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FROM THE EDITOR
Welcome to this issue of TTW.
The main purpose of this informal newsletter is to share information with those interested in the management of endoparasites of farmed animals, including sheep, goats and cattle.
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WORMMAIL VS TURNING THE WORM
As noted above, Turning the Worm is a newsletter for sharing worm management related information, especially information that otherwise would have a limited circulation or not otherwise be readily accessible. It is published on the Industry and Investment-NSW (Primary Industries) website and, is a registered serial (ISSN 1442-8466). See http://www.nla.gov.au/services/issn.html and http://trove.nla.gov.au/.

Normally we aim to publish TTW 3-4 times a year, but this does not always happen.

WormMail is the name of a mailing list, and serves as a conduit:

• WormFax, which is mailed (through the WormMail list) as well as posted on our website
• Issues of Turning the Worm
• Occasional, usually weekly, updates, which are referred to as ‘WormMails’, and of late have also been posted to http://wormmailinthecloud.wordpress.com/.

Recently much of the content that normally would have been published in TTW has been included in WormMails. So, some of the content of TTW and WormMails may overlap.

To subscribe to WormMail, go to: http://www.dpi.nsw.gov.au/agriculture/livestock/sheep/health/internal/worm-mail

WORMBOSS
WormBoss is a national repository of information and guidance on sheep worm management.


There have been some issues since the move, but please be patient: with the assistance of AWI information technology staff, we are working on ironing them out.

Have you subscribed to the monthly WormBoss News/Outlooks? If not, subscribe at the website.

PARASITES OF SHEEP IN TASMANIA
Paul Nilon, Animal Health and Production Consultant, Perth, Tasmania
(An invited article written for Turning the Worm)

GEOGRAPHY
Tasmania lies between 40° and 43° south in the path of the roaring 40s. Our rainfall has a winter bias but is not as winter dominant as, say, Western Victoria, or the true Mediterranean climates.
Despite its "Just like England" reputation, many areas of Tasmania are too predictably dry, and combined with the cold winters the southern midlands and Derwent Valley look more like the Monaro1 than any part of England.

Mild summers favour larval survival and environmental decontamination only works some years.

SHEEP INDUSTRY

Like many areas on the mainland our sheep numbers have declined from approximately 4.5 million in 1990 to about 2.5 million now. Further, meat sheep have replaced merinos and wethers are almost extinct.

Although sheep are found all over the State, the numbers are small in the high rainfall, intensively farmed areas on the north coast. Most sheep still live in the drier Midlands, Derwent Valley and East Coast. Over much of this area the long-term rainfall is 400 to 600mm, with prolonged drought reducing this in recent years.

While renowned for its superfine Saxon wool, the fact is that the majority of the Tasmanian clip is a medium fine one, and getting stronger by the day as producers scramble to get greater body size to facilitate lamb production.

Many farms are irrigated, and on these places specialist prime lamb production fits better than wool.

WORM SPECIES

Our fulminating, uncontrolled parasitism is caused by Trichostrongylus vitrinus 2 in mid to late winter. Wet years are particularly suitable for this species to cause problems. In 2002 sheep of all classes and ages were laid low by a particularly bad season for worms. Trichs seem to disappear from late spring to late May.

Teladorsagia (Ostertagia) circumcincta 3 is present year round, but predominates in late spring, and again in the autumn and early winter. It is most likely to be our drench-resistant worm, but its predations are rarely as severe as those of Trich.

Nematodirus spp 4 (don’t ask which species) predominates in dry summers and autumns. While it is regarded as relatively benign in other parts, in Tasmania it can cause significant parasitism, particularly in weaners. Moreover, because of sporadic egg output FEC 5 triggers for treatment are low (150epg).

Haemonchus 6 is a sporadic problem on the East Coast and on Flinders Island. It is occasionally found in sheep and cattle on irrigated pastures in late summer, so it may become more important in time. Other species (Coopera, Oesophagostomum and T. axei) 7 are frequent incidental findings from larval diffs, but are not regarded as important.

Fluke 8 is found in the range country on the headwater soils and springs. Old hands warn to beware of fluke when the wallabies and deer start to die from it in late autumn. In wet springs, both snails and intermediate stages (miracidia) are washed down to the lowland rivers and may set up temporary fluke cycles in marshy backwaters of the South Esk and Macquarie Rivers. More importantly, fluke habitat is being extended by widespread irrigation.

