared with 8,100. There was no effect of energy supplementation on worm burdens.

Discussion

Although results from Trials 1 and 2 had been equivocal, trends in faecal egg concentrations and worm burdens tended to support our hypothesis that the periparturient breakdown in resistance to nematodes could be modified by energy supply, even though statistically significant differences were generally not achieved. The design of these two trials was such that energy supply had not been altered independently of other nutrients, including protein, so it was not possible to determine the relative importance of energy or protein. Results from Trial 3 indicated the relative importance of MP supply over ME supply in the periparturient breakdown in resistance to parasites. These results are in

Sustainable control of internal parasites in ruminants 197
agreement with those of Bown et al.\textsuperscript{(14)} who reported that in lambs, post ruminal infusion of protein, as casein, had a greater impact in reducing the debilitating effects of \textit{T. colubriformis} infection, than did infusion of an iso-energetic amount of glucose.

It would appear then that the periparturient breakdown in resistance to parasitism and subsequent pasture contamination can be modified by nutrition. At this stage, however the mechanism by which this effect is occurring is unclear.

In the young animal there may be competition for nutrients between tissue growth and the immune system. There is evidence that the responses to protein supplementation, in terms of the development of immunity to parasitism, are greater in young than in older lambs.\textsuperscript{(15)} It has been suggested that in the young growing animal, parasitic infection may lead to competition for available nutrients between the requirement to maintain growth and at the same time to mount an effective immune response.\textsuperscript{(16)} Younger animals may be particularly responsive to protein supplementation due to the greater requirement for MP relative to ME, as a result of the rate and composition of tissue growth. MP requirement relative to ME declines with increasing body weight, viz. approximately 11, 8.8, 7.5 and 6.3 g MP/MJ of ME at 10, 20, 30 and 40 kg live weight, respectively.\textsuperscript{(17)}

In the periparturient ewe, MP demands, particularly in twin-bearing ewes, may be so great that the immune system is compromised. Requirement for MP relative to ME in the periparturient period is high, around 7-8 g MP/MJ ME. Results of the present work suggest that the ability to mount an effective immune response may be reduced by partitioning of nutrients to the growing conceptus and to lactation. This hypothesis is supported by the greater worm burdens of twin-bearing ewes compared with single-bearing ewes in Trial 3.

Other workers however, have questioned the concept of a nutrient cost for mounting and maintaining an immune response to parasitic infection. Kimambo and colleagues\textsuperscript{(18)} found that there was little nutritional cost associated with re-activation of the immunological mechanisms when adult sheep, resistant to \textit{T. colubriformis}, were re-challenged after a 24 week parasite-free period. In addition, van Houtert and others\textsuperscript{(19)} found that there
was no loss of acquired immunity to *T. colubriformis* resulting from a period of low nutrient supply and subsequent loss of live weight. More recently, Kyriazakis *et al.*\(^{(20)}\) stated that the expression of acquired immunity in resistant sheep is independent of protein nutrition. It follows that the precise significance of nutrition in the immune response requires greater investigation, as does the methodology for monitoring the immune response per se.

It remains to be determined if the results recorded in Trial 3, using fishmeal, can be achieved with any MP source or whether fishmeal provided a specific amino acid to trigger the response. The possibility that it is neither MP supply-nor amino acid-specific also can not be entirely discounted, though the fact that similar findings have been obtained in young lambs with casein strongly implicates protein supply as a determinant of resistance to parasitism.

At the moment supplementary feeding will, in most cases, be more expensive than the traditional anthelmintic drenching regime. In addition the use of fishmeal (used here as a 'research-tool' because of its capacity to escape rumen degradation) raises residue issues of its own and makes it important to identify alternative by-pass protein sources.

Whether similar results to those measured here can be obtained under grazing conditions remains to be determined. Grazing studies in growing sheep on different forage types have indicated that forages containing significant levels of condensed tannins (which reduce protein degradation in the rumen) appear to reduce the detrimental impact of parasitic infection on the host. What is yet to be determined is whether this is related to protein supply or to a direct effect of the tannins on nematodes.

Although it is in the early stages, results from the work described here are encouraging and indicate that the potential exists to reduce the contamination of pasture with parasite larvae and, consequently, to reduce our reliance on anthelmintic treatments. The results will be of particular relevance to prolific flocks, not only because of the greater capacity of ewes in such flocks to contaminate pasture, but also because twin suckling lambs are more likely to be exposed to infection at an early stage as a consequence of receiving a dietary protein supply inferior to that of single suckled lambs.
References


Donaldson: Dietary protein effects on parasitism in sheep
Models as a guide to sustainable worm control

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Introduction

One outcome of the revolution in information technology of the last decade has been a proliferation of computer models of complex systems. They are now ubiquitous, and are used to describe and predict the behaviour of systems varying in complexity from home mortgage repayments to global climate change. The use of models to describe, explain or predict behaviour of systems is not new, however. They have a long and distinguished history of successful use in science, engineering and economics. What is relatively new is the deployment of computers, particularly personal computers, to replace human beings in the intensive and laborious calculations required in most models. This replacement of the mathematician by the computer has meant that much more complex systems are now amenable to modelling, and that once constructed, a successful model is now accessible to virtually anyone with an interest in its output.

The population dynamics of the internal parasites of grazing sheep and their interactions with weather, management, immunity and drenching is a good example of a system that was simply too complex to model in its entirety before the advent of the computer. Nor was it really considered necessary, except by a few computer enthusiasts and techno-freaks, until the late 1980s. After all, if a better drenching programme was required for a particular livestock enterprise in a particular environment, it was a relatively simple matter to conduct a field trial over two or three years, choose the best programme on the basis of the results obtained, and the problem was then permanently solved. The occasional appearance of strains of worms resistant to drenches in the 1960s and 1970s did little to challenge the optimism of those advocating this approach; if worms were resistant to drench A, simply change to drench
B or C, or wait until the pharmaceutical industry developed D, E or F. We are now belatedly realising that as far as drenches are concerned, we may never be dealing with more than a one- or two-letter alphabet. The impetus for the rapid development of models of internal parasites of livestock in the 1990s was the outbreak of drench resistance in the trichostrongylid nematodes of sheep and goats in the 1980s, to the extent that it now occurs in all countries and threatens the sustainability of small ruminant production in many.\(^\text{(13)}\)

The challenge for pest and disease control in the 21st century is essentially similar in the fields of parasitology, entomology, bacteriology and weed control, namely, how to use biocides in such a way that the rate at which they become ineffective through selection for resistance does not exceed the rate at which new active compounds can be developed in an increasingly stringent regulatory environment. It is in this role that models have much to offer. I would go further and claim that there is no alternative approach - if we rely solely on classical methods of hypothesis testing and physical experimentation to explore strategies for delaying resistance, the best we can hope to achieve is to discover where we went wrong with the last compound, while having little that is useful to say about preventing the demise of the next. The difficulty with physical experimentation is simply that the time it takes to get an answer to a foreseeable problem is at least equal to the time it takes for future problems to become current ones. While parasitological models can be, and have been, used to evaluate and explore novel control strategies more quickly and economically than can be done by physical experimentation,\(^\text{(6)}\) it is in the understanding and formulation of procedures that retard the evolution of drench resistance where they have most to offer. It is in this field, too, that they have no real competition - experimentation is too slow, and gut feelings are subjective and unreliable.

**Kinds of models**

The simplest model of worms in livestock was probably the one formulated by JF Michel in 1970 to describe the results of his experiments on trickle infections at various constant daily rates of larval intake of *Ostertagia ostertagi* in housed calves.\(^\text{(11)}\) He found that their worm burdens did not continue to increase with time, but plateaued at a level proportional to the
rate of intake of infective larvae. This observation could be most economically explained by the simple assumption of a constant daily death rate of adult worms. The calculations required to estimate this parameter and thus fit the model to his data were probably done with pen and paper, or at the very most, with a mechanical calculator. Despite (or perhaps because of) its simplicity, this model was extremely influential in shaping the thinking of a generation of parasitologists. By focussing attention on influencing larval populations on pasture, rather than on removal of parasitic populations by drenching, Michel's model led to significant improvements in the control of Ostertagia and other parasites. It is still invoked today in attempts to explain the virtual absence of drench resistance in O. ostertagi; resistant survivors of a drench have only a short residence time in the host before being expelled as part of the normal daily 'turnover' of worms, and thus do not contribute disproportionately to the next generation of worms.

Much more complex computer models have been developed by research groups from the Universities of Strathclyde and Glasgow, from CSIRO in Australia and from AgResearch in New Zealand that simulate effects of weather, livestock management and drenching strategies on parasite populations in sheep and on pasture, and on their consequences for drench resistance. A simpler, but more generally applicable model of the evolution of anthelmintic resistance in nematode parasites has been developed at the University of Pennsylvania. Although the details, structure and uses of these four models differ widely, when asked the same questions they produce substantially the same answers - with one exception, which will be considered in more detail below.

These are currently the only models that incorporate selection for drench resistance, but probably the most widely-used parasitological model today is 'Paraban', a model of nematodiasis in cattle and its control by anthelmintics and grazing management. Developed by Dr Gary Smith at the University of Pennsylvania for MSD Agvet, Paraban is used by MSD Agvet sales representatives in several countries to prepare and demonstrate customized control programmes for individual cattle producers.
What do the resistance models tell us about sustainable worm control?

a. There are only two certain ways to avoid drench resistance, both equally impractical given current knowledge. These are not to use drenches at all, or to use only drenches that are literally 100% effective and thus leave no survivors. Selective pressure for drench resistance is determined by the genetic contribution that resistant survivors of a drench make to future generations of worms. If there are no survivors, they can make no contribution, and resistance will not evolve. Clearly, a small number of survivors will make a lesser genetic contribution than will a larger population of survivors. Hence the universal recommendation to use the most effective drug available at the full dose rate.

b. All else being equal, drench resistance evolves most rapidly if it is conferred by a single gene rather than two or more genes. The differences can be quite dramatic. In the example of a standard Australian strategic drenching programme simulated by Barnes et al., and under reasonable assumptions of additive effects for each resistance (R) allele and linkage equilibrium, it took around 30 years for R allele frequency to rise from 0.1% to 50% when resistance was controlled by three genes. Under two genes, the same drenching programme took 12 years to provoke the same degree of resistance, and this fell to only 6 years when resistance was controlled by a single gene.

c. Resistance evolves fastest when it is dominant, more slowly when it is co-dominant, and slowest when it is recessive. This is particularly worrying in the light of recent reports that macrocyclic lactone resistance in Haemonchus contortus is conferred by a single dominant gene.

d. In the absence of substantial reversion to susceptibility when the anthelmintic is withdrawn, rotation of anthelmintic groups, whether at each drench, annually, or at any other interval, has very little effect on the evolution of resistance. The experimental evidence so far indicates that reversion to susceptibility must be a rare phenomenon, if it exists at all.

e. In marked contrast to results obtained from drug rotations, combinations of unrelated drugs used simultaneously can profoundly delay selection for resistance, provided they are used initially when R allele frequency for
each constituent drug is low.\(^6, 12\) For example, R allele frequency to two unrelated drugs rose from 0.01% to 50% after around 17 years of annual rotation in a simulated strategic drenching programme. When the two drugs were used in combination, R allele frequency was still only 0.1% after 20 years.\(^6\)

f. Some forms of grazing management, in particular the provision of clean pastures at weaning, can substantially improve worm control and reduce selection for resistance,\(^6, 9\) even when drenching frequency is not reduced.\(^5\)

g. Within a given environment, production system and management regime, selection for drench resistance will intensify as drenching frequency is increased.\(^5, 6, 9, 10, 12\) In contrast, when comparing different environments, production systems or managements, drenching frequency is a poor predictor of selection pressure.\(^2, 10\) For example, selection for resistance has proceeded more quickly in drier environments in Australia and South Africa, where less frequent drenching is practised, than it has in the more humid environments of Europe and New Zealand where sheep production entails more frequent drenching.

h. Increased persistence of an anthelmintic, whether achieved by modification of the drug molecule or incorporation into a controlled-release device, increases efficacy against resistant worm genotypes, thus effectively making resistance more recessive. It also permits a reduction in treatment frequency. In these circumstances, use of persistent anthelmintic formulations need not increase selection for resistance.\(^5, 7\) Further, there is remarkably little contribution to future generations of worms by resistant infective larvae picked up during this period of drug persistence when compared with the contribution made by adult survivors of treatment.\(^7\) This counter-intuitive result is explained by the overwhelming reproductive advantage enjoyed by adult survivors of the drug during the persistency period. Even if resistant larvae establish during this period, they are unable to mature and begin producing eggs for a further period of around three weeks.

**Drenching ewes: for and against**

The consensus among Australian parasitologists has long been that periparturient drenching of ewes was a waste of time and money. Only in the
highly unusual situation where clean pastures were provided immediately following the drench was there any evidence of a production response to such drenching.\(^{(8)}\) It was recognized that lambing ewes were suffering production losses, or even clinical helminthosis, but this was tempered by the empirical finding that these losses could not be eliminated by pre- and/or post-lambing drenching. This is attributed to the profound and extended loss of immunity to worms by Merino ewes during lactation. Whatever the explanation, ewes drenched just before or during lactation are rapidly reinfected, with egg counts usually returning to pre-treatment levels within a month. More recently, controlled-release devices containing albendazole or ivermectin, which provide 100 days protection from reinfection have resulted in substantial gains in productivity in lambing ewes and their lambs,\(^{(3)}\) and the general view now is that lambing ewes should either not be drenched at all, or else given a controlled-release device pre-lambing, depending on the current price of wool and lambs. Recommended practice in most areas is to give ewes a drench at weaning to assist them in regaining their optimum mating live weight.

Recently Leathwick \textit{et al.}\(^{(10)}\) published results from their simulation model of nematodiasis and evolution of drench resistance in New Zealand ewes and lambs under various drenching and grazing management regimes. Their unexpected finding was that the output of unselected eggs from undrenched ewes, particularly through autumn and winter, was a major factor in delaying the progress of drench resistance through dilution of emerging resistance in pasture larvae derived from eggs passed by drenched lambs. This effect was so great that simply allowing undrenched ewes, and lambs drenched from 5 to 9 times to share common pastures after weaning more than doubled the time taken for drench resistance to evolve, when compared with the time it took when ewes and lambs did not share common pastures.

