



turning the worm

ISSUE 23, JULY 2008

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FROM THE EDITOR

Welcome to this issue of TTW.

WORMBOSS

Have you been to www.wormboss.com.au lately?

It is an easily accessible repository of information and tips on sheep worm control for every region of Australia.

To keep up to date and in touch, subscribe to the monthly WormBoss News at

<http://wormboss.com.au>

PATHOLOGY AND DIAGNOSIS OF INTERNAL PARASITES

(From WormMail 20080602)

If you are interested in this paper*, it is now retrievable from the NSW DPI website:

http://www.dpi.nsw.gov.au/__data/assets/pdf_file/0/003/34608/lh-pathol-int-para.pdf

OR <http://tinyurl.com.au/x.php?szc>

(126 kb, PDF, 27 pages incl. tables).

There are also links to this document from the sheep, goat and cattle health pages on the DPI website.

* Reproduced with permission: Love SCJ, Hutchinson GW (2003). Pathology and diagnosis of internal parasites in ruminants. In Gross Pathology of Ruminants, Proceedings 350, Post Graduate Foundation in Veterinary Science, University of Sydney, Sydney; Chapter 16:309-338.

WORMMAIL

WormMail is an informal electronic mailing list coordinated by Stephen Love, State Worm Control Coordinator. Subscription is free. Subscribers are treated to the following:

- Turning the Worm Newsletter - 2-3 times a year
- WormFax - a monthly 'digest' of WormTest information from around NSW.
- News, Views and Updates on matters parasitological - from time to time.

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NEW ANTHELMINTIC - 'MONEPANTEL' (AAD 1556)

(From WormMail 20080704b)

In WormMail 20080314 we mentioned a [Nature article](#) (Kaminsky et al) reporting a new anthelmintic class, the amino-acetonitrile derivatives (AADs). Go to <http://www.nature.com/nature/journal/v452/n7184/full/nature06722.html>

More recently Kaminsky et al have published on a particular candidate for development: monepantel (AAD 1556).



See abstract below, or go to <http://www.springerlink.com/content/b2g76x808x263807/>

The comments from WormMail 20080314 bear repeating:

Before you get too excited ('this new drug will solve all our worm problems'), consider the following:

- It takes a lot of time and money to get a new drug to market.
- Just because a new drug is discovered does not mean it will make it to market, or all segments of the market.
- No new anthelmintic class has reached the market in the last 25 years except the cycloheximides, and the drug from this class which has been marketed (Bayer) is only for use in cats.
- We have an unenviable history of 'killing off' new drenches sooner rather than later (see table below). If we get a new drug class, will we take better care of it?
- Even with the prospect of a new drug, it is more important than ever to implement an integrated approach to worm control, employing non-chemical approaches to parasite control as well as the judicious use of all available anthelmintics.

Drench	Released	1 st report resistance	Years
Thibenzole® (thiabendazole)	1961	1966	5
Rametin® (naphthalophos)	1960s	1981	~20
Levamisole	1968	1979	11
Closantel	1982	1988	6
Ivomec® (ivermectin)	1988	1993	5
Cydectin® (moxidectin)	1995	2001	6

Table. Adapted from Love S (2007). Drench resistance and sheep worm control. [NSW DPI Primefact 478](#).

What are some of the practices we should avoid or minimise to reduce selection for drench

resistance? Or, how should we look after a new drench class?

Pomroy (NZ Vet J Dec 2006, p 265 ff) recently outlined much of the current thinking. (Many of the articles in this issue of NZ Vet J are summarised in [Turning the Worm Issue 22, December 2007](#)).

An interpretive summary of this follows:

MANAGING DRENCH RESISTANCE

The following practices are regarded as high risk in relation to selection for drench resistance, and should be minimised:

- unnecessary treatment of sheep, especially adults
- moving newly drenched animals to very clean pasture
- failure to effectively quarantine drench bought-in animals
- treating ewes pre-lambing with long-acting anthelmintics
- unknowingly using ineffective drenches.