Tasmania is (notionally) hydatids free, so deworming dogs is not done as diligently as many mainland areas. Consequently, condemnations for sheep measles (Cysticercus ovis) are higher than it should be.

CONTROL

Your correspondent’s merino clients are urged to use 1 or 2 summer drenches, depending on rainfall and specific seasons. This is given at lamb marking or weaning. Strategic drenches work so-so. Plenty of larvae seem to survive our summers. The good news is that strategic drenches have less impact on resistance status than they do in WA or western Victoria.

Therapeutic drenches are triggered by FECs. Weaners would receive 2-4 drenches outside the summer drenches, and adults 1-2, depending on season. Pre-lamb drenching is common, but not universal. Some clients did away with it last

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1 The Monaro is a region in southern NSW and is in a rain shadow. Average annual rainfall varies from 470 to 700 mm. http://en.wikipedia.org/wiki/Monaro,_New_South_Wales
2 One of the species of ‘black scour worm’.
3 (Small) brown stomach worm.
4 Thin-necked intestinal worm.
5 Faecal worm egg count.
6 Barbers pole worm.
7 Coopera sp: small intestinal worm; Oesophagostomum: almost certainly Oes. venulosa (large bowel worm) rather than Oes. Columbianum (nodule worm); T. axei: stomach hair worm.
8 Liver fluke: Fasciola hepatica.
spring, and surprise-surprise, the sky did not fall. It is not a strategy for every farm or all years.

Like most other parts of the world there has been widespread and dedicated use of long acting products. They are marvellously convenient, and, let’s face it; they work a treat until they fail. Weaners are often treated in early winter, ewes prelambing. Some properties have an uninterrupted history of use for 10 or more years. Those who have done resistance tests have had some ghastly surprises with macrocyclic lactones (MLs).

As mentioned, environmental control is not as reliable as on the mainland. There are opportunities to integrate grazing management with both cattle and cropping, but it is frequently all too hard. A few dedicated individuals have used “smart grazing” to great effect for 4-5 years. Others should follow.

Worm control on specialist prime places is relatively straightforward (at least on paper). Ewes sometimes get a pre-lambing drench; lambs are drenched at weaning and then on FEC results. As up to 30% of lambs are sold as suckers drench use is often limited. Brassicas and vegetable aftermaths (particularly left over broccoli) finish many lambs safely. The big problem is irrigated perennial pastures and short rotation ryes grass. These pastures become worm farms within 12 months and remain so until they are ripped up as part of the cropping rotation or become unusable. There is heavy reliance on white capsules.

Integrated grazing with cattle and mature sheep has had limited success. There are several PhDs awaiting the intrepid researcher able to devise a workable system.

Fluke burdens are rarely so onerous as to require really tight control. A spring strategic drench and a late autumn therapeutic drench are generally all that is given.

RESISTANCE

Tasmania is perhaps 10 years behind the mainland in drench resistance. This is for two reasons: firstly, summer refugia slow resistance development; secondly we are less than diligent in looking for it. ML resistance is in its infancy. Most properties come back at, say, 99% for full ML and maybe 97% for 1/2ML. Teladorsagia are our most resistant species. Trichs are frequently resistant to levamisole, but rarely to BZs. Many properties find standard combinations still work well, and using OP combinations is in its infancy. Properties with an unrelenting history of ML use get a bit shocked when they see their results.

Of course, strategies to slow resistance are usually not adopted until it becomes a problem. This is very much the case here as sheep production is often the second or third string operation. Sustained sheep meat prices or the return to good wool prices may bring more focus to bear on this and other sheep production issues.

Author details:

Melton Farm Health
Paul Nilson. BVSc, MVS, MACVSc; Animal health and production consultant, RD Box 129, Perth, Tas. 7330.
Phone: 03 63981566 Fax: 03 63981677
Mobile: 0410 399585 Email: pnilson@bigpond.com.au

Beyond the gate

A MOISTURE INDEX TO PREDICT DEVELOPMENT SUCCESS OF BARBER’S POLE WORM AND ALLOW BETTER MANAGEMENT OF PASTURES

Lewis Kahn
School of Environmental and Rural Science, University of New England, Armidale

(An invited article written for Turning the Worm)

Barber’s Pole worm, also known as Haemonchus contortus, is one of the major infective worm species of sheep in summer rainfall regions, such as northern NSW and southern QLD. Death due to the effects of infection from Barber’s Pole can occur suddenly, mortality rates can be high (up to 20% of a mob) and this represents a significant component of the cost of worms in a summer rainfall region. A better understanding of the factors that control the life cycle of Barber’s Pole worm may prove useful in the management of...
integrated worm control programs and reduce the impact of this parasite.