Even more astonishing was the effect of a single drench given to the ewes at either tail-docking or mating. Just one such drench given to the ewes selected much more strongly for resistance than up to four additional drenches given to the lambs. When ewes were drenched, allowing them to share common grazing with the lambs then did very little to alleviate the acceleration in drench resistance provoked by drenching the ewes.
We were surprised by these results, and ran some simulations with the CSIRO model to see if they could be confirmed. As far as possible, we started with the same initial conditions as in the AgResearch model, but with local (Armidale) weather data. Our standard management system was to set stock lambs after weaning on a spelled paddock that ewes were always excluded from, to give them 3 drenches at two-monthly intervals starting from weaning, and to drench the ewes once, at weaning. This programme conforms with extension recommendations for this region. When a flock of 100 ewes and lambs was simulated over a 20-year period, resistance to the drench (defined as 50% R allele frequency in larvae on pasture in the weaner paddock) occurred after 8 years, and there were a total of 26 lamb deaths and no ewe deaths attributable to worms over the 20 years of the simulation.

When the single ewe drench was omitted, and everything else remained the same, resistance on the weaner paddock still occurred after 8 years, but did not occur on the ewe paddock until well after 20 years, compared with 14 years when ewes were drenched once. Lamb mortalities rose marginally to 44. When the single ewe drench was reinstated, but given at marking rather than weaning, resistance on the weaner paddock was again unaffected, lamb mortalities dropped back to 30, and resistance occurred after 16 years on the ewe paddock.

Clearly, under our standard management system where ewes and lambs do not graze over common pastures after weaning, drenching ewes has very little effect on either selection for drench resistance or worm control, which is consistent with our experience in the real world.

We then decided to allow the simulated ewes and lambs to share common pastures after weaning, as this was the management system that, in the AgResearch model, permitted the greatest dilution of emerging drench resistance by the eggs passed by undrenched ewes. The results were equally as astonishing as those of Leathwick et al., but in an entirely different direction.

Under our standard drenching programme of a weaning drench for the ewes and three drenches at two-monthly intervals for the lambs, starting at weaning, but with ewes and lambs rotated over the same pastures after weaning, resistance took almost 9 years to develop on the common pasture, but worm
control was catastrophically bad, with 26 dead ewes and 494 dead lambs over the 20 year period - an average lamb mortality rate of almost 25%. If the weaning drench for ewes was dropped, resistance took slightly more than 9 years to develop, and mortalities were similar to the simulation where ewes were drenched. Essentially similar results were obtained regardless of when the ewe drench was given (marking or weaning), whether it was given at all, or if a series of up to 4 drenches at 30-day intervals from marking was administered to ewes. In other words, our model suggests it is impossible to control helminthosis in lambs in our environment with only 3 drenches per year unless they are grazed on separate pastures from the ewes, regardless of how often the ewes are drenched. Furthermore, it tells us that drenching of ewes contributes very little to the evolution of drench resistance, even when undertaken at what we would regard as suppressive levels.

**Why is there such a difference between the two models?**

There are at least two questions implied here. What is the immediate cause, in terms of model structures and mechanisms, for the vastly different output? and Which model is more faithful to reality? Or possibly a third - Does AgResearch reality differ from CSIRO reality? I am happy to answer the first question, not confident of my impartiality in answering the second, and will therefore probably avoid the issue by addressing the third!

The relevant difference between the two models is the way that the lactating ewe's temporary loss of immunity to worms is handled. In the CSIRO model, it is assumed that at lambing, the ewe loses its acquired immunity completely, and from then on, must acquire it again through progressive experience of infection. In this regard, it is in much the same predicament as its newborn lamb, with the exception that, because of its greater feed intake, it accumulates the necessary worm burden faster than the lamb, and because of its greater age, mounts an effective immune response more quickly. Full details can be found in (5) but basically, establishment rate of incoming infection rises from around 1% during pregnancy to 65% at lambing, and then declines at a rate determined by subsequent larval intake. This process takes up most or all of the lactation period in an average year, with the result that ewes are very susceptible to reinfection during lactation as discussed previously. As a
corollary, any resistant worms surviving a drench are very quickly diluted by susceptible worms acquired from pasture. Detailed examination of the CSIRO model output shows that for around 4 weeks following a drench, R allele frequency in worms in lactating ewes is elevated above that in larvae on their pasture, but from around 5 weeks, the genetic composition of the lactating ewe’s worm burden is roughly in equilibrium with that of the larvae on pasture. This means that a drenched ewe is only contaminating the pasture with a significantly higher frequency of resistant eggs for 4 or 5 weeks following drenching. In this respect, the ewes in the CSIRO model more closely resemble the lambs in the AgResearch model than they do the ewes.

By contrast, the loss of immunity in lambing ewes in the AgResearch model is a much more modest affair. My interpretation of its description in (10) is that establishment of new infection is constrained between 1% and 3%, and the normal daily turnover of worms in adult ewes rises from 1% to 2% per day for a 6-week period centred around lambing. This means that any worms in a New Zealand ewe are going to be there for a long time - an average of 100 days for most of the year and 50 days around lambing. If these worms are susceptible, because the ewe has not been drenched, then the egg output by the ewe will consist largely of eggs of susceptible worms. If the ewe has been drenched, the worms will tend to be the resistant ones and will consequently produce resistant eggs. Either way, it will take much longer for the genetic composition of the AgResearch ewe’s worm burden to return to equilibrium with that of the pasture on which she grazes than it will for the CSIRO ewe, because only 1% of the worms will be replaced in any one day, or 2% if she is within three weeks of lambing. This can be clearly seen in Fig. 6 of the paper by Leathwick et al.,(10) where R allele frequencies in eggs passed by drenched ewes are orders of magnitude higher than those in larvae on pasture for around 5 months after drenching, rather than around 5 weeks in the CSIRO model.

The differing outcomes of the two models are thus direct and reasonable consequences of the different assumptions about loss of immunity used in their formulation, and these assumptions are readily testable experimentally. To the best of my knowledge this has not been done, but would require no more than a few weeks’ work with lactating ewes and marked cohorts of worms. On the other hand, it could be argued that each model is appropriate
for its own environment. Australian ewes are usually Merinos, New Zealand ewes are probably Romneys, Merinos are more susceptible to worms than Romneys and susceptible breeds have a more marked periparturient loss of immunity to worms.\(^{(1)}\)

**Conclusion**

Comparison of the greatly differing predictions of two models concerning the effects of drenching and grazing management on worm control and selection for drench resistance has highlighted an area about which there is little quantitative knowledge. The extent to which lactating ewes lose their immunity, and the rapidity with which they regain it, are thereby identified as having important consequences for the efficiency of worm control and the evolution of drench resistance, as also might breed differences in susceptibility. I am quite sure that these particular issues would not have been identified as worthy of investigation without the aid of models, and therein lies what I believe to be one of their most important attributes.

**References**


Barger: Use of models in worm control
Introduction

The rapidly escalating problem of anthelmintic resistance and the increasing concerns of chemical residues in livestock products and the environment pose serious threats to the future of chemical control of worm parasites of livestock. Alternatives, or at least adjuncts, to control of parasites by drenches are no longer simply desirable, but now essential research goals. Not only do they need to be discovered and developed, but most importantly, they need to be adopted by sheep farmers if they are to remain in business. To become sustainable, parasite control schemes need to be based on the principles of integrated pest management.

Although nematode control will continue to rely on anthelmintics, at least in the medium term future, there is a great need to explore the opportunities for greater use of biotechnology and biological control. Certain aspects of this approach are well served, such as the very large research programmes in many laboratories worldwide on developing worm vaccines and breeding animals naturally resistant to worm parasites. In contrast, there has been very little systematic investigation into the potential of biological control of worm parasites.

The concept of biological control

By definition, biological control does not assume to be a substitute for chemotherapy where the expectation, if not the reality, is that parasites may be eradicated by the frequent use of drugs with efficiencies approaching 100%. Biological control agents rarely eliminate the target organism, but reduce the numbers to acceptable levels and maintain a balance between the pathogen and the antagonist. In contrast also to chemical control of nematode parasites...
which is directed entirely at the parasitic stage within the host, biological control will almost certainly be focussed on the free-living stages on pasture. Within this environment, the pre-parasitic stages of nematodes are subject to a variety of both abiotic and biotic factors that can profoundly influence their development and survival. The most important abiotic factors are temperature, oxygen and humidity – extremes in these can be lethal on these free living stages. With regards to biotic factors, there exists a vast assemblage of living organisms that can affect the success of worm eggs developing to infective larvae. From these may come candidate(s) for biological control of worm parasites.

Before considering these, it is useful to describe briefly the general concepts of biological control. Essentially, it can be divided into two broad categories.

**Natural biological control**

Natural biological control is control produced by native (or co-evolved) natural enemies in the normal environment. Although such organisms certainly exist against worm parasites, under most livestock grazing enterprises they are likely to have little impact, otherwise there would not be a problem with worm parasites in the first instance. It has been argued that the major ecological disturbances that followed the intensification of livestock grazing systems, have tipped the balance in favour of parasites by providing an abundance of susceptible hosts and favourable pasture micro-environments for the free-living stages.

**Applied biological control**

Applied biological control is control produced by human intervention. This is further divided into classical biological control, which is effected by the introduction of exotic natural enemies, or augmentative biological control which is brought about by the enhancement of natural enemies already present in a given environment. Most people associate biological control with the former. Although there have been some examples of classical biological control that have been spectacularly successful, such examples in Australia are the use of the Cactoblastis moth to control prickly pear and Myxomatosis to control rabbits, there have also been some spectacular disasters. Again Australia can provide an example, with the cane toad introduced to control cane beetles, but which has now spread widely, causing inestimable damage to both
beneficial invertebrate and vertebrate fauna alike. As a result, regulatory authorities in many countries insist on thorough environmental assessments to be conducted before they sanction field release of introduced organisms. Control of nematode parasites of livestock is likely to be by the augmentative approach, either by manipulation of the environment or of the existing natural enemies of parasites.

**Biological control of parasites by manipulation of the environment**

There are good examples of environmental manipulation, or management, for the biological control of insects. These include changes in land use, habitat provision, reducing natural enemies of beneficial species, and improved pesticide utilisation – particularly more selective use. There is good reason to consider that it is possible to lessen the effects of worm infections in livestock by similar environmental manipulation. In support of this, there is evidence that organic farming practices increase the abundance and variety of dung-dwelling microorganisms, particularly fungi, which may include nematophagous species.\(^1\) These findings may partly account for the good levels of parasite control in organically reared lambs in New Zealand.\(^2\) There is also some evidence that the type of plant species used in pastures can influence the species and type of fungi that colonise the dung of livestock that graze on the pastures.\(^3\)

The practice of ‘green manuring’ of land, by the ploughing-in of various crops, as a replacement for synthetic fertilizers, is now being strongly advocated in Western Europe. This is not only more ecologically responsible, but another ‘spin-off’ benefit is that it encourages the proliferation of earthworms which can have an important influence on the free-living stages of parasites, as described in more detail below.

**Biological control of parasites by manipulation of the organisms**

Direct manipulation of natural enemies of parasite larvae consists of mass production and field release of individuals of a given species of organism.
There are two types of release, namely inoculative and inundative. Inoculative release refers to the release of relatively small number of individuals where the expectation is that the progeny of these individuals will provide long-term pest suppression. In contrast, inundative release is the release of massive number of individuals with the aim of providing immediate pest suppression. It is in this latter category of augmentative, inundative release that future biological control of worm parasites of livestock will be developed.

Candidates for biological control of worm parasites

A. Dung removers

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Dung beetles_ Dung beetles are found throughout the world and these are often capable of rapid and often complete dung removal and thus are indirectly responsible for significant reductions in the number of free-living stages of parasites.\(^4\) However, such dung dispersal activity is notoriously labile, being dependent on ideal weather conditions, therefore little opportunity exists to exploit these organisms in attempts to achieve cost-effective and reliable biological control of nematode parasites.

_Earthworms_ Earthworms take over the role of dung beetles in the cool, moist regions of the world. In northern Europe for example, earthworms play an important and often dominating role in removal of cattle dung from pastures and can be responsible for significant reduction of infective larvae on pasture.\(^5\)

B. Parasite antagonists

A number of organisms have been identified that exploit the free-living stages of parasites as a food source. These include microarthropods, protozoa, predacious nematodes, viruses, bacteria and fungi.\(^4\) Although all are of intrinsic interest, it is from the latter two groups of organisms that breakthroughs in biological control are likely to emerge.

_Bacteria_ Many species of bacteria are associated with the cuticle, body cavity and gut of nematodes and some of these are pathogenic. _Bacillus penetrans_ is a promising candidate for the control of parasitic nematodes of plants. It produces highly resistant spores, which attach to the cuticle and then invade the nematode host. This bacterium is highly host-specific, which is both a good and bad thing. It is good from the standpoint that only the target nematode
pest will be affected, but bad insofar as the search for the specific *B. penetrans* pathogen for each of the whole range of nematode pests would be most laborious, expensive and fruitless in many cases. Another factor that is hampering the exploitation of this organism is the difficulty in culturing large quantities of *B. penetrans*, which is an absolute pre-requisite for commercialisation. Many bacteria and closely related organisms, the Actinomycetes, produce important secondary metabolites, which include antibiotics, insecticides and anthelmintics. As such they should be regarded as microbial control agents, rather than true biological control agents.

**Fungi** Fungi that exhibit anti-nematode properties have been known for a long time. They consist of a great variety of species which include nematode-trapping (predacious) fungi, endoparasitic fungi, fungi that invade nematode eggs and fungi that produce metabolites that are toxic to nematodes.\(^6\) The most important groups of nematophagous fungi are the first two, namely:

- **Nematode - trapping fungi** These fungi produce specialised hyphal trapping devices, such as adhesive networks, knobs, and constricting or non-constricting rings. Fungi in this class may also produce nematode chemoattractant and/or chemotoxic substances.\(^7\) Within a short period of time following capture of the nematode, the fungus penetrates the worm and destroys it.

- **Endoparasitic fungi** These fungi invade the nematode (i) from adhesive spores that stick on the cuticle, from spores that are ingested by the nematode, or (ii) from motile spores in water.