(Source: WestWorm. Primefact 736, revised edition)

With respect to managing drench resistance, using drenches in combination is also advocated, at least by most advisers in Australia and NZ.

Reference

Kaminsky et al (2008). Identification of the amino-acetonitrile derivative monepantel (AAD 1566) as a new anthelmintic drug development candidate. Parasitology Research.

Retrieved 20080704 from <http://www.nature.com/nature/journal/v452/n7184/full/nature06722.html>

Abstract. Anthelmintic resistance has become a global phenomenon in gastro-intestinal nematodes of farm animals, including multi-drug resistance against the three major classes of anthelmintics. There is an urgent need for an anthelmintic with a new mode of action. The recently discovered amino-acetonitrile derivatives (AADs) offer a new class of synthetic chemicals with anthelmintic activity. The evaluation of AADs was pursued applying in vitro assays and efficacy and tolerability studies in rodents, sheep, and cattle. Amongst various suitable compounds, AAD 1566 eliminated many tested pathogenic nematode species, both at larval and adult stages, at a dose of 2.5 mg/kg bodyweight in sheep and 5.0 mg/kg bodyweight in cattle. The same doses were sufficient to cure animals infected with resistant or multi-drug-resistant nematode isolates. These findings, complemented by the good tolerability and low toxicity to mammals, suggest that AAD

1566, monepantel, would be a suitable anthelmintic drug development candidate.

HYDATIDS IN NZ

(From WormMail 20080704a)

The following is from NZ-based parasitologist Dr Paul Mason, and is reprinted with permission:

Steve - Hydatids (*Echinococcus granulosus*) is potentially a much greater problem in Australia than NZ, because of your much wider range of both final and intermediate sylvatic hosts. In NZ it is eradicated apart from a couple of off-shore islands. Here the only functional intermediate hosts were domestic animals: sheep (most important), goats, cattle and horses (though this may have been a separate strain); with the dog as the only final host. Most gains in control were made before praziquantel became available, through education of farmers to fence off the sheep slaughter area on the farm and not to feed offal. I managed the National Hydatids Testing Station on the Taieri from 1974 until it closed in the mid 1980s. – Paul M.

CONTROLLING HYDATIDS

(From WormMail 20080703)

Below are some excerpts from a soon-to-be published Primefact on hydatids.

Hydatids is a human health hazard, as well as a wealth hazard (condemnations at abattoirs).

"At its intermediate stage, cysts form in the internal organs of a number of animals. Humans can also be intermediate hosts, with serious health consequences".

*"Control is by preventing or eliminating hydatid tapeworm infections in the final hosts – dogs, foxes and dingoes. **Controlling hydatids will also help to control sheep measles, caused by a tapeworm with a similar lifecycle**"*

"The sylvatic (wildlife) life cycle may involve dingoes, dogs and foxes as final hosts and kangaroos and wallabies as intermediate hosts."

"CONTROLLING HYDATIDS

Simply, this involves preventing or eliminating hydatid tapeworm infections in final hosts, notably dogs. To prevent the disease in humans, hygiene is important.

FEED ONLY MANUFACTURED DOG FOOD

Even cooked meat or meat by products from stock slaughtered on farm may contain viable hydatid tapeworm heads from ruptured cysts.

PREVENT ACCESS TO OFFAL OR DEAD STOCK

Dogs on farms and in public places should be restrained or closely supervised. Sheep provide the greatest risk because they have the largest proportion of viable cysts when infected.

ELIMINATE INFECTIONS

The only suitable tapewormer for treating dogs is praziquantel. This active ingredient is found in many dog wormers (Check the label).

When treating potentially infected dogs, take great care in disposing (by deep burial, or burning) of droppings for 3 days after treatment.

Dogs at on-going risk of infection will need to be treated with praziquantel every 6 weeks.