The life cycle of Barber’s Pole consists of eggs being shed by adult female worms, resident in the true stomach (or abomasum), that are passed from the sheep in faecal pellets. The egg-laying potential of adult females is very high, compared to most other major worm species, and has been estimated to reach up to 15,000 eggs a day. Within the faeces, eggs hatch and develop through to infective larvae which migrate onto pasture and soil. Susceptible sheep become infected when they consume pasture which carries the infective larvae of Barber’s Pole.

Development from egg to infective larvae requires adequate temperature and moisture. For example, development of Barber’s Pole eggs occurs with minimum and maximum temperatures that exceed 10°C and 18°C respectively. Temperatures below these values are unlikely to lead to development. The optimum temperature range for development is 25–35°C. Greater temperatures lead to faster development with the time taken for development from egg to infective larvae likely to fall from 6 days at 20°C to 4 days at 30°C.

Adequate temperature is insufficient for the successful development of Barber’s Pole eggs and negligible development to infective larvae will occur without rainfall. Development requires sufficient moisture at the right time in relation to when eggs are deposited onto pasture in faecal pellets. The term, development success, is used to describe the percentage of Barber’s Pole eggs in faeces that successfully develop to infective larvae. For example, a development success of 5% indicates that 5 out of every 100 eggs developed to infective larvae. The other 95 eggs, in this example, were not successful and perished along the way.

The emphasis on moisture rather than rainfall alone is an important consideration for estimating development success. For example, under conditions of low evaporation (2.5 mm/day), development success may be rise from 0.2% with a rainfall event of 12mm, to 2.0% with 24mm and to 6.0% with a 32mm event. Under conditions of higher evaporation (4.8 mm/day) development success may be 0.1%, 0.5% and 2.0% for the same rainfall amounts of 12, 24 and 32mm. It is apparent that the success of development depends not just on the amount of rainfall but also on the rate of evaporation.

The timing of rainfall events, and hence moisture availability, is also critical for the development of Barber’s Pole infective larvae. Rainfall amounts of 32mm delivered either on the same day that faeces are deposited compared to just 3 days later may result in development success falling from 6.0% to 0.5%.

The effects of rainfall and evaporation can be combined to produce an index that may be useful to estimate the development success of Barber’s Pole eggs and as a consequence the likelihood of sheep infection from grazed pastures. Work from our research group, has built upon the earlier suggestions of the late Dr Ian Barger, and suggests that the cumulative ratio of rainfall to evaporation over a 3–day period is a useful predictor of development to infective larvae. An example is a useful way to understand this concept. If rainfall on days 1, 2 and 3 following egg deposition in faeces was 16mm, 0mm, 0mm and evaporation rate was 4mm, 5mm, 4mm then the cumulative ratio on day 3 would be:

\[
\text{Rainfall/ Evaporation} = \frac{16+0+0}{4+5+4} = 1.2
\]

The greater the ratio of rainfall to evaporation the greater the development success of Barber’s Pole eggs. Values less than 1.0 at day 3 are unlikely to lead to development of infective larvae.

It is at this stage, that attention can be drawn to the duration of moisture, that is, how many days does the rainfall to evaporation index need to stay above a minimum value to permit development. Our research suggests that development will be minimal if the ratio falls below 1.0 within 4 days of deposition. Beyond that minimum value, the longer the ratio stays above 1.0 the greater will be the likely development.

So let’s put these concepts into a practical example and try and predict the extent of development success of Barber’s Pole eggs. We are not trying to predict a particular percentage success but rather if development is likely. In this example, the location is Armidale, NSW and faeces containing Barber’s Pole eggs are deposited onto pasture on the 1st December. A rainfall event of 40mm occurs the following day but no other rainfall is recorded for the next 6 days. The evaporation rate was 5 mm/day for every day of that week.

The first consideration is temperature, which ranged from 15–30°C and so we know development was possible. The second consideration is the timing of the rainfall event which was just 1 day after deposition and so we know that the timing was OK. The third consideration is the moisture index, which was calculated to be 2.7 on day 3 after deposition (rainfall = 0 + 40 + 0; evaporation = 5 + 5 + 5), and 2.0 on day 4 after deposition, indicating that moisture was of sufficient duration to permit
development. It would be concluded that infective larvae would develop. However, if the rain had fallen 4 days after faecal deposition or had only amounted to 15mm then little, if any development would be predicted.