Fungi from these two classes are found in all environments throughout the world, but are particularly abundant in rich agricultural soils. Under laboratory conditions, where fungi are grown as a monoculture on standardised, generally nutrient-poor media and are provided with a nematode prey that cannot escape, results can be spectacularly successful. Total capture and destruction of nematodes can occur within a matter of hours. However this type of work provides little relevant information as to how these fungi would perform as practical biological control agents against animal parasitic nematodes. Testing needs to be done to determine the limitations and opportunities for parasite control associated with the livestock production systems being considered.
Methods for selecting fungi as biological control agents

The most important principle for selecting candidate fungi as possible biological control agents is to obtain isolates from the field in the region, or country, where this work is to be performed. This is important for several reasons. Firstly, it has been observed that laboratory stocks of fungal isolates lose various attributes, which may include nematode-destroying capacity, following repeated passage. Secondly, most countries have stringent requirements regarding the importation and field release of exotic living organisms. These two drawbacks would apply if strains of fungi with known nematophagous activity were obtained from the major fungal collections or repositories in Europe or North America. Fungal species that have evolved to survive under local environmental conditions would be much better strains to work with than those derived from centralised fungal collections.

The most relevant sites for sampling would be the environments where the fungi are expected to exert their effects, notably fresh faecal deposits, but in intensive animal production systems, animal bedding may also be appropriate. The reason for restricting the sampling to these sources is simply to save unnecessary labour at a later stage, because in almost all circumstances, fungal deployment will be in ways which require it to survive passage through the gastrointestinal tract of animals and then to trap nematodes in freshly deposited faeces. Almost certainly, a large number of nematophagous fungi would be isolated from other sources such as soil, pasture etc. However almost all would fail the most important test of gut survival and thus their isolation (and any other testing) would be wasted effort.

The use of animals as a stringent screening procedure means that the number of occasions on which isolations can be expected is very few. Therefore if a serious attempt is to be made, a large number of small samples should be collected per rectum, from livestock found on a comprehensive range of farms in the region. Suitable procedures have been described. Following isolation by these means, pen trials should be carried out to confirm the gut survival and nematophagous capabilities of the fungal strains.
Possible Fungal Products

Direct Application

Direct application could only be considered in the most intensive forms of animal production where animals are closely confined, and of course, where internal parasitism is a problem. Such an example would be the intensive calf-rearing units in the southern islands of Japan where *Strongyloides papillosus* can cause sudden death in massively infected animals in the hot summer months.\(^9\) A practical solution to this problem may be the direct application of fungal elements to the bedding. Therefore, the requirement for fungi to survive gut passage is not relevant in this circumstance. All that would be required is for the fungi rapidly to colonise the bedding and to reduce the overwhelming number of *S. papillosus* larvae responsible for the sudden death syndrome, but to allow sufficient numbers to survive to provoke the normal, rapid acquisition of immunity which characteristically occurs against this parasite.

However, apart from similar forms of highly intensive livestock production, it is beyond the bounds of reality to conceive of a practical means of applying fungal material, especially to the grazing environment, to produce reliable and substantial reduction in the free-living stages of parasites.

Supplementary feeding

Danish workers have demonstrated that a daily supplement of barley grains supporting the growth of *D. flagrans* will reduce parasitism and increase productivity in grazing cattle, pigs, horses and sheep.\(^{10}\) These results are particularly exciting as they demonstrate that the principle of biological control of nematode parasites using nematophagous fungi is particularly robust, being applicable across the whole spectrum of grazing livestock species. Clearly then, the transfer of this technology to those industries where long-term daily supplementary feeding is a common management procedure, would be relatively straightforward. The major impediment would be the need to scale-up production to satisfy the commercial requirements for the fungal grain supplementary feed option for biological control of nematode parasites.

Feed blocks

Administration of feed blocks, developed mainly for mineral supplementation
and to a lesser extent for anthelmintic medication, is now undergoing a resurgence of interest as a means of low-cost nutrient supplementation of livestock. These blocks can be manufactured using simple, low-cost technology and generally incorporate surplus plant by-products as the nutrient source. These by-products may well prove to be suitable growing substrates for locally isolated strains of nematophagous fungi. A range of block formulations containing *D. flagrans* chlamydospores have been tested and the results are very encouraging (PJ Waller & MR Knox, unpublished data). These blocks have also been shown to have a shelf life of at least 6 months. Fungal blocks could prove to be a particularly important control option in the humid tropics and sub-tropics where tethered husbandry and night housing with stall feeding are common animal management practices and where anthelmintic resistance is a serious problem.

**Controlled release devices**

Intra-ruminal sustained or controlled release devices are a modern advance in anthelmintic medication. Although the unit costs of these devices is high, they allow great flexibility in animal management insofar as they provide protection against parasite infection for an extended period of time. Rather than using anthelmintic compounds, devices containing fungal spores could provide this extended prophylactic effect. The objective would be to develop a device which would release sufficient spores for an extended period (60 days or more) to result in a substantial reduction in the number of infective larvae which succeed in migrating to pasture over the same time period. These devices could be administered at epidemiologically critical times to reduce seasonal peaks in larval numbers but would allow sufficient larvae to escape and thus provoke the development of naturally acquired immunity in grazing livestock.

Investigations have shown that chlamydospores of *D. flagrans* can withstand tablettting pressures required for manufacture of these devices. The devices have a good shelf life and can release optimum concentrations of spores for effective parasite control *in vivo* (PJ Waller & K Ellis, unpublished data). Further work is required to test the time/release profiles of fungal chlamydospores in these prototype devices and to verify the long-term *in situ* viability of spores in devices administered to livestock. Although it is premature to speculate as to whether commercially attractive, fungal controlled release devices will be
developed, they have an enormous potential market as a non-chemotherapeutic, environmentally benign form of parasite control to all the grazing livestock industries throughout the world.

**Conclusion**

Modern control methods of worm parasites of livestock need to shift away from the reliance on anthelmintics to a more integrated approach to pest management. Biological control is a major tactic in integrated pest management (IPM) of insect pests and there are grounds for optimism that this will also apply to animal nematode infections in the near future. With the current move towards ‘sustainable’ agriculture, biological control can be expected to play an even more substantial role in IPM of worm parasites. However, this view must be tempered with the inescapable fact that the commercial, financial and animal management dependence of anthelmintics is too great to allow for any rapid change. But the goad will be the spectre of widespread, high level anthelmintic resistance.

In comparison with other non-chemotherapeutic approaches to parasite control in livestock, progress in biocontrol using nematophagous fungi in recent years has been remarkable. Although commercial interest is high, there has been a general reluctance by companies involved in the anthelmintic business to invest in this research. Part of this is due to the fact that as distinct from the anthelmintic discovery and development, where new drugs can be tightly protected by patents, this is not the case for naturally occurring organisms. However, there is an ever increasing interest worldwide, by potential consumers of biological control products which are in tune with the move towards the sustainable, ecologically and environmentally acceptable systems of livestock management and disease control. Therefore there is a clear market for biological control products against worm parasites of livestock.

Biological control has many obvious attractions and advantages over other non-chemotherapeutic means of worm control. For example, it will be applicable to the range of worm parasites not only within, but also between, species of livestock, which is one of the major shortcomings of the worm vaccine approach. It will provide the opportunity for livestock producers to capitalise on the increasing demands of consumers for chemical-free livestock.
products. Finally, it is also difficult to envisage the development of resistance mechanisms which casts a dark shadow over the future of anthelmintics.

References


Cestode parasites of ruminants in New Zealand

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Moniezia spp.

There are only two valid species in the genus Moniezia, *M. expansa* and *M. benedeni*. The former is the common species in sheep and the latter in cattle although both can be found in either host. Whether *M. benedeni* has been seen in New Zealand is in doubt.\(^{(1)}\) *M. expansa* has also been recorded from red deer.\(^{(2)}\)

In the definitive ruminant host the parasite lives in the small intestine and may reach lengths of up to 600 cm.\(^{(3)}\) At the anterior end there is a scolex (holdfast) which has four suckers but no hooks. The proglottids (segments) are broader than long. Eggs of *M. expansa* are roughly triangular in shape (with a pronounced pyriform apparatus) and accumulate in the gravid proglottids. These proglottids are eliminated in the faeces either singly or commonly still attached to each other in short chains. Some proglottids will break up and allow free eggs to be detected in faecal examinations. Shed proglottids are obvious to the naked eye as their white colour stands out against the darker colour of the faeces. Elliot\(^{(4)}\) reported the largest number of individual tapeworms (counted as the number of scolices) seen in one lamb was 41 while 68% of 75 infected lambs had 4 or less. Southworth *et al.*\(^{(5)}\) reported as many as 55 scolices per lamb with a mean burden of 24 in 8 lambs. Due to a ‘crowding effect’ the actual size of individual tapeworms tends to decline with increasing numbers.\(^{(6)}\) Tapeworm mass is generally measured in terms of volume and rarely exceeds 200 ml in lambs\(^{(7)}\) but can be as large as 280 ml.\(^{(8)}\) Southworth *et al.*\(^{(5)}\) reported mean worm volumes ranging from 15.5-48.1 ml in 4 groups of lambs in New Zealand.
The intermediate hosts of *Moniezia* spp. are free-living oribatid mites. Larvae (oncospheres) still within the egg are ingested and leave the egg and make their way into the body cavity of the mites where they develop into cysticercoids which are the infective stage for ruminants. Oribatid mites are a very diverse group with 127 species included in 27 families being implicated as intermediate hosts for *Moniezia* and related cestodes. However, oribatid mites do vary in their susceptibility and not all species are suitable as intermediate hosts. Most infected mites have only 1 cysticercoid but up to 13 cysticercoids have been found in individuals of some species with the maximum number tending to be proportional to the size of the mite. The majority of oribatid mites are found in the soil humus layer with as many as 2.5x10^7 per ha recorded on a permanent sheep pasture in the northeast USA with 3.9% of these being infected. Few studies have been reported in New Zealand on oribatid mites and *Moniezia*. Sligo reported 2.6% infected mites from a pasture in New Zealand. The number of mites on herbage has been found to correlate positively with temperature, relative humidity, rainfall and soil moisture on the day of collection. The seasonality of mite numbers is not clear and probably varies with species. Kates and Runkel found as many mites in frozen soil taken in the middle of a northern American winter as in summer. Ingestion of eggs by infected mites is accidental as they are not coprophagous. The development rate of cysticercoids in mites depends on temperature and host species and can be as short as 28 days. *Moniezia* eggs have been shown to survive up to 4 days exposure to direct sunlight, 20 days at about 0°C and at least 7 months between 5-80°C. The longest report of infectivity being maintained on pasture appears to be 22 months.

The minimum prepatent period (time after infection until eggs are produced) for *M. expansa* is about 35 days. The prevalence and intensity of infection will vary with season, host age and availability of the infected mites. Lambs infected in spring become substantially resistant after 4-5 months. In a trial with lambs in New Zealand, Sligo reported an infection rate of 100% (19/19) in November falling to 9% (1/11) in June with the mean volume of tape-worms falling from 100 ml in November, to 28 ml in January to <1ml in June.
Anthelmintics against *Moniezia*

Table 18.1 shows the reported efficacy of several anthelmintics against *M. expansa*. It is apparent from this that most commonly used benzimidazole anthelmintics are highly effective at their standard recommended dose rates except perhaps fenbendazole which appears to have an efficacy of about 95%. In New Zealand there have been 2 cases reported where it appears there may be anthelmintic resistance to albendazole,\(^5\) There are other anecdotal reports of inefficacy of benzimidazoles against *Moniezia* and these may also be cases of resistance. Praziquantel, which has recently been formulated for use against *Moniezia* in this country, also has a high efficacy at 3.75 mg/kg. Niclosamide would appear to leave some scolices behind at the recommended dose rate although at 100 mg/kg Prichard,\(^{16}\) in his review, rated it as 95-100% effective.

**The effect of *Moniezia* on productivity**

The effect of *Moniezia* on productivity is the subject of some continuing debate. Little to no work has been done with *M. benedeni* in cattle with most being

**Table 18.1**: Efficacy of anthelmintics against *Moniezia expansa*.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose rate (mg/kg)</th>
<th>Efficacy</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>albendazole</td>
<td>3.8</td>
<td>19% and 50%</td>
<td>5</td>
</tr>
<tr>
<td>albendazole</td>
<td>2.5</td>
<td>100%</td>
<td>36</td>
</tr>
<tr>
<td>albendazole</td>
<td>3.8</td>
<td>100%</td>
<td>37</td>
</tr>
<tr>
<td>albendazole</td>
<td>5</td>
<td>95%</td>
<td>38</td>
</tr>
<tr>
<td>albendazole</td>
<td>10</td>
<td>100%</td>
<td>39</td>
</tr>
<tr>
<td>febantel</td>
<td>5</td>
<td>100%</td>
<td>37</td>
</tr>
<tr>
<td>fenbendazole</td>
<td>5</td>
<td>100%</td>
<td>40</td>
</tr>
<tr>
<td>fenbendazole</td>
<td>7.5</td>
<td>94%</td>
<td>41</td>
</tr>
<tr>
<td>niclosamide</td>
<td>100</td>
<td>100%</td>
<td>38</td>
</tr>
<tr>
<td>niclosamide</td>
<td>75</td>
<td>91%</td>
<td>4</td>
</tr>
<tr>
<td>oxfendazole</td>
<td>5</td>
<td>100%</td>
<td>42</td>
</tr>
<tr>
<td>oxfendazole</td>
<td>5</td>
<td>99%</td>
<td>37</td>
</tr>
<tr>
<td>oxyclozanide</td>
<td>12.5</td>
<td>28%</td>
<td>5</td>
</tr>
<tr>
<td>praziquantel</td>
<td>3.75</td>
<td>96%</td>
<td>37</td>
</tr>
<tr>
<td>praziquantel</td>
<td>3.75</td>
<td>98-100%</td>
<td>5</td>
</tr>
</tbody>
</table>
done with *M. expansa* in sheep. Elliot\(^7\) comprehensively reviewed the literature up to 1986 and concluded there was “no justification for treating sheep for *M. expansa* on the basis of any likely benefit to the health or production of the animals”. Most experiments investigating this issue and claiming some effect on productivity have been poorly designed and/or reported and/or have only had access to anthelmintics with less than 100% efficacy against scolices.\(^7\) Clearly the tapeworms are growing body mass at the expense of the host but is this sufficient to produce a measurable loss? With nematodes the response of the host to their presence is the factor most responsible for pathology and clinical disease but the extent of this with *M. expansa* remains largely unknown. More recently Southworth *et al.*\(^5\) reported a trial where they showed a significant effect of treating lambs (100 per treatment group) with a levamisole-praziquantel combination compared to a levamisole only treated group. Two treatments were given over a 54 day period in spring with a significant difference of 2 kg in favour of the praziquantel treated group by the end of the trial. However, this one positive result must be considered against other trials in New Zealand which did not show a difference\(^4,17,18\) where all were using niclosamide as the cestocide but one of these\(^17\) used a low dose rate. There appear to be only 2 reports in the literature of artificial infections of lambs. In one,\(^19\) significant differences were reported in growth rate between infected and worm free controls in groups of apparently 6 animals, but as it was only a conference abstract no details of infection rate or burdens are available. The other experiment\(^6\) compared average growth rates over a 2 month period in 8 infected versus 4 uninfected lambs and with means of 4.65 kg and 4.88 kg respectively. However, in this latter report only limited data was presented and there was no statistical evaluation undertaken although it seems unlikely to be a significant difference given the small group sizes and variable growth rates noted in the infected group.