BE AWARE OF WILDLIFE SOURCES

Farm dogs are not the only source of hydatids infection. Wild and straying dogs and foxes carry hydatid tapeworms. Direct or indirect contact with faeces from these animals can result in the transmission of hydatids to humans.

HYGIENE

As with many zoonoses (diseases transmissible from animals to humans), attention to hygiene can markedly reduce the risk of infection.

Always thoroughly wash hands before putting your hands near your mouth (for eating, cigarette smoking etc), especially after handling dogs or being in potentially contaminated areas such as around kennels. Wash vegetables and fruit before eating. Teach your children to do the same, by precept and example."

References

King and Hutchinson (2007). Hydatids-you too can be affected. Primefact 475 NSW DPI; retrieved 7 July 2008 from <http://www.dpi.nsw.gov.au/agriculture/livestock/sheep/health/internal/hydatids>

Love S (2008). Hydatids-the basics. Primefact 812 (in press). NSW DPI.

Sarre A (2000). Hydatids-when a dog is not man's best friend. Retrieved 7 July 2008 from [/www.science.org.au/nova/056/056key.htm](http://www.science.org.au/nova/056/056key.htm)

STRANGE DRENCHTEST RESULTS – A CONVERSATION

(From WormMail 20080701)

Following the Wormmail of 20 June (Sheep drench resistance - a case report; see below), I got the following inquiry:

"Dear Steve,

"I was wondering what the possible explanations for the results in the 1st case study that show the individual actives of BZ (benzimidazoles) and Lev (levamisole) out performing the BZ/LEV combination for brown stomach worm (*Teladorsagia* sp)?

"I have had this happen to me a couple of times while conducting faecal egg count reduction tests (FECRTs; DrenchTests) for various clients.

The following is based on my reply:

"Hi Mark

"Well, it doesn't make sense, does it?

"I think part of the explanation lies in the variability and vagaries of biological systems. You can't say a result for drench X is exactly 45% (or whatever), because in re-test it might be 64% or 32%....but hopefully still in the same ballpark.

"And this assumes that everything was done right in the DrenchTest: on-farm and in the lab. (I think mistakes in the lab are rare, accredited labs at least).

"Normally we work out '95% confidence intervals' (at least NSW DPI Vet Labs do) to get an idea of where the 'true' number lies, especially if the numbers are around the 95% mark and we are trying to work out if the result is 'resistance' or not.

"So, with the example above, for drench X: our calculated figure might be 45%, but the '95% confidence interval' might be from, say, 30% to 70%, depending on the variability of the data. i.e. the 'true' figure probably (95% likely) lies in the range 30% to 70%.

"This is one reason to choose young sheep for a DrenchTest: as well as being likely to have higher worms burdens (high enough for a meaningful DrenchTest), there is also less variation between egg counts from animals that have not yet fully developed their immunity. In older sheep, the egg counts may be too low, but also there will be more variation between animals. When the egg counts are highly variable, you become less confident that the calculated drench efficacy is close to the 'real' figure. (This is one reason to calculate '95% confidence intervals' for each estimate of drench efficacy).

"Just while I think of it, with black scour worm (*Trichostrongylus* species; I know you were talking about brown stomach worm), the different species of this worm, while closely related, have different temperature preferences, and also different resistance profiles for some drenches (The PhD thesis by Michelle Wooster touches on this). So, a drench test in say summer, may give slightly different results from say a drench test in early Spring.

"And, as mentioned, above, we are assuming that there have been no mistakes in the conduct of the DrenchTest: i.e. drench guns are calibrated, the drenches aren't expired or otherwise compromised, a sample of the sheep have been weighed, and bodyweights are fairly even, the right dose rates are used (and the drench is correctly administered), the sheep have been randomly allocated to the various groups and correctly identified etc.