The moisture index is still being investigated by our group, particularly how robust the cumulative ratio is in a commercial situation. The application of this index would allow prediction of the rainfall events likely to have led to development of infective Barber’s Pole larvae and therefore identification of the more infective paddocks. These paddocks could be managed in a number of ways to reduce the threat of Barber’s Pole infection and the resultant sporadic but high rates of mortality and financial loss. There are probably not many development events in a year for Barber’s Pole in some locations but because of the egg-laying potential of this species these are sufficient to cause major financial loss. At Armidale, historic records suggest only 30-40 days each year are permissive for development of Barber’s Pole infective larvae. This index may eventually form part of an integrated approach to parasite management in summer rainfall regions to better manage Barber’s Pole infection.

ACKNOWLEDGEMENTS AND REFERENCES

This work has been conducted by Dr Lauren O’Connor, Ms Khadijah Saad, Professor Steve Walkden Brown and myself. Support was provided by Australian Wool Innovation through the project ‘Integrated Parasite Management in Sheep’ and the Cooperative Research Centre for Sheep Industry Innovation. A more detailed description of this work can be found in the following publications:


CONTROL OF ACUTE, SUBACUTE AND CHRONIC FASCIOLOSIS IN SHEEP AND CATTLE (AN ESSAY FOR GENERAL INFORMATION)

Joseph C. Boray
Specialist Veterinary Surgeon (Pathobiology); Consultant for Parasitology

INTRODUCTION

A well planned strategic treatment schedule is essential for the control of fasciolosis to reduce economic loss by liver condemnation, mortality, secondary bacterial infections, interference with fertility, reduced wool, milk and meat production and through the expense of control measures. About 250 million sheep and 300 million cattle are potentially affected by the disease world-wide. The clinical disease is more often manifested as a chronic anaemia. However, we have to emphasise the important role of acute and sub-acute fasciolosis which also cause production loss and mortalities.

EPIDEMIOLOGY

Completion of the life cycle of Fasciola hepatica and potential infection of sheep and cattle depends mainly on rainfall or the presence of moisture and temperature. The moisture necessary for the reproduction of snails and the hatching of fluke eggs is usually provided by small permanent creeks, normally fed by springs. Those creeks running through paddocks and gullies support the amphibious intermediate hosts Lymnaea tomentosa in shallow muddy habitats preferred by the snail. Similar conditions are created by seepage from canals in the irrigation areas. In drought some of the springs dry up but some moisture may be still present to maintain the growth of grass which has the infective stage of the fluke. The sheep and cattle congregate around those gullies and graze the contaminated herbage, resulting in heavy acute infection in the animals.

During drought the sheep and cattle congregate around the moist areas and can obtain heavy infections.

During the winter the metacercariae may survive for some time on the herbage under moist conditions. The first invasion of herbage with the fluke cysts commences in late spring when the larval stages of fluke which are obtained from infection of snails in autumn. The fluke larvae complete the development when the temperature increases (overwintering infection). At the same time the snails rapidly multiply under the more suitable conditions and become infected by the fluke larvae (miracidia) which hatch out from the fluke eggs produced by the adult flukes in sheep and cattle. Within 2–3 months more fluke cysts will invade the herbage during the summer months (summer infection) and reach high contamination by the end of summer and the beginning of autumn. Heavy infections may occur during this period but the clinical symptoms of acute and sub-acute fasciolosis are often unnoticed. The disease produces obvious symptoms in most cases when the parasites reach the chronic adult stage about 2 months later.

Due to progressing anaemia the economic loss is more pronounced, reducing the wool growth and bodyweight in sheep, particularly in younger animals. The clinical symptoms of the acute disease will not be obvious for 2-3 months in the spring and early summer period unless the pastures are heavily contaminated and at that time increasing mortalities may occur.