**Taenia ovis**

The life cycle of *Taenia ovis* involves the definitive host, dogs and the intermediate hosts, sheep and goats. The adult tapeworm lives in the small intestine of dogs and can be up to 2 metres long.\(^3\) Dogs become infected by eating sheep or goat meat containing the viable cysticercus stage (*Cysticercus ovis*) which is located in intramuscular connective tissue of the intermediate
host. Once ingested worms can mature as early as 35 days.\(^{(20)}\) In general most infected dogs harbour only 1 mature worm.\(^{(20)}\) The egg output from an infected dog can be as high as 750,000 eggs per day with the average life span of the worm being about 6 months although some can live as long as 5 years.\(^{(21)}\) There is no evidence that dogs develop any protective immunity and can get reinfected throughout life.\(^{(21)}\) Taeniid eggs can be dispersed over a very wide area. In one report most eggs were concentrated within a small area of about 10 ha but some travelled as far as 10 km from the deposited faeces.\(^{(22)}\) Dispersal of eggs can occur either by the dog’s movement distributing faeces or, as in the above example, by other means most probably in flies\(^{(21)}\) in which eggs have been shown to survive.\(^{(23)}\) Sheep and goats rapidly develop an immune response after infection but this declines over a few months in the absence of reinfection.\(^{(21, 24)}\) Thus in a situation of partial control it is possible for sheep to develop further cysticerci later in life whilst in a heavily contaminated environment their immunity is continually reinforced and only the initial cysticerci have a chance to establish. Most cysticerci die within a few months but small numbers may survive for 1–2 years or more.\(^{(21, 25)}\) Live cysticerci are 3–4 mm in diameter with a scolex visible inside a clear bladder whereas dead cysticerci develop into 5–10 mm caseous or calcified lesions\(^{(26)}\) that are quite easy to see with the naked eye. According to one authority \textit{C. ovis} are infective about 46 days after sheep ingest the eggs\(^{(3)}\) although Gemmell and Lawson\(^{(25)}\) found it took longer than 3 months. In heavy infections cysticerci may be found scattered throughout the musculature of the host whilst in lighter infections there do seem to be relatively more in the heart and diaphragm compared to the rest of the carcass given the respective weight of these organs.\(^{(26)}\)

In 1970 \textit{Taenia ovis} was included together with \textit{Taenia hydatigena} and \textit{Echinococcus granulosus} in the hydatid eradication campaign. The history of this national programme for \textit{T. ovis} has been summarised by Lawson.\(^{(27)}\) Regulations concerning dog feeding and the use of periodic treatment of dogs with cestocides were the mainstay of the control programme that was introduced. Compulsory dog dosing was discontinued after 1991. At present there are no restrictions with regard to control of this parasite. Although it poses no public health risks \textit{per se} it has led to the rejection of sheep meat consignments to North American markets from Australia in the 1960s\(^{(27)}\) and
from New Zealand in the early 1990s\textsuperscript{(21)} and may create similar problems again in the future. In 1990 the national prevalence of \textit{C. ovis} in lambs was approaching 1\% being slightly higher in the North Island.\textsuperscript{(1)} In 1995 the prevalence was similar being 0.7-1\% in lambs.\textsuperscript{(29)} In adult sheep the figure in 1995 was 2.8\%.\textsuperscript{(29)} However, due to the low sensitivity of cysticercus detection at meat inspection this figure would be a gross underestimate, particularly in lightly infected carcases.\textsuperscript{(26)}

A serological test was developed to monitor the level of infection in dogs following the cessation of compulsory 6 weekly praziquantel dosing. The intention was that every rural dog would be tested every 2 years. In 1990 the prevalence of infected dogs was about 1.9\% rising to a peak of almost 3.5\% in 1992 before declining and rising to another peak of 3.5\% in 1995 (DD Heath pers. com.). Serological testing of dogs ceased in mid-1996 as the problem of \textit{C. ovis} infected meat was not deemed to require a national control programme.

A vaccine for sheep has been developed by expression of a cloned gene of a \textit{T. ovis} host-protective antigen and has been shown to provide greater than 90\% protection in the field.\textsuperscript{(30)} However, this vaccine has not been released commercially for a number of reasons which includes the absence of a direct relationship between the market returns for the farmer who chooses to use such a vaccine and those that do not.\textsuperscript{(24)}

\textbf{Echinococcus granulosus}

In New Zealand, the only definitive host for \textit{Echinococcus granulosus} is the dog. Adult cestodes are found in the small intestine and are only 2-7 mm long and rarely possess more than 5 proglottids. In contrast with \textit{Taenia} spp. there may be many hundreds or thousands of individual worms in one dog. Eggs appear in faeces from 42 days after infection.\textsuperscript{(22)} The rate of egg production is very low with one proglottid released every 7-14 days with each containing about 1500 eggs.\textsuperscript{(31)} Adult worms generally live for up to about 2 years.\textsuperscript{(31)}

Intermediate hosts for \textit{E. granulosus} are ungulates, marsupials and man. In New Zealand the principal intermediate hosts are sheep with a large percentage of hydatid cysts in other animals being sterile. In the intermediate host each
egg develops into one hydatid cyst that can contain many thousand scolices. Each of these scolices can then develop into an adult worm if ingested by a dog. Hydatid cysts are principally found in the liver and lungs but can be found in other organs. Scolices have been observed in hydatid cysts from 2 years after infection but some cysts take several more years to develop and contain scolices. However, hydatid cysts will survive for the life of the host.

New Zealand is on the verge of eradicating *E. granulosus*. There have been two notable outbreaks of hydatid infection in recent years. One was in Otago in 1990-92 and appears to be the result of one infected dog in 1988. The other was on Arapawa Island in 1996. Other findings of cysts have generally been individual animals. Since January 1994 there have been 3 properties with sheep containing hydatid cysts identified at slaughter and 6 with cattle.

For a review of the hydatid control programme in New Zealand readers are referred to Lawson. A national eradication campaign for *E. granulosus* began in 1959 and was carried out under the Dog Control and Hydatids Act 1982 until 30 June 1996. This has now been replaced from 22 August 1996 with a Notice under Section 131 of the Biosecurity Act 1993. These controls are:

- All ruminants and pigs to be slaughtered in home killing facilities in the controlled area may only be slaughtered if those facilities are located within a dog-proof enclosure in order to ensure that raw offal is not accessible to dogs.
- Dogs within the controlled area shall not be fed the offal of sheep, cattle, pigs and goats unless the offal is first cooked by boiling for a minimum of 30 minutes.
- Dogs within the controlled area shall not be allowed access to dead livestock.
- Dogs within the controlled area shall not be allowed access to raw offal of feral ruminants killed in the controlled area
- All landowners within the controlled area are responsible for controlling their livestock and preventing them from straying onto neighbouring properties.

**Taenia hydatigena**

The life cycle of *T. hydatigena* involves dogs as the definitive hosts with sheep being the principal intermediate host although it has also been found in...
goats, deer and pigs. The adult tapeworm is found in the small intestine of the dog and can be up to about 500 cm long.\(^{(3)}\) In the intermediate host the larvae migrate via the portal vein to the liver where they migrate through the parenchyma for up to 30 days\(^{(3)}\) by which time they are about 5-10 mm in size.\(^{(20)}\) They then leave the liver through the liver capsule into the peritoneal cavity where they become enclosed in a layer of peritoneum and are attached to mesentery, omentum or any abdominal organs. They mature into infective *Cysticercus tenuicollis* which are about 6 cm long and contain a single scolex invaginated on a long neck.\(^{(3)}\)

The mature cysticercus is regarded as a harmless parasite\(^{(20)}\) but the migrating immatures in the liver can cause extensive damage and the parasite emerging into the abdominal cavity has been associated with haemorrhage and jaundice.\(^{(20)}\) The main loss is through condemnation of livers at slaughter due to scar tissue from healed migration tracks. There are no public health implications other than unsightly lesions in livers.

The prevalence of *T. hydatigena* in New Zealand is unknown but it is generally considered to be uncommon. This parasite was included in the hydatid eradication campaign along with *T. ovis*. At present there are no specific controls in place but those for *E. granulosus*, specifically not feeding uncooked abdominal contents of sheep, goats and pigs to dogs, should ensure that no rapid increase in prevalence occurs.

**Taenia saginata**

Adult tapeworms of *T. saginata* species are found in the small intestine of humans. The infective stage for humans is *Cysticercus bovis* which is similar in size to *C. ovis* and is found in the intramuscular tissues of cattle. It is not considered to be endemic in New Zealand but is occasionally found at meat inspection with a prevalence of 0.01% in 1995,\(^{(29)}\) presumably due to travellers picking up infections overseas and a small number of eggs from these individuals being ingested by cattle in some way. Good sanitation in New Zealand should prevent dispersal of eggs to places where cattle have access although birds have been implicated in their spread.
References


Pomroy: Cestode parasites of ruminants
Trematode parasites of ruminants in New Zealand

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Introduction

There are only two trematodes infecting ruminants in New Zealand, the common liver fluke (Fasciola hepatica) and the rumen fluke (Calicophoron calicophorum). These differ in many respects and will be dealt with separately.

Liver Fluke

Life cycle

The liver fluke, Fasciola hepatica, lives in the bile ducts of ruminants and many other animals. The life cycle depends on the presence of water, suitable snail intermediate hosts, and a temperature of 10°C or more. For development to proceed at optimum rates, temperatures of around 25-27°C are needed. Note that this refers to water temperatures as that is where the snail intermediate hosts are found.

The adult flukes lay eggs which enter the gut in the bile and pass out in the faeces. A ciliated larval stage, the miracidium, develops in the egg. This takes a minimum of 9-10 days at 25-27°C but usually considerably longer - a month or more at 15°C. Successful development requires that the egg is separated from faeces and kept wet, i.e. normally in water. When fully developed, the miracidium hatches and swims around in search of a suitable snail host which it must find and infect within about 24 hours. Suitable snails are always species of Lymnaea in the family Lymnaeidae. Being air-breathing, these snails can survive for a time out of water and many species, particularly those involved in the transmission of liver fluke, live at the margins of bodies of water or in boggy areas in pastures.

Sustainable control of internal parasites in ruminants
The miracidium enters the snail by boring through its integument and becomes a **sporocyst**. This gives rise to several **rediae** which migrate to the digestive gland (hepatopancreas) of the snail where they feed on the tissues. In each redia, several larvae called **cercariae** develop. These have a tail with which they swim and so can leave the snail provided it is in water. They then attach to some solid object such as vegetation, shed their tails, and encyst to become **metacercariae**; these are about 0.2 mm across.

Development in the snail is temperature-dependent and takes a minimum of five weeks at 25-27°C - usually much longer (2-3 months or more) under field conditions. The level of multiplication in the snail depends on how well-fed and how heavily infected it is but, theoretically, one miracidium can give rise to several hundred cercariae.

When fully encysted (after about 24 h), the metacercaria is infective to animals such as sheep or cattle that ingest it. Cercariae that have not encysted are not infective so that animals are extremely unlikely to become infected simply by drinking water in which snails live, particularly from water troughs. The metacercarial wall is tough and protective to the enclosed juvenile fluke. Metacercariae can remain viable for several weeks or months in ideal conditions, though in the field usually for relatively short periods.

After ingestion, the young flukes excyst in the small intestine and bore through the intestinal wall into the peritoneal cavity from where they make their way to the liver. They enter by boring through the liver capsule, mainly into the ventral (left) lobe where they migrate preferentially. They then spend at least five, sometimes up to eight weeks wandering about in this region of the liver feeding on the parenchyma. After this, they enter the bile ducts and develop to maturity. With light infections, the **minimum** time from ingestion of metacercariae to the appearance of eggs in the faeces of sheep and cattle (prepatent period) is approximately 8 weeks. The flukes are not fully grown at this stage, reaching full size and maximum egg production some weeks later.

With heavy infections and repeat infections the migratory phase is prolonged, the growth of flukes is retarded and the prepatent period lengthened, as a result of the liver damage and fibrosis.
Liver fluke in New Zealand

Liver fluke was first reported in New Zealand in 1896\(^{(13)}\) at Te Hauke in Hawkes Bay. It was probably introduced via Australia with sheep but could never have established had it not been for the fact that there was a suitable indigenous snail host, *Lymnaea tomentosa*, already here. By 1945 liver fluke was reported to be established in Hawkes Bay County, Poverty Bay, small areas near Opotiki and Ngaruawahia, and several small foci in the South Island.\(^{(13, 79)}\) Since then it has spread considerably, particularly over the last 30-40 years, mainly in association with the spread of the exotic snail *Lymnaea columella*. This snail was first recognised in New Zealand in 1969 but by then it was widespread in the North Island and present in some parts of the South Island.\(^{(52, 54, 56, 57)}\)

*Lymnaea columella* occupies similar habitats to those of *L. tomentosa* though doing somewhat better in ponds, water troughs and the like.\(^{(26, 29, 57)}\) It is particularly well-suited to New Zealand temperatures and has a much higher reproductive capacity than *L. tomentosa*.\(^{(30, 31)}\) Although there have been no recent surveys of the distribution of lymnaeid snails, *L. columella* has continued to spread in both Islands and it appears to have replaced *L. tomentosa* in several known habitats in Hawkes Bay and the Manawatu, and along the West Coast of the South Island (WAG Charleston, unpublished observations).

*Lymnaea truncatula*, the European host of *Fasciola*, is also present in New Zealand but as far as is known, it is confined to a small number of habitats in Nelson and Marlborough and is of little importance in the transmission of *Fasciola*.\(^{(57)}\)

Prevalence and distribution

The spread of liver fluke has been reflected in an approximate doubling of the prevalence in sheep between 1969 and 1984/85.\(^{(17, 55)}\) The later survey revealed a prevalence of 7.5% and 1.1% in the North and South Islands respectively.\(^{(17)}\) Of particular note in the North Island were the 2-3 fold increases in the South Auckland and Taranaki regions, and in the South Island, prevalences of 18% and 29% for Nelson and Westland provinces compared with approximately 3% recorded from the Stoke (Nelson) freezing works in 1969.