"Don't forget commonsense either. It is always good to 'eyeball' the raw data for example, casting your eye over the individual egg counts to see if they make sense.

"I remember being at one field day where a speaker said there was resistance to a particular drench (moxidectin in that case) in a DrenchTest because the average reduction in egg count was somewhat less than 95%. A quick perusal of the individual egg counts on the screen however revealed that two animals had high egg counts, and the rest of that group of ten had zero egg counts: a case of mis-drenching perhaps.

"Some results are more unlikely than others too. So, a DrenchTest showing *Haemonchus* resistance' to naphthalophos+LEV+BZ, or *Trichostrongylus* 'resistance' to say moxidectin, or a macrocyclic lactone (ML)-based triple combination, should invite closer scrutiny and repeat testing.

"To reiterate what we often say to farmers and others, it's good to involve the drench companies if you can in any suspected cases of resistance involving their products. It gives them 'a fair go' and, subsequent investigations can be to the producer's advantage, either confirming or disproving suspected cases of resistance, or suggesting better courses of action. Of course, if the farmer doesn't like their suggested products or strategies, they can always so no. It's their call.

Regards

Steve

References

Le Jambre LF, Geoghegan J, Lyndal-Murphy M (2005). Characterization of moxidectin resistant *Trichostrongylus colubriformis* and *Haemonchus contortus*. *Veterinary Parasitology* 128 (2005) 83–90.

Green PE, Forsyth BA, Rowan KJ, Payne G (1981). The isolation of a field strain of *Haemonchus contortus* in Queensland showing multiple anthelmintic resistance. *Aust Vet J* 1981 Feb; 57(2):79-84.

SHEEP DRENCH RESISTANCE - A CASE REPORT

(From WormMail 20 June 2008).

Regarding the results depicted below, if some results don't seem to make sense, or you are investigating possible early cases of a drench that hitherto has shown no signs of resistance, then you should repeat the test.

efficacy. (NSW DPI labs normally do these calculations when reporting DrenchTest results)

Most important of all is to actually do the testing, whether by way of a full blown resistance test (DrenchTest), or using doing a worm egg count after a routine drench (DrenchCheck).

The unseen production losses - and accelerated resistance - that occurs from unknowingly using a

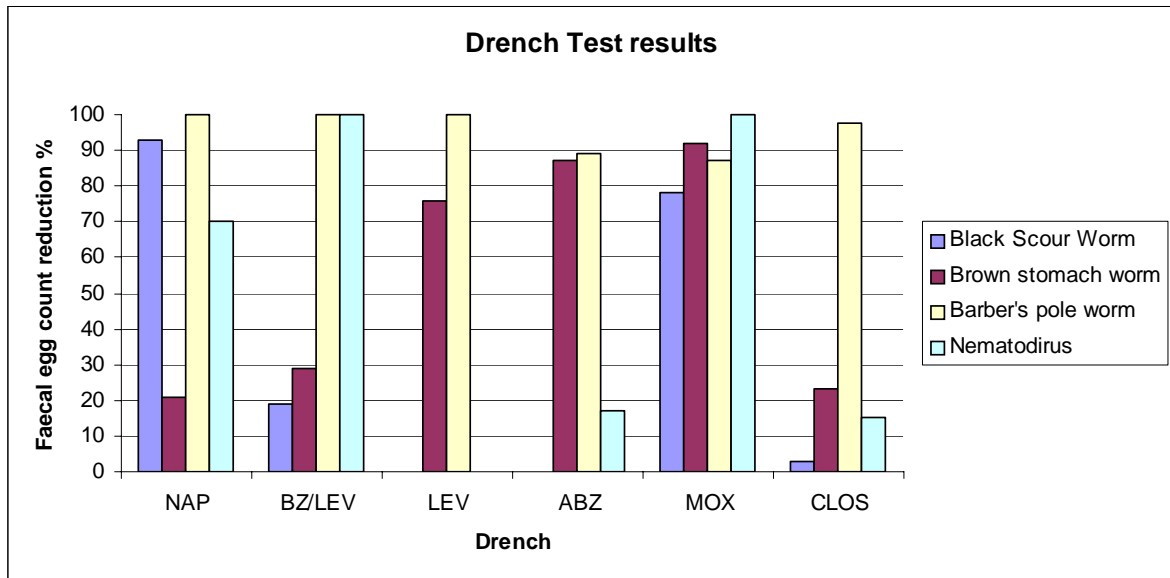


Figure 1.