PATHOLOGY OF ACUTE FASCIOLOSIS

We should emphasise the pathological effect of acute and sub-acute fasciolosis in sheep and cattle. In sheep the acute disease is due to a mechanical damage when large numbers of immature flukes migrate through the liver tissues and destroy the functional liver cells. The inflicted damage to the liver tissues also causes a retardation of growth of the flukes and tissue migration period will be extended which causes severe sub-acute fasciolosis. Peracute, acute and sub-acute fasciolosis is caused by the tissue migration of immature flukes. The pathological damage produces cell destruction causing extensive haemorrhage. Deaths are normally due to profound anaemia resulting from blood loss and the failure of liver function. However, the role of the excretion of proline and subsequent tissue changes should also be considered (Symons & Boray, 1968, Boray, 1985). Outbreaks may occur with considerable losses when seasonal and climatic conditions result in a large intake of metacercariae during a relatively short period.

The second important condition for the completion of life cycle and the survival of metacercariae is suitable temperature. In winter all stages of fluke development and reproduction of snails cease when the temperature is around 10°C or less, but the snails survive together with the dormant fluke larvae. The snails and the fluke larvae within the snails also survive in the mud during dry periods for about a year. After rain the snails emerge and complete the life cycle of the fluke, producing cercariae, contaminating the pastures with the infective metacercariae, attached to grass.
Much work on the pathology of fasciolosis was carried out in the McMaster Laboratory, CSIRO (Boray, 1967, 1969). Trials were carried out with experimentally infected sheep, which involved a total of 269 animals. It was shown that in sheep with an average fluke burden of 103, clinical disease was not evident until the fluke matured and a large proportion of the sheep was suffering clinical chronic progressive anaemia causing death in some of the sheep in the higher fluke recovery groups. In two groups of sheep which had an average of 204 flukes after experimental infection, early liver damage causing a reduced liver function was demonstrated with serological tests by detecting a very high level of the enzyme glutamate dehydrogenase (GLDH, see Fig. 1). In the tests as early as two weeks after infection, the high enzyme levels persisted for 16 to 18 weeks, demonstrating the presence of liver damage, caused by acute and sub-acute fasciolosis. All of those sheep died of progressive profound anaemia 26 – 36 weeks after the inoculations.

In a group of sheep which had an average of 708 flukes in their liver after infection, the animals had acute and sub-acute clinical fasciolosis, resulting in haemorrhages and severe anaemia. All the sheep eventually died after 15 to 22 weeks infection. During decades of field work similar fluke numbers were often found in sheep. In one occurrence of acute and sub-acute fasciolosis in sheep an average of 1,384 flukes was present in the livers at necropsy.

In further experimental work in merino sheep aged 5 years, serious acute and sub-acute fasciolosis was observed and in a group of 58 sheep an average of 1,535 flukes was present at necropsy. All those sheep died within 7 to 10 weeks after infection suffering from severe haemorrhages and with the evidence of acute and sub-acute liver damage.

All the above sheep, including those with only around 100 flukes in the liver, had loss of appetite, reduction of weight, anaemia and thus subsequently died indicating the potential pathogenicity in the field if the animals are not treated.

In one experiment a group of sheep was infected with 500 metacercariae each and was treated with triclabendazole at 10 mg/kg ten weeks later to achieve eradication of the fluke. Ten weeks after the treatment the same procedure was repeated to inflict heavy damage in the liver and then remove the fluke. In another group a similar procedure was carried out, but each sheep was infected with 100 metacercariae only. The sheep showed evidence of successful treatment and ten weeks after the second inoculation and treatment all the sheep were inoculated with 500 metacercariae each. One group of sheep remained uninfected and untreated as controls. The high level of liver damage was demonstrated by the increased GLDH levels in the serum. Similar numbers of flukes were present at necropsy 14 weeks after the challenge infection in all the sheep, including the controls. This experiment showed that a previous infection did not generate an immune reaction against the second infection and the serum enzyme test was a useful tool for diagnosing acute fasciolosis in sheep (see Fig. 2).

In all the above experiments there was always sufficient liver damage by the flukes to explain deaths. However, in the majority of cases, secondary pathological lesions, such as peritonitis, pleuritis and traumatic damage in the lungs and pancreas, contributed to the condition. The primary damage due to the migrating flukes was detected with a single bromsulfalein clearance test as early as three weeks after infection (Symons and Boray, 1968), thus demonstrating the occurrence of liver function failure caused by immature flukes. Those results were in accordance with results of experimental work in Wales (Sinclair, 1967).

STRATEGIC CONTROL IN SHEEP

In an endemic area a curative drench has to be given in April/May, when a high level of infection is anticipated. For this treatment a product should be used which is highly effective against both early immature and adult fluke. The best treatment for this period is an oral dose of triclabendazole and particularly the highly effective formulation of Flukazole S, which has an improved efficacy by the addition of oxendazole. The increased efficiency is achieved by a synergistic effect of the two ingredients.