The prevalence of infection in cattle was not estimated in the 1984/85 survey but trace-backs of infected lines showed that they originated from all counties...
in the North Island. In the South Island, most infected lines originated from the north and west.\(^{(17)}\) Independent surveys showed approximately 10% affected livers at the Moerewa meat works in Northland in 1984 (Kearns pers. com.), about 2.5 times that recorded in 1969; and 35% at the Kokiri works in Greymouth in the same year (Edington, pers. com.). This compares with only 2.7% in cattle slaughtered at Stoke in 1969\(^{(55)}\) where, presumably, many cattle from the West Coast would have been killed as there was no West Coast slaughter house at the time.

**Epidemiology of infection**

Two studies of the epidemiology of infection using tracer sheep have been made in New Zealand. One was on a *Lymnaea tomentosa* habitat in Hawkes Bay over a 2.5 year period,\(^{(53)}\) the other on a *L. columella* habitat in the Manawatu over 5 years.\(^{(28)}\) Both showed that the main period of availability of infection was between January and July/August. In the Hawkes Bay study there was a peak in April/May and in one year there appeared to have been some overwintering of infection in snails with metacercariae becoming available in November/December.\(^{(53)}\)

The pattern of seasonal availability of infection is largely determined by temperature. Except in the warmest areas of the country, average temperatures are in the region of 10°C or lower (in some areas much lower) for several months in winter and for all practical purposes the development of fluke stages ceases. As temperatures rise in spring, the development of fluke stages can begin but is very slow, needing 3-4 months until the first cercariae are released. That is why little or no infection is likely to become available before January over much of the country. At the end of the season when temperatures fall below 10°C, further development of larvae and release of cercariae ceases. Metacercariae, if kept wet, can survive for a time - our observations indicate a month or two on pasture in the Manawatu.\(^{(28)}\) This explains why transmission ceases in July in this area.

There will be some regional differences in transmission period but these have not been studied. In colder areas of the South Island, one would expect the transmission period to start later and end earlier than in the Manawatu. Conversely, in Northland, where mean monthly temperatures exceed 10°C all
year, some development of infection may occur throughout the year and there is some evidence to suggest that infection can be acquired year-round there (Brown, pers. com.) though the main infection period will still be in the late summer and autumn.

The seasonal pattern of availability of infection is only one component of the epidemiology of infection. The risk of exposure of grazing animals to infection is greatly influenced by the proportion of the grazing area that is snail habitat. This varies widely between farms. Another important factor is the effect of weather conditions on the likelihood of animals grazing marshy areas that are snail habitat.

Although both *L. tomentosa* and *L. columella* will breed successfully in ponds and dams, it is marshy areas of pasture that are most important in the transmission of infection. Typically, these are poorly drained areas that are kept permanently wet by seepages and springs, or the margins of slow-moving streams or irrigation ditches.\(^{(14, 31, 57)}\) Observations in New Zealand indicate that snails are not found in habitats that dry out completely in summer.\(^{(26, 31)}\)

The presence of snails in farm dams and ponds, and even water-troughs, is of little significance to transmission of infection unless metacercariae are encysted on vegetation at the margins of ponds which is then eaten. There is a slight possibility that if metacercariae have encysted on mud at the bottom of a pool or marsh and are stirred up, perhaps by animals walking in the water, animals drinking may ingest some metacercariae. It is unlikely that more than a few would be acquired this way.

Large numbers of snails can occur in irrigation channels and become infected by animals defaecating into them. Animals grazing these areas will be exposed to infection but, in addition, metacercariae can be distributed over the whole grazing area when it is flood-irrigated.

In Europe, there is a well-established relationship between the wetness of the summer and the severity of the fluke problem in that year and this is the basis of forecasting systems used there.\(^{(45, 46, 66)}\) Studies in New Zealand, however, have shown no positive relationship between the wetness of the summer and the acquisition of infection but rather suggest the reverse.\(^{(28, 31)}\) Observations indicate that the level of infection of stock is likely to increase
in dry summers as the animals selectively graze marshy areas or the margins of streams or irrigation ditches as they provide green feed. This is analogous to the situation in parts of Australia.\(^{11, 47, 48, 49}\)

The level of infection available on a snail habitat, is not directly related to the numbers of snails present. A few, well-fed snails can produce more cercariae than large numbers that are competing for food resources in the habitat.\(^{4, 28, 37}\) Furthermore, high levels of transmission of fluke do not necessarily require a large proportion of snails to be infected. While infection levels in field populations of \(L.\ tomentosa\) of 1-5\% or more have been recorded, particularly during transmission periods,\(^{5, 12}\) this is not necessarily the case with \(L.\ columella\) with which the numbers infected can be extremely low (less than 0.2\% in our study).\(^{28}\) For this reason there is no point in submitting snails to a laboratory to see if they are infected. Although many infected \(L.\ columella\) die, those that survive produce almost twice as many cercariae as \(L.\ tomentosa\).\(^{6}\)

A further factor to be considered under the heading of epidemiology is the reaction of the host to infection. It is well-established that sheep do not acquire resistance to \(Fasciola\) as a result of previous infection.\(^{5, 25}\) With cattle, previous infection does lead to a substantial level of resistance to reinfection and animals may reject established fluke infections either spontaneously or in response to reinfection.\(^{5, 25, 38, 62, 63, 64}\)

There is some debate about whether this resistance is, in fact, the result of immunological responses per se or attributable to fibrosis of the liver and fibrosis and calcification of the bile ducts, interfering with the ability of flukes to develop and survive.\(^{5, 38, 65}\)

The result is that young cattle are more susceptible to infection and older animals, following exposure to infection, become relatively highly resistant. This resistance does not always provide total immunity to the effects of fluke. Reinfection can cause further damage to the liver even if few or no flukes reach maturity; any that do mature are unlikely to survive long. The development of resistance by cattle also has implications for the relative importance of cattle and sheep as sources of infection for snails.\(^{5}\)
Pathogenesis of disease and its clinical consequences

The disease caused by *Fasciola* can be considered under three headings: that caused directly by migrating juvenile flukes, that associated with adult flukes in the bile ducts, and the clostridial toxaemia secondary to fluke damage commonly referred to as Black Disease or infectious necrotic hepatitis.

Most experimental studies of the disease have been carried out on sheep but are generally applicable to cattle. The main differences are that in cattle the reactive fibrosis in the liver is more marked and affected bile ducts become calcified. The disease processes have been described in detail in numerous papers and reviews (e.g. \(^{(5, 22, 41, 72)}\)).

Acute and subacute fasciolosis

The migrating flukes cause traumatic damage to the liver parenchyma as they migrate through it for a minimum of 5 weeks and, especially in cattle, often for longer. They feed on liver tissue, damaging blood vessels and liver parenchyma, and the damage increases as they grow. This phase of the life cycle is the cause of acute fasciolosis which results from the migration of large numbers of flukes, usually a few thousand, acquired over a short period of time.

The acute disease in sheep is sudden in onset and outbreaks are often signalled by deaths. Affected animals are weak and lethargic with pale mucous membranes, signs of abdominal pain and possibly ascites. At necropsy, the liver is swollen with haemorrhagic tracks caused by the migrating fluke clearly visible. The ventral lobe is most affected but most of the liver can be involved. Subcapsular haemorrhages, fibrinous material attached to the liver capsule, and a blood-tinged exudate in the abdominal cavity are usually present. The liver is easily broken up in water, and if this is done, large numbers of immature flukes, about 5-10 mm long will be seen. Deaths usually occur 4-6 weeks after ingestion of the metacercariae, but sometimes earlier, in which case the flukes will be smaller. Acute disease has rarely been reported in New Zealand.\(^{(14, 31)}\)

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Acute fasciolosis is very rare in cattle although it has been produced experimentally and a field outbreak has been described overseas.\(^6\) It has not been recorded in New Zealand.

**Subacute** disease in sheep is also associated with ingestion of large numbers of metacercariae but less than in the acute disease. Deaths usually occur 6-10 weeks after infection so there is more time for animals to develop clinical signs. Affected animals lose condition rapidly, are severely anaemic and hypoalbuminaemic, with consequent clinical signs. The liver is enlarged and shows extensive migration tracks, large numbers of flukes in the parenchyma and bile ducts, and fibrinous tags on the liver capsule.

Little has been published on subacute disease in cattle although a field outbreak has been recorded in Switzerland.\(^23\)

**Chronic fasciolosis**

This is associated with adult flukes in the bile ducts and it is by far the most important in all classes of stock. Depending on the level of infection and its duration, it is characterised clinically by poor growth or loss of condition, decreased productivity (e.g. of wool), anaemia, hypoalbuminaemia and, in some cases, diarrhoea. The pathogenesis is complex.

The adult flukes in the bile ducts feed on bile duct lining, ingesting and causing loss of blood and plasma proteins into the bile.\(^2, 19, 21, 71\) Anaemia and hypoalbuminaemia develop over a period of weeks - the rate depending on the numbers of flukes present and the nutritional status of the animal. The anaemia is primarily caused by blood loss with secondary effects on the bone marrow due to induced iron deficiency and disruption of protein metabolism. Plasma albumin loss is of major importance and is caused by leakage of plasma albumin through the bile duct epithelium in addition to that lost with blood.\(^19, 21\) Levels of plasma globulins increase, probably reflecting antibody responses to infection.

In both sheep and cattle, fluke infections cause inappetance, reducing intake of energy and nutrients.\(^5, 21, 34\) Reduced protein intake also affects iron absorption.\(^2\) The severity of fasciolosis is increased markedly by poor nutrition.\(^1\)
Erosion and inflammation of the bile ducts leads to hyperplasia of the duct lining and reactive fibrosis of the walls which, in cattle, is usually followed by varying degrees of calcification. Bile ducts, particularly those of the ventral lobe where most of the flukes are found, become enlarged and visible on the visceral surface of the liver. Fibrosis of the liver parenchyma, chiefly of the ventral lobe, results mainly from the physical damage and necrosis caused by migrating fluke.

At necropsy, the enlarged bile ducts and fibrosis of the ventral lobe of the liver are characteristic lesions. Poor carcase condition, and signs of anaemia and hypoalbuminaemia are other prominent features. Overall the liver is usually enlarged as although the ventral lobe is fibrosed and often reduced in size, there is hypertrophy of the remainder. However, in longstanding or very severe infections, the whole liver may be shrunken. The numbers of adult flukes present will vary with circumstances but, as a guide, it is considered that 100-300 adult flukes can kill an adult sheep in 3-5 months.\(^5\) In clinical fasciolosis in calves or yearlings, fluke numbers usually exceed 200.\(^{58}\)

**Black Disease: infectious necrotic hepatitis**

This is a sporadic bacterial disease secondary to invasion of the liver by *Fasciola*. Necrosis of the liver caused by migrating fluke can provide anaerobic conditions suitable for the multiplication of clostridia (*Clostridium novyi* type B) present in the liver. The bacteria produce toxins which are rapidly fatal. Black disease is more commonly recorded in sheep than in cattle. The disease does not require the presence of large numbers of migrating fluke. It can be prevented by vaccination.

**Diagnosis and detection of infection**

The diagnosis of **acute** and **subacute** disease is usually straightforward as dead or moribund animals are available for necropsy. Cases would be most likely to occur between late summer and early winter when maximum numbers of metacercariae are available. Aspects of the history may also be suggestive, such as recent flood-irrigation of pastures, or drought forcing animals into marshy areas. Detection of sublethal levels of infection before the infection is patent is more difficult although serum levels of glutamic dehydrogenase (GD) which are raised by damage to the liver parenchyma may be useful in subacute cases.
Diagnosis of chronic fasciolosis is based primarily on clinical signs and the presence of fluke eggs in the faeces. A complication is that even where fluke is causing significant production losses on a farm, the actual prevalence of infection may be relatively low. This affects the numbers of samples that may be needed in an investigation and the care with which they are selected.

In both sheep and cattle, clinical fasciolosis is most likely to be seen in the autumn and winter during or after the main period of infection, often in association with poor nutrition and climatic stress. In sheep, the stress of pregnancy is another factor. Disease can occur in all ages of sheep as there is no acquired immunity. Because cattle do develop resistance, significant production losses and clinical disease are more likely to be seen in young stock. Disease in adult cattle is usually subclinical unless they are previously uninfected (or possibly not reinfected for a year or so\(^5\)) and exposed to a substantial intake of metacercariae. The history of the animals and of the farm and its locality are further points to be considered although, as the infection spreads, cases will occur on farms where it has not been recorded previously.

In sheep there is a reasonable relationship between *Fasciola* egg counts and numbers of mature flukes in the liver although the egg production per fluke declines as the level of infection rises. In round figures, the numbers of eggs/g faeces representing one fluke ranged from approximately 30 at subclinical levels of infection to about 10 at levels that would cause severe clinical disease (>250 flukes).\(^{24}\) In cattle, interpreting faecal egg counts is much more difficult as they are affected by the effects of resistance on the development and survival of fluke.\(^5\)

Changes in the levels of various enzymes in serum following infection have been investigated in numerous studies involving both sheep and cattle (e.g. \(^{15,70,74,81}\)). The general conclusion of these studies is that GD and gamma-glutamyl transferase (GGT) are the most sensitive and reliable indicators of *Fasciola* infection, GD being particularly indicative of parenchymal damage early in infection and GGT of biliary damage later. However, there is considerable variation between animals and the usefulness of GGT estimates is very limited in areas where facial eczema occurs as it causes very marked and often persistent elevation of GGT levels.\(^{77}\)
A number of serological tests for antibodies to *Fasciola* have been developed but are not widely used. It appears that none are sufficiently sensitive and specific to reliably detect infections in individual animals though they may be of some value on a herd basis.\(^{(50)}\)

**Effects on production of sheep**

Much of the published work has been reviewed by Dargie.\(^{(20)}\) Experiments with single or trickle infections have shown significant decreases in growth or loss of weight with subclinical burdens of as few as 45 flukes. It appears that these are mainly attributable to decreased food intake\(^{(32, 75)}\) although decreased food conversion efficiency has also been described in some cases.\(^{(32)}\) Most experiments have been carried out with housed animals and weight loss may be greater under field conditions where the sheep have to graze to meet their requirements and they are exposed to the weather. In addition, increases in liver weights occur which can obscure effects on body weights\(^{(75)}\) (Charleston and Nottingham, unpublished). In a trial in which lambs at pasture were trickle-infected with varying numbers of metacercariae over a 14 week period, weight gains were significantly affected after 8 weeks. Relative to controls, average weight gains over the 22 weeks of the trial were reduced by approximately 20% with 27-100 flukes, 35% with 101-175 flukes and 46% with 176-261 flukes, after deduction of liver weights (Charleston and Nottingham, unpublished).