Notes: NAP = Naphthalophos BZ/LEV = BZ/Levamisole combination. ABZ = Albendazole. MOX = moxidectin oral. CLOS=Closantel, at full dose. LEV and ABZ both had zero efficacy against black scour worm. The egg counts for Nematodirus (thin-necked intestinal worm) were low, so results may be unreliable. Faeces collected 10 days post-treatment

For example, the result for 'Rametin (naphthalophos) Combo' (only 30% efficacy against *Haemonchus*) is quite surprising, especially if the 'Combo' is naphthalophos + BZ + LEV. Some follow up work is required.

Remember also, that naphthalophos on its own is usually only 70-90% effective against *Trichostrongylus* sp (black scour worm) and *Ostertagia/Teladorsagia* (small brown stomach worm), which does not necessarily indicate resistance, but highly effective (~ 100%) against adult *Haemonchus* (barber's pole worm). To my knowledge, there are just two cases of confirmed resistance in Australia to naphthalophos (Le Jambre et al 2005, Green et al 1981).

Also, ML resistance in *Trichostrongylus* (black scour worm) is somewhat less common in Australia than in *Ostertagia/Teladorsagia* (small brown stomach worm) and *Haemonchus* (barber's pole worm). So, an investigator might consider double-checking results for that worm.

It is almost important to 'eyeball' egg count data for individual sheep in a drench trial, to see if it all makes sense. It is also good to have '95% Confidence Limits' for estimates of anthelmintic

less than effective drench can be quite significant.

But, following is a case report, an outline of results from a faecal egg count reduction test DrenchTest) I recently discussed with a northern tablelands merino producer and his adviser.

This test was done in April 2008 on weaners weighing 25-30 kgs. The untreated controls had an average egg count of 2338 eggs per gram of faeces, with the larval culture showing that 35% were black scour worm (*Trichostrongylus* sp), 10% small brown stomach worm (*Ostertagia/Teladorsagia* sp) and 55% barber's pole worm (*Haemonchus contortus*).

The results, used with permission, are summarised in the graph ('DrenchTest Results') below (figure 1, above).

This is by no means an unusual result overall for a northern tablelands property. A number of farms have more severe resistance than indicated above, including the macrocyclic lactones (MLs).

ML resistance is common in barber's pole worm in northern NSW, with 70% or more of farms having resistance (a similar figure for the number of farms in WA having ivermectin-resistant brown stomach

worm). Resistance is no longer rare even in moxidectin, the most potent of the MLs.

Farmers in central and southern NSW cannot rest on their laurels either. It is thought that 30% or more of farms in these areas have resistance to the MLs, and, like the north of the state, resistance to levamisole and the benzimidazoles has been quite common (>80% of farms) for a number of years.

Unlike the great majority of sheep producers, the farmer in this story has done resistance testing, and now has solid information to work with. If he continued to proceed 'in the dark', he may well have had 10-20% losses in production through use of ineffective drenches, as well as hastening the complete demise of existing drenches.

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FURTHER INFORMATION

NSW DPI

<http://www.dpi.nsw.gov.au/agriculture/livestock/sheep/health>

WORMBOSS

wormboss.com.au

[Turning the worm] is a newsletter for those interested in the management of endoparasites of farmed animals.

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Quote of the Day...

Some cause happiness wherever they go; others whenever they go.- Oscar Wilde