The second essential treatment (preventive treatment) is very important at the end of the winter or early spring (August/September) to eliminate the flukes surviving in the sheep and reduce the contamination of the pasture before the active period commences with increasing temperatures. At that time most of the flukes would have reached an advanced immature or adult stage when another product which is effective against those stages could be used with good results. Many products are available for but a product containing closantel would be the most effective for this purpose.

The above products include chemicals which belong to groups different from triclabendazole. This treatment would achieve an effect of drug rotation, reducing the chances of the development of resistance to triclabendazole.
In endemic areas with high rainfall in spring an additional treatment in January/February is recommended with drugs highly effective against immature fluke as mentioned above. At that period a high proportion of the flukes in the liver would be immature.

PATHOLOGY IN CATTLE

It has been generally recognised that cattle are more resistant to fasciolosis than sheep (Boray, 1967, 1969, Ross, 1967) due to more intensive tissue reaction in cattle than in sheep and in the bovine hosts a considerable age resistance is present. It has been concluded that the resistance observed in cattle is due to the combination of an early and a late tissue reaction forming a mechanical barrier against re-infection. The normally observed preferential migration of young flukes into the ventral lobe produces an effective mechanical resistance and the subsequent hypertrophy of the right lobe facilitates the survival of the host by leaving sufficient undamaged liver tissue. The dystrophic calcification of the bile ducts and the fibrosis proliferating into the parenchyma in chronic cases causes the elimination of the flukes. Calcification is not present in sheep. Some results of experimental infections carried out in McMaster Laboratory (Boray, 1969) may give reasonable information on the clinical pathology expected to occur in the field.

Severe anaemia was diagnosed in a group of calves aged 6 to 8 months after experimental infections with 1,000 metacercariae each. One calf died but three calves recovered spontaneously. A group of 4 month old calves which had a mean number of 1,358 flukes in the liver, showed profound anaemia and high egg counts when the flukes reached maturity. In another group of 6 calves aged 6 to 8 months, one calf died, two showed severe anaemia and two of the calves showed no clinical symptoms. They had a mean number of 1,381 flukes in the liver. When a group of calves aged 17 months were infected with the same number of metacercariae only a mean number of 620 flukes were recovered from the liver and the calves showed no clinical symptoms of fasciolosis. In another experiment cattle aged 6 to 8 months or 2 years were infected with 10,000 metacercariae. All the younger animals showed profound anaemia and all died of sub-acute or chronic fasciolosis and a mean number of 4,671 flukes was recovered at necropsy. The two year old cattle showed no serious clinical symptoms and a mean number of 512 flukes were recovered from the livers. It was also shown that calves in good condition showed more resistance than poorer ones. It was also shown that some breeds of cattle were more or less resilient to fluke. In a comparative experiment, Jersey calves aged 4 months showed more serious clinical symptoms compared to Herefords of the same age after experimental infections resulting in a similar number of flukes recovered at necropsy.

FASCIOLOSIS - CONCLUSIONS

It can be concluded that acute and sub-acute fasciolosis causing serious clinical disease occurs mainly in younger animals with severe anaemia and death occurring on heavily contaminated pasture and more often when susceptible sheep are grazed together with calves. Flukes in sheep normally produce more eggs than in cattle contaminating the pastures. However, there is considerable evidence that even a low infection in young cattle may result in reduced growth rate, reduced pregnancy rate and delayed conception of heifers. In adult cows milk production is reduced in sub-clinical infections due to Fasciola hepatica.

STRATEGIC CONTROL IN CATTLE

Strategic liver fluke control is essential to maintain productivity of cattle even if no visual signs of clinical fasciolosis are present but positive egg counts, serological tests or ELISA tests using milk samples confirm the presence of fasciolosis. The most important treatment should be carried out in April/May when the highest levels of infective metacercariae are present on herbage. At that time an anthelmintic should be used which is highly effective against early immature and adult flukes. The most effective product for that purpose is Flukazole C plus Selenium drench, which is a combination of triclabendazole and oxendazole with synergistic action, or other products applied orally which contain triclabendazole, or Nitromec® injection, which is a combination of clorsulon, nitroxynil and ivermectin with high efficacy against early immature and adult flukes and gastrointestinal nematodes. The use of Nitromec® has the advantage that it does not include triclabendazole in the formulation and it represents a useful rotation treatment, reducing the chances of producing resistance against triclabendazole. At that time none of the other products, including pour-on treatments, are useful because they are only effective against adult fluke. In dairies, triclabendazole preparations and Nitromec can be used in young heifers and in dry cows. In lactating cows the ivermectin + clorsulon