Wool production and quality are particularly sensitive to adult fluke infections. There is evidence that as few as 30-50 flukes can reduce wool growth by over 20% (see Dargie\(^{(20)}\)). Reproductive performance can also be impaired, particularly in heavily infected ewes.\(^{(20)}\)

It is clear that significant effects on sheep production can result from very modest fluke burdens but more research under field conditions is needed.

**Effects on production of cattle**

There is no question about the potential seriousness of fasciolosis for cattle but while the consequences of levels of infection sufficient to cause clinical disease are relatively easy to demonstrate, determining the significance of subclinical infections is much more difficult.
Nutrition and environmental conditions play critical roles in determining the significance of infection. This is graphically illustrated by two studies in which similar levels of infection were established in calves kept, in one experiment, indoors and, in the other on pasture in the autumn/early winter in Scotland.(59, 69) The most heavily infected of the housed calves developed a moderate anaemia but no other clinical signs, whereas outdoors, severe clinical disease developed with deaths occurring after 13-17 weeks. This was attributed to the declining level of nutrition and increasing environmental stress in the calves outdoors.(58, 59)

Some experiments involving pen-fed animals artificially infected with *Fasciola* have shown significant effects on growth and body weights(34, 44) whereas others have not,(16, 33) in one case despite the establishment of average burdens of almost 300 flukes over 20 weeks in calves 2-3 months old at the start.(16) However, interpreting such data is complicated by the liver enlargement that occurs obscuring decreases in carcase weight.(16, 20) Another complication is that animals may shed part or all of their infection during an experiment and their performance return to control levels.(34) Decreased feed conversion efficiency in infected animals has been recorded in some studies.(33, 54, 44)

How well the results of pen-trials apply to field conditions is unclear. Some attempts to assess the effect of fasciolosis on growth of cattle at pasture or in feedlots by the use of anthelmintics have not shown significant responses(39, 67) but this may be because recovery of lost production is very slow. In Australia, artificial infections superimposed on natural infection in grazing Hereford yearlings, resulted in substantial reductions in growth and body weights, the effect varying with infection level and stocking rate.(18)

In summary, there is clear evidence that fluke infections can have serious effects on the growth and production of young cattle but the extent of the effect depends not only on the level of infection but also on the circumstances of the animals concerned, particularly their level of nutrition. Again, more research under grazing conditions is needed.

Studying the effect of liver fluke infection on milk production of cattle is difficult and costly. Some authors have shown beneficial effects of treatment on milk yield,(43, 51, 67, 73) others have not,(78) or have found no effect of artificial infection.
Some data suggested an effect on milk quality (total solids) but no further evidence seems to have been published.

Much of the trial data is difficult to interpret for various reasons, and Dargie concluded that "claims by some authors that drug treatment of cattle improves milk yield or quality must be viewed with scepticism, and certainly more and better controlled work is required...".

A significantly poorer conception rate has been recorded in experimentally infected heifers, but no such effect was found in a field trial in Oregon comparing treated and untreated animals.

In summary, it appears from the limited data available that the effects of liver fluke infection on the productivity of adult cattle and the benefits from treatment are uncertain.

**Liver condemnations**

One of the consequences of liver fluke infection is the rejection of livers or their grading as unfit for human consumption. This can be of considerable economic significance. Although this has received some attention in overseas assessments of the economic importance of liver fluke infection (see Dargie), it has not been examined in this country. At present in New Zealand, there is apparently some concern among meat processing companies about the impact of the increasing prevalence of fasciolosis on yields of edible livers (Seal, pers. com.).

**Treatment**

Most of the drugs used against *Fasciola* increase in effectiveness as the age of the flukes increases. Mature flukes are much more easily removed than immature ones, the parenchymal stages being particularly difficult to kill. Even within the category of ‘mature’, those 12 or more weeks old are more easily removed than those 8 weeks old. It is necessary, therefore, to be quite specific in comparing efficacies. Furthermore, killing flukes in cattle tends to be more difficult than in sheep. These points need to be borne in mind in selecting the most appropriate anthelmintic for use in particular circumstances.

The anthelmintics with claims for efficacy against liver fluke that are currently marketed in New Zealand fall into various categories: benzimidazoles
(albendazole, oxfendazole, ricobendazole, triclabendazole); salicylanilides (oxyclozanide, closantel); aromatic amines (nitroxynil); sulphonamides (clorsulon). Some of these are combined with antinematode drugs to provide a wide spectrum of activity. Several only claim efficacy against adult fluke. Some are marketed for use in both cattle and sheep, others for one or the other. Space does not allow a detailed review of the relative efficacies of these drugs against flukes of various ages and for further information the reviews and papers by Boray, Richards et al. and McKellar and Kinabo should be consulted. The following brief comments are based on these publications and others cited.

The efficacy claimed for benzimidazoles, with the notable exception of triclabendazole, is against adult fluke, albendazole and ricobendazole (which is albendazole sulphoxide) requiring a higher dose-rate than that used for nematodes; oxfendazole is only claimed (and only by some suppliers) to "assist in the control of fluke". Trial data indicate that in both sheep and cattle, the efficacy of albendazole is variable. It is considered that the performance of ricobendazole is similar to that of albendazole at bioequivalent dose rates.

In contrast, triclabendazole has been shown consistently to be highly effective (about 90%) against both immature (from one week of age) and mature flukes in sheep. Similarly high efficacy has been reported in cattle although in some later trials the efficacy against 1-6 week-old flukes was found to be somewhat more variable ranging from 80-98%. In various trials, efficacy against fluke aged 8 or more weeks has been consistently high (95-100%) at the recommended dose rate. Interestingly, although a benzimidazole, it has no effect on nematodes.

Oxyclozanide is reported as effective against fully adult fluke about 12 weeks old in sheep and about 14 weeks old in cattle but some trials have shown very low efficacies against 12 week-old fluke in cattle. Closantel is more effective against 6-8 week-old and adult fluke and has the additional advantage of being only slowly excreted so that it has persistent activity, continuing to kill fluke as they mature after the treatment has been administered (Maes et al. cited by McKellar and Kinabo). Closantel is only marketed for use in sheep in New Zealand.
Nitroxynil is again most effective against adult fluke about 8 weeks old in both cattle and sheep but is considered to be erratic and less effective against younger stages.\(^{(8,60)}\)

In cattle, clorsulon has been shown to be approximately 90% effective against 8 week-old flukes and 97.5% effective against adult flukes when administered by injection at the recommended dose rate of 2 mg/kg.\(^{(82)}\) In New Zealand, it is marketed as an injectable formulation in combination with ivermectin for use in cattle but it is not available for use in sheep.

In summary, where removal of both developing and adult Fasciola is the objective, triclabendazole (for sheep and cattle) and closantel (for sheep) are the drugs of choice, with clorsulon and nitroxynil next in line for cattle. Where the removal of fully mature fluke is all that is required, oxyxyclozanide can be used. Benzimidazoles other than triclabendazole will only give partial control and they cannot be recommended for treatment of clinical cases or where efficient preventive measures are needed.

It should be noted that there have been a number of instances of Fasciola developing resistance to salicylanilide anthelmintics (rafoxanide and closantel) in Australia.\(^{(9,10)}\) Experiments indicate that selection for resistance to other drugs is also possible.\(^{(10)}\) So far, resistance to flukicides has not been recorded in New Zealand.

**Control**

**General considerations:** Various aspects of the control of fasciolosis in a New Zealand context have been reviewed by Brunsdon\(^{(14)}\) and Harris and Charleston.\(^{(27,31)}\) While, theoretically, control measures can involve such things as the fencing off or drainage of snail habitats, the use of molluscicides to kill snails or the avoidance of grazing of snail habitats at critical times of the year, in practice under New Zealand conditions it is almost entirely dependent on the use of anthelmintics.

In general terms, the objectives are to prevent clinical disease and subclinical losses in the autumn and winter, during and after the main infection period, and particularly to remove infection before the stresses of winter and pregnancy arise. Ideally, the level of treatment should be related to the severity of the
problem on the farm but this is not always easy to assess, particularly if the level of infection is subclinical and/or the prevalence of infection is low.

The incidence and prevalence of infection on individual farms vary widely. The situation is entirely different from that involving gastrointestinal nematode infections where, in any group of grazing animals, it can safely be assumed that all are infected to some extent or other. That is not the case with *Fasciola*. The proportion of animals that are infected can vary from <1%, in which case the infection is of little economic importance, to over 50% where it is almost certainly substantial. It is often under 10%. The difficult issue is to decide at what point it is economic to apply preventive treatments across a group of animals most of which are uninfected. The development of resistance by cattle and resulting loss of infections complicates matters further.

Treatment trials do not provide a satisfactory basis for assessment as responses to therapy are slow to develop. Instead, one has to rely on the collection of information on the prevalence of infection (e.g. by faecal sampling and the examination of livers of slaughtered animals) and an assessment of the severity of liver damage. The extent of snail habitats on the farm is an important indicator of the likely size of the problem so veterinarians and other investigators need to be able to identify lymnaeid snails in order to correctly identify snail habitats. It should be noted that snails, particularly *L. columella*, may largely disappear in winter so that determining which likely areas actually are snail-infested is best done in summer.

In estimating prevalence by faecal examination, it is best to sample sheep as they do not develop resistance to *Fasciola*, although the prevalence of eggs in faeces at any given time may reflect infections acquired over more than one season. With cattle, the prevalence of infection is likely to be underestimated because of the effects of host-resistance on parasite survival and egg production. Note that meatworks data actually measure the prevalence of liver damage rather than of actual infection because lesions persist even though no infection is present.

**Sheep:** The usual recommendation is for 1 to 3 treatments to be given in the autumn/winter period, though in some localities more may be needed to give effective control. This will be determined by the length of the transmission season and the seriousness of the problem. The treatment interval can be

252  *Charleston: Trematode parasites of ruminants*
extended with those drugs that provide high levels of control of immature stages. In most circumstances, it is unlikely that anthelmintic treatments would need to start before February or continue beyond July. There might be a need to start earlier in Northland but there is no information on which to decide this. Where only one or two treatments are given, this should be later in the season to remove the accumulated burden before winter, and preferably using a drug effective against immature fluke.

Very high levels of control can be achieved with drugs that are effective against both immature and adult flukes, as was shown in a trial in Otago in which stock were treated with triclabendazole at 8-11 week intervals for 14 months.\(^{(12)}\) Although this would not be normal farm practice in most circumstances, it led the authors to suggest that regular treatments within the prepatent period for the whole season might be a means of eradicating the infection or reducing it to extremely low levels.\(^{(12)}\)

**Cattle:** The situation is more complicated with cattle because of their ability to cope with larger intakes of metacercariae, their development of resistance, and the lack of information on the significance of infection for production under grazing conditions. It has been suggested that routine preventive treatment of cattle is not usually necessary and recommended that treatment should only be given when losses of production have been specifically diagnosed.\(^{(14)}\) However, in parts of the country where there is a high prevalence of infection, routine control programmes are likely to be needed on many farms. In other areas, the needs will differ markedly from farm to farm.

As the most significant effects of infection are likely to be seen in young cattle, treatment of animals infected in their first autumn/winter period is likely to produce the greatest production benefits. The removal of flukes earlier in their development will be advantageous to reduce liver damage and the numbers of fluke eggs produced.

Whether treatments of cattle in their second year and beyond is likely to be economically worthwhile and, if so, under what conditions, is unclear. Published trial data suggests that the benefits of treating cattle that have been exposed to infection earlier in life and have, therefore, developed resistance to infection, are likely to be small or non-existent. However, where the incidence of infection is low, the majority of animals may not be infected.
in their first year of life, and so remain susceptible. The effect on production of infecting previously uninfected cattle in their second or subsequent years of life, has not been studied.

In most circumstances, the practical approach with cattle may well be that, as recommended by Brunsdon,\(^{(14)}\) treatment should only be given where production losses attributable to fasciolosis have been specifically diagnosed.

Finally, a further general comment relating to control. It has been suggested that, particularly where there is little or no overwintering of infection in snails, there could be considerable advantages to be gained in treating farm stock \textbf{in the spring} to eliminate or substantially reduce the excretion of fluke eggs at that time as these are the principal source of infection for the new season's snail population.\(^{(31)}\) This should significantly reduce the numbers of metacercariae released later onto pasture and, in turn, the impact of infection on stock and the need for treatment over the subsequent autumn/winter period. However, this has \textbf{not} been investigated experimentally. It should be remembered that sheep are potentially much more important than cattle as a source of fluke eggs.

\textbf{Rumen Flukes - Paramphistomes}

\textit{Life cycle}

One rumen fluke, \textit{Calicophoron calicophorum} (syn. \textit{C. jimai}) (Paramphistomatidae) has been described from cattle and sheep in New Zealand. The life cycle, though involving a different snail intermediate host, is broadly similar to that of the liver fluke.\(^{(35,36)}\) The adult paramphistome is pear-shaped with a large posterior acetabulum with which it attaches to the lining of the reticulum and rumen. Eggs are produced that are passed out in the faeces and those that are in water develop. A miracidium develops (in 10 days at 27°C), hatches and invades the intermediate host, the flat-spiralled planorbid snail (\textit{Gyraulus corinna}) (syn. \textit{Planorbis kahuika} = \textit{Gyraulus kahuika}). This snail is widespread in New Zealand and is found in streams, ponds and swampy areas. Development proceeds through sporocyst and redial stages, and from the latter, cercariae are released. These encyst to become metacercariae which are infective to the definitive host.\(^{(35,36)}\)
After being ingested, the metacercariae excyst in the small intestine and then migrate up the intestine, through the abomasum and into the reticulo-rumen. This migration takes about 6 weeks, longer with heavier infections. It appears that they may first develop in the rumen before moving into the reticulum.\textsuperscript{[36]} The prepatent period has not been established for this species.

**Prevalence and distribution**

The parasite is probably widespread although no surveys have been published. Infections have been recorded in cattle in the Wairarapa,\textsuperscript{[36]} and clinical cases have been described from Westland, the Manawatu, Hawkes Bay and Coromandel. Unpublished reports indicate that infection is very common in cattle in the west and northwest of the South Island. Infections are apparently much more common in cattle than in sheep.