13 Enzyme-linked immunosorbent assay.
14 For information on various commercial anthelmintic products, go to www.apvma.gov.au and search in the ‘PUBCRIS’ section.
triclabendazole products can be used which have clearance for lactating cows. However those products are only effective against adult flukes. **NB:** Various triclabendazole products, including some pour-on formulations, are registered by the APVMA ([www.apvma.gov.au](http://www.apvma.gov.au)) in Australia as being ‘effective against all three stages of fluke (adults, immatures, early immatures)’. Note that the definition of ‘effective’ may vary in different contexts. Nitromec® is not registered in Australia for use in dairy cattle. Not all triclabendazole products are registered for use in dairy cattle. It is important to read and follow the (APVMA-) approved product labels. –SL (Editor), 2010-03-31.

The second important treatment (preventive treatment) is recommended to be carried out in August/September to eliminate the flukes surviving in the cattle after the Summer/Autumn period. This time most of the fluke have reached adult stage and combination treatments such as Virbamec Plus®, Ivomec Plus® or other products effective against adult flukes can be used. Another triclabendazole treatment and particularly a pour-on (topical) application of the drug should be avoided. Delayed absorption of the drug from these formulations may contribute to the development of drug resistance. The use of an alternative drug, such as Nitromec® would achieve chemical rotation and reduce the chances for the development of resistance to triclabendazole.

In endemic properties with a history of heavy infections, a third treatment may be necessary in January/February, particularly when spring and early summer rain would stimulate the reproduction of snails or dry periods when the animals congregate in moist pastures. This treatment is highly recommended for young cattle which are more susceptible to infection and likely to develop clinical fasciolosis. During this period a high contamination of the herbage is expected through the “overwintering” larval stages of the parasite when the temperature increases in late spring. Increased numbers of cercariae will also complete their development in the snails which were infected in early summer. This treatment in January/February should be carried out with an oral drench preparation of triclabendazole or as an injection with Nitromec® which are highly effective against immature flukes. Dairy heifers can be treated until 4 weeks before their first calving.

Triclabendazole resistance in sheep and cattle is present in the Goulburn Valley irrigation area around Echuca, Pyramid Hill and Shepparton. In those areas an alternative product should be used such as an injectable application of the combination products containing ivermectin and clorsulon, which is suitable for both dry and lactating cows but they’re only effective against adult flukes. The new combination product, Nitromec® with high efficacy against early immature flukes and adults can be used for calves, beef cattle and dry cows.

**ORAL APPLICATION OF TRICLABENDAZOLE COMPARED TO POUR–ON FOR THE TREATMENT OF FASCIOLIOSIS IN CATTLE**

Recently pour-on products were released to the market and the problems of the treatment with those products will be discussed below.

Triclabendazole showed high efficacy against both early immature and adult *Fasciola hepatica* in sheep (Boray et al., 1983) and in cattle (Boray, 1982). The drug is a halogenated benzimidazole derivative, but the presence of chloride atoms and a thiomethyl group and the absence of a carbamate moiety clearly distinguishes it from all other benzimidazole compounds. Its spectrum of activity is unusual. Triclabendazole is very specific for *F. hepatica*, *F. gigantica* and *Fascioloides magna*. It lacks activity against nematodes and cestodes and other trematodes as well.

Triclabendazole is metabolised by the liver into two active forms, triclabendazole sulphoxide and triclabendazole sulphone. The first metabolite is more effective than the second against *Fasciola* sp. It is clear that the rate at which these metabolites are produced and in what concentration, will determine their efficacy against liver fluke. To achieve high efficacy against early immature liver fluke a high concentration of those metabolites are required to act against immature fluke, which are migrating in liver tissues. The adult flukes in the bile ducts are killed by those metabolites as they are excreted into the bile.

Triclabendazole given orally as a drench is absorbed from the gastrointestinal tract and quickly transported to the liver via the portal blood flow, which drains directly into the liver, achieving a high concentration of the drug, which will be quickly metabolised. Triclabendazole given either parenterally or as a pour-on will travel through the entire vascular system before it can be metabolised in the liver. The delayed absorption will produce a dilution effect and will reduce the concentrations of active triclabendazole metabolites in the liver, resulting in lower efficacy for early immature flukes aged 2 to 4 weeks. It is reasonable to say that oral dosing of triclabendazole will produce a greater concentration of the metabolites in a shorter time because the drug has direct access to the liver.
from the gastrointestinal tract via the portal system.

The mode of action of triclabendazole was reviewed by Fairweather & Boray (1999). Triclabendazole has a multiple action against the flukes. It seems to affect the energy-producing pathways resulting in a decrease of motility. Triclabendazole also damages the reproductive system of *F. hepatica* reducing egg production and growth of the fluke. The most significant effect of the drug is the inhibition of protein synthesis which in turn, produces morphological damage to the integument of flukes. Most of the experimental data conform to a microtubule-disrupting action and disruption of protein synthesis. Additional studies showed that triclabendazole is also capable of uncoupling oxidative phosphorylation and this action was greater by the sulphoxide than that of the parent compound.

During the development of triclabendazole in the second half of the 1970s, the sheep and cattle experiments were carried out in the CIBA-GEIGY Research Centre in Australia, supervised by Dr. Boray, who was then Director of Research and Development in the company. It was shown that at comparative dose rates the oral formulations were superior to the injectable or pour-on formulations.

The pour-on formulation produced by CIBA-GEIGY in Basel used an excellent solvent, resulting in very good absorption from the surface of the skin. However, even at drastically increased dose rates of up to 30 mg/kg, high efficacy was only achieved against adult flukes. Experience from trials with other pour-on products, which were carried out by J.C.Boray at the Elizabeth Macarthur Agricultural Institute, NSW Agriculture in the late 1980s, has shown that the age and breed of cattle and the season when the treatments were carried out greatly influenced the efficacy of a pour-on formulation. The absorption of the drug may be impaired by the dense hair growth during winter, particularly on beef cattle.

When the choice of drug for the treatment of cattle is triclabendazole, it can be concluded that the best results will be achieved by using the products, which are formulated for oral application or use another combination product, Nitromec® injectable, which has no triclabendazole in its formulation, reducing the chances of producing resistance.

Author details:
Joseph C. Boray, DVM, PhD, Dr Med Vet Habil, FACVSc.
Specialist Veterinary Surgeon (Pathobiology);
Consultant for Parasitology

Tel: 02/88505515
Email: jbo56991@bigpond.net.au

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Further to the scientific treatise on liver fluke (above), following are some points of clarification, mostly of a regulatory nature.

TRICLABENDAZOLE PRODUCTS IN DAIRY ANIMALS AND POSSIBLE RESIDUE ISSUES

Check the label for the particular triclabendazole product you wish to use, particularly with respect to withholding periods and whether they are registered for use in dairy cattle. Of course, the label should be read and followed for any product that you use.

TRICLABENDAZOLE PRODUCTS AND LABEL CLAIMS

Some pour on triclabendazole products have met APVMA \(^{15}\) requirements to allow label claims of being ‘effective against all three stages of liver fluke (adult, immature, early immature)’. In the case of liver fluke, APVMA allows a claim of ‘effective’ if the product has an efficacy > 90% efficacy (c.f. > 95% for nematodes).

Notwithstanding this, Hutchinson and others (2009) showed that, with respect to very young (2 week old) fluke, an oral formulation of triclabendazole (TBZ), although not particularly effective, was more effective than a pour-on formulation. Martin and others (2010) reported an oral formulation of triclabendazole (TBZ + oxfendazole) had greater efficacy than a pour-on formulation (TBZ + abamectin) against 28 day-old fluke. Check the papers for the details.

NITROMEC® INJECTION

Nitromec® injection, which was launched in early 2009, is not registered for use in dairy cattle (cattle which are producing or may in the future produce milk which may be used in products for human consumption.

Again, it is important to read and follow the label.

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\(^{15}\) The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an Australian government authority responsible for the assessment and registration of pesticides and veterinary medicines. www.apvma.gov.au/
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[Turning the worm] is a newsletter for those interested in the management of endoparasites of farmed animals.
Editor: Stephen Love
Veterinarian/State Worm Coordinator
Building C02, Ring Rd North
University of New England
Armidale NSW 2351
Phone 02 6738 8519
stephen.love@industry.nsw.gov.au
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