**Epidemiology of infection**

The seasonal pattern of infection has not been studied but it is likely that, as with *Fasciola*, most cercariae will be released from snails in the summer/autumn period. Circumstantial evidence indicates that clinical cases are often preceded by flooding of pastures which carries released cercariae over the paddocks so that metacercariae are distributed over the grazing area. In addition, in dry weather, snail habitats can shrink leaving metacercariae available to grazing animals along their margins.

**Pathogenesis of disease and its clinical consequences**

The adult flukes are generally considered to be of little or no significance. Very heavy infections may cause some low-grade rumeno-reticulitis. It is the migrating immature flukes that are the pathogenic stage of the life cycle. If several thousands of these are migrating simultaneously, they cause severe damage to the upper small intestine and abomasum. This results in severe diarrhoea, rapid loss of condition and dehydration and, in some cases, death.

Most reports of disease outbreaks are unpublished and involve cattle. It is generally considered that cases occur more commonly in the West Coast regions of the South Island than elsewhere. There is one report of probable clinical disease in sheep in the Manawatu.\textsuperscript{[80]}
**Diagnosis**

The presence of adult infections can be established by the detection of eggs in the faeces. The eggs resemble those of *Fasciola* but are almost colourless whereas those of the liver fluke are yellow-brown in colour. The presence of eggs is, of course, of no relevance in the diagnosis of clinical disease caused by migrating immature flukes.

Diagnosis of these cases is best attempted by sieving the diarrhoeic faeces to recover immature flukes as numbers of these are passed out. The immature flukes may be as small as 1-2 mm in length so a sieve mesh of about 0.5 mm aperture should be used. A considerable amount of faeces (e.g. half a litre) may need to be sieved. A history of recent flooding of pastures associated with appropriate clinical signs is strongly suggestive.

At necropsy, severe duodenitis and abomasitis will be seen with very large numbers of immature flukes. If samples are to be sent to a laboratory for diagnosis, it is important either to ensure that the organs are tied off to retain the contents or, if the organs have been opened, to send their contents as after death of the animal, the flukes may become detached from the mucosa and be free in the lumen.

**Treatment**

Treatment for adult flukes is rarely necessary but they can be removed reasonably effectively with oxyclozanide at 15 mg/kg but a dose rate of 18.75 mg/kg may be more effective. Immature flukes can also be treated in both cattle and sheep with the same drug at 18.75 mg/kg but treatment should be repeated after three days (Rolfe, pers. com.). Oxyclozanide is sold in New Zealand in combination with levamisole (Nilzan®). Note that the dose rate is 1.25 times the recommended dose rate for liver fluke in cattle. Niclosamide (Mansonil®) at 50-100 mg/kg is also highly effective against immature paramphistomes in sheep but is erratic in cattle; it has no effect on adults in either host.

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*Sustainable control of internal parasites in ruminants* 257


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Sustainable control of internal parasites in ruminants


Integrated control systems for the management of internal parasites in ruminants

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Introduction

The integration of farm management decisions with biological and chemical control of pests is central to all integrated pest management strategies. Integrated control programmes (ICP) for internal parasites of grazing ruminants have received considerable attention both at the theoretical, experimental and practical levels.\(^1,2,3,4\)

Management decisions involved in ICP are centred on the premise that the risk of developing an internal parasite infection and the severity of any infection can be reduced by minimising larval challenge from pasture. There are a number of New Zealand reports (Table 20.1)\(^5,6,7\) which show a significantly greater live-weight gain of lambs grazing pastures with low levels of contamination.

**TABLE 20.1:** Advantage in growth rate of lambs grazed on low contamination pasture. From \(^5,6,7\).

<table>
<thead>
<tr>
<th>Pasture larval contamination</th>
<th>Advantage (%) to low contamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (g/day)</td>
<td>Lower (g/day)</td>
</tr>
<tr>
<td>Trial 1 99</td>
<td>137</td>
</tr>
<tr>
<td>2 99</td>
<td>134</td>
</tr>
<tr>
<td>Trial 3a 70</td>
<td>77</td>
</tr>
<tr>
<td>3b 85</td>
<td>90</td>
</tr>
<tr>
<td>Trial 4 52</td>
<td>160</td>
</tr>
</tbody>
</table>

\(^1Tavendale and Co, P O Box 528, Ashburton, New Zealand\)
Leading farmers and their advisors identify minimization of larval challenge to susceptible stock as the main aim of integrated control programmes and their management and animal health programmes are designed around this objective.

In this chapter we first outline the general principles and practices being adopted by farmers in their ICPs. We then identify why many of the theoretical components of ICPs do not feature in current on-farm programmes and finally outline how further improvements in on-farm ICPs could be made.

**On-farm integrated parasite control**

Details of any ICP are farm specific, but the principles and practice for typical intensive sheep properties where lambs are sold for slaughter and ewe lambs retained as replacements are outlined here.

The objective is to minimise the larval challenge to the most vulnerable and economically sensitive class of stock, the naive lamb pre- and post-weaning. Any reduction in lamb growth rate due to internal parasites, (a) reduces carcass weight (the major determinant of income per lamb) and/or (b) extends the time period from weaning to slaughter which:

- decreases lamb value ($/kg carcass weight)
- increases competition between finishing lambs and ewes (pre-joining) for late-summer pasture and
- increases the total pasture consumption of lambs to a given carcass weight.

There are three components to on-farm ICPs: These are summarised in Table 20.2.

**Minimise contamination by the ewe through control of the periparturient rise in faecal egg output**

Control of the periparturient rise has two advantages. It reduces exposure of the lambs to pre-weaning larval challenge and as importantly, the lower contamination reduces the infectivity of these areas when these are subsequently grazed by lambs post-weaning.
TABLE 20.2: Summary of on-farm integrated parasite control systems on intensive sheep farms.

<table>
<thead>
<tr>
<th>Aim:</th>
<th>minimise exposure of lambs to larval challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Means:</td>
<td>(1) reduce ewe contamination</td>
</tr>
<tr>
<td></td>
<td>- control post-parturient rise</td>
</tr>
<tr>
<td></td>
<td>- control post-parturient rise</td>
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<tr>
<td></td>
<td>- control post-parturient rise</td>
</tr>
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<td>- control post-parturient rise</td>
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<tr>
<td></td>
<td>- control post-parturient rise</td>
</tr>
<tr>
<td></td>
<td>(2) utilise lower-contamination pasture</td>
</tr>
<tr>
<td></td>
<td>- new grass, brassicas</td>
</tr>
<tr>
<td></td>
<td>- ex cattle grazing</td>
</tr>
<tr>
<td></td>
<td>- ex hogget grazing (with anthelmintics)</td>
</tr>
<tr>
<td></td>
<td>(3) control/prevent infections in lambs</td>
</tr>
<tr>
<td></td>
<td>- post-weaning preventative drenching</td>
</tr>
<tr>
<td></td>
<td>- faecal egg counting</td>
</tr>
</tbody>
</table>

Control of the periparturient rise is achieved by:

- minimising the extent of the breakdown in ewe immunity by maintaining good body condition and correcting major dietary deficiencies. Recent evidence with adult ewes suggests the immunity of ewes is improved by both higher live weight (condition score) and higher protein intake (see Chapter 15).

- control of the periparturient rise by strategic pre- and /or post-lambing anthelmintic treatment or through slow release anthelmintic administered pre-lambing. This control procedure has been shown to reduce faecal egg output very markedly in ewes. Ewes in poorer condition may require anthelmintic protection before lambing whereas, a drench at tailing may be adequate control for ewes in better condition.

**Grazing lambs post-weaning on areas of lower larval concentration**

There are three potential sources of these areas:

- cultivated areas sown in summer brassicas, spring sown new pasture and hay and silage regrowth.
- areas grazed by cattle.
- areas grazed by non-infective sheep.
New pasture and summer brassicas

Pasture or brassica crops which have been newly established on intensive farms are considered to be free of endoparasite larvae. Whether the same can be said if they are established by spraying and over-drilling is unknown. Under cooler, wetter conditions larvae of many species could readily survive in the decaying vegetation or in the soil for the minimum 6-8 weeks between spraying old pasture and grazing the resown pasture.

The area of new pasture established annually on intensive farms is only 3-5% effective farm area (Table 20.3, Reference 9), so the quantitative contribution of new pasture to that required by lambs after weaning is small. Similarly, although increasing in popularity, any area specifically sown into summer crop for finishing lambs will be limited by the fact that these areas are not available for grazing in autumn or winter.

Pasture conservation

There are three limitations to regrowth from hay and silage as sources of lower larval concentration pasture. Firstly, if the areas used for silage or hay were grazed by a contaminating class of stock, say, lactating ewes, before being closed for conservation, significant populations of larvae may still exist even after hay and silage removal because the spelling interval between grazings; particularly for silage may be no greater than 60-70 days.

Secondly, cutting height is seldom less than 5 cm, a height below which most larvae are located so they will not necessarily be removed during conservation. Thirdly, the availability of hay and silage regrowth (Dec/Jan) may synchronise with the demand for lower-contamination pasture but it is a limited source. Only 3-5% of intensive New Zealand farms are used for hay or silage (Table 20.3), equal to about one tenth of the lower contamination pasture needed with a lambing % of 120%. This is in contrast to many farms in the U.K. where up to 40% of the area is conserved prior to grazing in spring.

Hay and silage regrowth exists as a potential, but not guaranteed, source of a small amount of post-weaning pasture but cannot be viewed as a major contributor.

Cattle grazing

Cattle and sheep are generally not susceptible to the same species of internal
TABLE 20.3: Proportion of stock units as cattle and areas of new pastures, forage crops and conservation in various New Zealand farm classes. From (9).

<table>
<thead>
<tr>
<th>Farm class</th>
<th>Total area (ha)</th>
<th>Total cattle no./farm</th>
<th>Cattle as % total s.u.</th>
<th>Area (ha) of new pasture</th>
<th>Area (%) of forage crops &amp; hay</th>
<th>Total Max. area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI intensive finishing</td>
<td>190</td>
<td>16</td>
<td>3.1</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>SI breeding/ finishing</td>
<td>365</td>
<td>95</td>
<td>14.8</td>
<td>11</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>SI hill country</td>
<td>1520</td>
<td>233</td>
<td>21.0</td>
<td>9</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td>SI mixed finishing</td>
<td>270</td>
<td>50</td>
<td>14.1</td>
<td>15</td>
<td>23</td>
<td>8</td>
</tr>
<tr>
<td>SI high country</td>
<td>10,500</td>
<td>274</td>
<td>15.7</td>
<td>11</td>
<td>13</td>
<td>50</td>
</tr>
<tr>
<td>NI intensive finishing</td>
<td>220</td>
<td>250</td>
<td>45.0</td>
<td>3</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>NI hill country</td>
<td>385</td>
<td>340</td>
<td>40.6</td>
<td>3</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>NI hard hill country</td>
<td>610</td>
<td>380</td>
<td>37.0</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

* Maximum safe pasture area assumes all areas of new pasture, forage crops, silage and hay and from cattle grazing available for lambs after weaning.

NI = North Island, SI = South Island
parasites\(^{(11)}\) and thus one animal species can in theory be used to ‘clean-up’ pasture contaminated by the other. There are good examples in the literature where interchange of cattle and sheep has lead to effective parasite control, particularly when appropriate spelling intervals have been adopted,\(^{(12, 13)}\) Warnings have been issued\(^{(14)}\) that alternate grazing of species is likely to increase the importance of species which can cross-infect and perhaps reduce the host-specificity of others. To date there seems to be little evidence for this occurring.

On-farm ICPs make use of sheep-cattle interchange where possible. For example, areas grazed by cows and calves or finishing cattle from calving to lamb weaning, are often grazed by lambs after weaning. Provision of sufficient pasture from cattle grazing for lambs after weaning requires 30-50% of stock units as cattle.\(^{(15, 16)}\) No intensive finishing New Zealand livestock farms contain this proportion of cattle (Table 20.2, Reference 9) although on many North Island hill country farms cattle make up over 40% of the stock units. Because of low cattle numbers, many on-farm ICPs can only make use of the ‘dilution’ effect of cattle (faeces returned by cattle will not contain infective sheep nematode eggs, thus lowering the average faecal contamination) in less formal mixed grazing. This mixed grazing of sheep and cattle may involve rotational grazing, set stocking or set stocking of sheep with cattle rotationally grazed through the mobs of sheep. Where cattle are used in this ‘dilution’ role, simultaneous rotational grazing induces less competition between sheep and cattle and enhances cattle live-weight gain.\(^{(17)}\) Another way of using a limited number of cattle is to graze them for shorter periods of time on areas known to have a high concentration of infective larvae.

**Hogget areas**

Areas grazed exclusively by ewe hoggets or by hoggets in association with cattle are also used for lambs after weaning. For these areas to be of low larval concentration, prevention of contamination by hoggets has to be ensured by monitoring the development of parasitic burdens and controlling them. The benefits of good parasite control are also manifest in increased hogget fleece weight and two-tooth mating weight.\(^{(18)}\)

In combination, areas grazed by cattle or hoggets plus new pasture and hay silage regrowth only provide sufficient lamb grazing for a maximum of 6-8
weeks post-weaning. Inevitably then, lambs will return to areas previously grazed by lactating ewes.

**Anthelmintic control in lambs**

To minimise the risk of reduced post-weaning live-weight gain and reduce re-contamination of areas being grazed by lambs, anthelmintic control of lambs is a feature of on-farm ICPs. These programmes follow a preventative drenching schedule involving anthelmintic treatment at weaning and at three to four weekly intervals until slaughter (about 3 months). This programme is associated with regular monitoring of faecal egg counts which may allow for some relaxation in the drenching schedule, particularly later in the season with replacement ewe lambs.

To summarise this section; the control of internal parasites in lambs on intensive sheep farms involves integrating appropriate anthelmintic treatment of both adult ewes and hoggets to reduce contamination by these classes of stock, the use of pastures of lower larval contamination by lambs after weaning and the control of any infection in lambs to maintain growth rate and limit recontamination of the pasture.

**Other components of ICPs**

Those conversant with the literature on ICPs will have noted the omission, in the above outline of on-farm ICPs, of many of the sacred cows of ICPs. In particular, no reference has been made to the generation and use of 'safe pasture', to appropriate spelling intervals between successive grazings or to the potential of various pasture species or pasture management to influence parasitological status of pasture and animal.

In this section we outline reasons for these omissions.

**Safe pasture**

Most proponents of ICPs refer to preparation and use of 'safe' pasture, defined as those areas with sufficiently low larval populations not to impair the production of susceptible animals grazing them. Farmers have been criticised for not fully embracing the safe-pasture concept through an inability to accept the discipline involved or understand the underlying biology. We dispute this. Many farmers have conscientiously tried to prepare and use...
safe pasture and although there have been some success stories (2) many farmers have been disillusioned with the concept when so-called ‘safe’ pasture failed to live up to expectations. We now know that many of the reasons for these failures were due to a lack of understanding of parasite biology by those promoting safe pasture rather than those trying to use it.

Safe pasture does not feature in current IPC for three reasons:

- inappropriate spelling intervals
- unsuitable classes of stock
- insufficient areas

These are discussed below.

**Spelling intervals to produce safe pasture**

In theory, if the interval between grazing by stock which have contaminated an area of pasture and the subsequent grazing covers the period of infective larval development and death, the pasture will self-decontaminate. Alternatively, the spelling interval between grazing with contaminating (infective) and resistant classes of stock needs to synchronise with the time period for maximum development of infective larvae on the pasture (Fig. 20.1). There is a wide literature concerning appropriate spelling intervals and their success in achieving these objectives but the period required for decontamination is very variable. For example:

Under hot wet, tropical conditions where hatching and development of eggs is rapid and continuous and survival short (3-7 weeks), a 35 day spelling interval in a 10 paddock rotational grazing system was very effective by reducing the need for anthelmintic treatment in goats (Fig. 20.2).\(^{(21)}\)

In Taranaki, New Zealand on areas not grazed by ewes from lambing to weaning, a 70 day interval between the first and second lamb grazing maintained levels of pasture infectivity below 200 larvae per kg pasture\(^{(13)}\) although even this level can cause very significant damage.

On areas not grazed by lactating ewes from lambing to weaning, larvae deposited in the previous autumn should have fallen to minimum levels by weaning.\(^{(11)}\) At Wallaceville, New Zealand over a 2-3 month period over summer, pastures grazed by non-lactating sheep or two-tooth wethers, were
FIG. 20.1: Schematic illustration of use of cattle to produce lower-contamination pasture.

<table>
<thead>
<tr>
<th>Options</th>
<th>Grazing sequence</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe pasture</td>
<td>cattle</td>
<td>insufficient cattle available</td>
</tr>
<tr>
<td>Dilution approach</td>
<td>cattle, sheep</td>
<td>undocumented outcome</td>
</tr>
<tr>
<td>Strategic cattle</td>
<td>cattle, sheep</td>
<td>requires good prediction</td>
</tr>
<tr>
<td>Alternate grazing</td>
<td>cattle, sheep</td>
<td>inappropriate spelling interval</td>
</tr>
</tbody>
</table>

Pasture larval concentration

FIG. 20.2: Faecal egg count of set-stocked or rotational grazed goats. From (21). (Arrows represent anthelmintic treatment)

Reduced in infectivity by 93-98%.(1) The most common general statement(11, 14) is that a spelling interval of 2-6 months (a huge range in terms of the implications to farm management) will produce safe pasture.

However, there are also examples where extensive spelling intervals have not resulted in safe pasture. For example, grazing irrigated pasture in Canterbury by cattle for 6 months before use by lambs after weaning was not effective in producing safe pasture due to survival of larvae from contamination by ewes and lambs the previous season.(22) Extending the period of cattle grazing to 9 months (from April to November) did give lower worm burdens in tracer lambs and higher lamb live-weight gain (Table 20.4, Reference 23). Worse still, alternating calves and sheep annually was ineffective as an IPC.
system in the West of Scotland (Fig. 20.3).\(^{(24)}\) Ostertagia survived for 18 months until favourable conditions led to levels of infection in calves as high as in the control groups. There are also many on-farm examples of failure to produce safe pasture using supposedly appropriate spelling intervals.

**TABLE 20.4:** Post-weaning live-weight gain of lambs grazing areas prepared by cattle, suppressively drenched ewes and untreated ewes from April until weaning (Nov.) and worm burdens of tracer lambs (average of 2 years). From (23).

<table>
<thead>
<tr>
<th>Pasture prepared by</th>
<th>live weight gain (g/day)</th>
<th>tracer lamb worm burdens (worms/lamb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cattle</td>
<td>155</td>
<td>725</td>
</tr>
<tr>
<td>drenched ewes</td>
<td>140</td>
<td>850</td>
</tr>
<tr>
<td>undrenched ewes</td>
<td>120</td>
<td>2200</td>
</tr>
</tbody>
</table>

It is not currently possible to predict accurately the length of time pastures need to be spelled to self-decontaminate or show maximum levels of infectivity under the wide range of climatic conditions that exist in New Zealand. This is critical information for effective ICPs. Spelling intervals that are too long are to be avoided as much as those that are too short. The former impose greater than necessary demands on the system for alternative use of the area.

The inability to define effective spelling intervals is one of the major reasons why the safe pasture concept does not feature in on-farm ICPs. Because of the bad image the term ‘safe’ pasture has with farmers, we prefer the term ‘lower-contamination’ pastures to refer to areas on which measures have been taken to keep larval populations low.

**Appropriate classes of stock**

**Sheep**

Non-lactating ewes and ewe hoggets have been advocated as suitable groups of animals for producing safe pasture for lambs and indeed several successful demonstrations of the value of safe pasture have involved pasture prepared by these classes of stock.\(^{(5, 6, 7)}\) However, much of the dissatisfaction with safe pasture (e.g. significant parasite infections in lambs grazing safe pasture)
FIG. 20.3: Faecal egg count of calves grazed on the same area; (a) for four consecutive grazing seasons or, (b) grazed alternately with sheep. From (24).

probably results from these classes of stock not being as resistant or non-contaminating as originally thought. Ewe lambs can develop significant infections with consequent high levels of egg production (700-900 epg) during April to June and later.(22) Furthermore, it has been pointed out that although faecal egg output in pregnant adult ewes in winter may be low (low feed intake and low FEC/g), their contribution to pasture contamination under winter rotational grazing can be high by virtue of the high stocking rate (1500-2000 ewes/ha/day). With higher than expected winter survival of these larvae, significant spring pasture larval levels can be found on areas grazed by adult ewes.(25)

Consequently, we must be much less dogmatic about the potential of various classes of sheep to produce lower-contamination pasture for lambs unless their parasite status is known.

**Beef cattle and deer**

Cattle are readily accepted (see above) as an appropriate alternate species to sheep. However, the effectiveness of cattle as co-grazers acting in their 'dilution' role is not well documented.

Transmission of internal parasite species from deer to sheep is also limited so deer have been suggested as an alternative to cattle in producing safe pasture for sheep.(11) However, grazing for alternate species (sheep) within a deer unit is normally only available in late spring (to complement the low fed demand of hinds) whereas the need for lower-contamination pasture for lambs
occurs in summer/autumn when most deer units are fully stocked with deer. Furthermore, there are unresolved animal health issues (e.g. malignant catarrhal fever) associated with sheep and deer integrated grazing.

**Areas of safe pasture**

It has already been pointed out that the areas of new pasture, silage/hay regrowth and those grazed by cattle seldom quantitatively meet the requirements for areas of lower-contamination pasture.

On mixed livestock farms there are many reasons for adopting a particular ratio of stock species. For example, the ratio of sheep to cattle depends not only on the relatively profitability of the two enterprises but on the pattern and quality of pasture supply (a function of geography, topography, level of subdivision and pasture development), and labour supply of each farm. It is unrealistic to expect that farmers will significantly adjust this mix solely to increase the area of lower-contamination pasture produced by cattle.

Furthermore, the current national trend to higher lambing % and lamb carcass weight in response to market requirements (Fig. 20.4, Reference 9) will increase the demand for lamb grazing after weaning. For example, increasing weaning % from 120 to 160% and decreasing the proportion of lambs sold at weaning from 40 to 10% increases the area required as safe pasture at weaning by almost 50%, from about 40% of the farm area to 60%.\(^{(15)}\)

It must be accepted then, that intensive sheep farmers will have no option but to graze susceptible sheep (lambs) on areas previously grazed by infective sheep (ewes and lambs).

It is the inability to produce ‘safe’ pasture reliably and in sufficient quantities which has lead to its demise as a concept in on-farm ICPs.

**Alternative pasture species**

There is considerable current New Zealand interest\(^{(26)}\) in the extent to which pasture species and morphology (height, density, etc.) affect (a) the survival/supply of larvae and/or (b) the likelihood of an infection developing in animals and thus whether there are advantages in producing specific kinds of pasture for IPC (although this is not a new concept). Pastures modify the microclimate which may directly affect larval development and survival, affect egg and
FIG. 20.4: Trends in average lamb carcass weight, lambing % and stocking rate on New Zealand sheep and beef farms. From (9).

![Graph showing trends in lamb carcass weight, lambing % and stocking rate](image)

larval predators and pathogens and/or alter the rate of faecal decomposition. Rate and extent of larval migration may be affected by sward plants differing in morphology and composition. Some plant species may contain chemical moieties which either help animals resist infection or make them more resilient to an infection.\(^{26}\)

The results some of the New Zealand work in this area are illustrated in Fig. 20.5.\(^{27,28}\) There is some difficulty interpreting these data because feed and larval intake have not been controlled in many cases. However, there are some general comments which can be made.

**Grasses**

Grasses promote moderate live-weight gains in non-parasitised lambs, but low live-weight gain in parasitised lambs which show large faecal egg counts. Larval survival is high, but distribution is mainly in the lower levels of the sward. Of the grasses, brown top supports lower growth rate, and higher faecal egg counts than average and Yorkshire fog shows relatively low faecal egg counts and better growth rate in parasitised lambs. Perennial ryegrass is about average.
FIG. 20.5: Influence of various pasture species on lamb faecal egg count and live-weight gain of parasitised lambs. From (27, 28).

<table>
<thead>
<tr>
<th>Plant</th>
<th>Lamb LWG (parasitised as % non-parasitised)</th>
<th>Lamb FEC (as % mean FEC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucerne</td>
<td>60</td>
<td>120</td>
</tr>
<tr>
<td>Chicory</td>
<td>80</td>
<td>140</td>
</tr>
<tr>
<td>Sulla</td>
<td>40</td>
<td>120</td>
</tr>
<tr>
<td>Maku L. Comi</td>
<td>40</td>
<td>120</td>
</tr>
<tr>
<td>Plantain</td>
<td>40</td>
<td>120</td>
</tr>
<tr>
<td>Rye/WC</td>
<td>40</td>
<td>120</td>
</tr>
</tbody>
</table>

**Legumes and chicory**

Legumes and chicory are well known for producing high live-weight gain in unparasitised lambs. The decline in live-weight gain due to parasitism on these species is similar to that on grasses. A major advantage to legumes is that larval survival is lower but with lucerne the larvae are carried higher in the sward than with grasses. Larval survival on chicory is also lower than on grasses and LWG is not so severely reduced by parasitism.

**Plants containing condensed tannins**

Parasitised lambs grazing Maku lotus or sulla show much less depression in LWG than lambs on other species, but the faecal egg count remains as high as...
from lambs grazing grasses or legumes. Tannins may increase the amino acid supply to the small intestine. Protein supplementation has been shown to increase the resilience of lambs to parasite infection.\(^\text{29}\)

In summary, there are clearly no pasture species which produce lower-contamination pasture when grazed by infective stock. There are some in which larval survival is poorer (tall fescue, white clover, lucerne and chicory), and so may become safer with shorter spelling intervals and there are some (sulla, Maku lotus) which reduce the effects of parasitism on lamb growth rate (the lambs are more resilient but contamination is not markedly reduced).

However, most of these differences are small and there are many other important features of pasture species, for example seasonal pattern of pasture growth and susceptibility to damage by heavy winter stocking rates which influence the choice of pasture species used on farms. It is unlikely that those current species which may have some parasitological advantages will dominate on New Zealand pastoral farms.

**Stocking rate**

Associated with the increase in per head production on New Zealand sheep farms is a slight decrease in stocking rate (Figure 20.4). There is a general concept that well fed animals (lower stocking rate) are less susceptible to developing parasitic infections although this is not always confirmed in well controlled experiments.\(^\text{29,30}\) Although animals at a higher stocking rate are more likely to be grazing at lower pasture heights (the lower sward horizons) where there is a greater concentration of nematode larvae,\(^\text{10}\) their feed intake is lower thus total larval intake may not necessarily be significantly greater. Furthermore, grazing to lower height (at a higher stocking rate) may sufficiently modify the larval environment to decrease larval survival.

The effect of stocking rate *per se* on internal parasitism is not clear. We must not be complacent that increasing levels of individual animal performance through lower stocking rate will inevitably decrease the risks of internal parasitism.

In summary, there appears to be increasing scientific evidence for the dissatisfaction or low uptake of some of the concepts commonly promulgated as components of IPCs.
Towards improved IPCs

Clearly, current on-farm IPCs are not ideal. They involve considerable anthelmintic use in situations which may encourage anthelmintic resistance to develop in worms (anthelmintic treatment of adult ewes) and reduce the development of natural immunity of hosts (preventative drenching of lambs). For example, is a lower drenching frequency in lambs (to encourage immunity to develop), but probably requiring a greater number of drenches before lambs reach target slaughter weight, likely to increase the risk of drench resistance? Current IPCs are not able to utilise the ‘safe’ pasture concept.

There is plenty of potential for improvement. We identify four key issues which would assist farmers in developing improved IPCs. These are:

- better prediction of appropriate spelling intervals to ensure effective decontamination or maximum infective larvae concentrations (e.g. see Fig. 20.1)
- a rapid, reliable and cheap method of measuring infective larvae concentration on pastures
- better understanding of the parasitological consequences of mixed species grazing
- consensus on components of IPCs which will minimise the risk of development of parasite resistance and maximise host immunity.

Summary

ICPs are a concept that must have a place in animal production systems. In intensive sheep farming systems this involves making best use of pastures, pasture plants and management systems which minimise the opportunity for exposure of grazing animals to levels of infection which cause clinical parasitism. Unfortunately there are no existing pastures, pasture species or management systems which can guarantee success in achieving the above aim. Therefore strategic use of anthelmintics is part of current IPCs. On-farm experience with some IPC concepts suggests the comment that IPCs are “elegantly simple in concept and in execution”\(^4\) is somewhat inappropriate and that there are many good reasons why on-farm IPCs are difficult to design and implement.
The on-farm application of ICPs will continue to improve as the success in predicting and measuring the parasite status of the pasture improves and we develop a better understanding of the role of mixed animal species grazing and specific pasture species with potential anthelmintic properties. Development of animals less affected by internal parasites would also help. Farmers and advisors await developments in ICPs with enthusiastic anticipation.

References


280 Nicol & Everest: Integrated control systems


