The sheep that turned

Australian Merino breeders are learning that genetic variation holds the key to sustainability as well as profit. A worm-control program that reduces chemical dependence marks the beginning of their new approach. **Bryony Bennett** reports.

Every August, at a place called Willalooka in South Australia's south-east, a mob of moleskinned graziers descends on the Pocock family farm, Panlatinga.

Penned up for the occasion are 80 of Panlatinga's finest young Poll Merino rams. As the Willalooka Progress Association prepares lunch, the graziers set about deciding which rams might best raise the productivity of their flocks. After lunch, they will parry with a wise-cracking auctioneer, determined to coax keen bidding for every ram in the catalogue.

The auction at Panlatinga is one in a string of ram sales held annually by Merino studs across the country. The sales are an integral part of the rural calendar, attracting a pilgrimage of woolgrowers, many travelling interstate in search of rams to match budgets and breeding objectives.

At each sale, a stroll around the pens and a few deft partings of pearly-white fleece reveal potential candidates with the right look and feel. But there's more to this game than meets the eye.

To help their clients meet specific production goals, many studs test their rams for measurable traits such as body size, fleece weight, fibre diameter and fertility.

For 20 years, Panlatinga's sale catalogue has featured four neat columns ranking each ram according to these production traits: a valuable guide for potential buyers. In 1995, stud principals Michael and Jim Pocock added a fifth column recording each ram's level of resistance to gastrointestinal worms. So far, few buyers have considered this information when choosing rams. In five to 10 years' time, more may wish they had.

Happy travellers

Gastrointestinal nematode parasites are a significant problem in most sheep-breeding regions of the world. The worms have spread across the globe in the bodies of their host animals, in much the same way that rats found free passage in the bellies of ships. From a worm's point of view, a sheep's gut is an ideal place to live and breed. After picking up infective larvae from pasture grasses, sheep can become highly-productive worm factories, nurturing new generations of eggs, and dispatching them in their faeces.

While all this industry is a boon for worm populations, the effects on their hosts can be horrendous. The black scour worm (*Trichostrongylus specis*) causes illthrift and scouring in young sheep, which in severe cases leads to death. The brown stomach worm (*Ostertagia* species) also causes illthrift, and anaemia, and death can rapidly follow the blood-sucking activities of the barber's pole worm (*Haemonchus contortus*).

These worms are estimated to cost Australia's sheep industry $220 million a year through reduced lambing percentages, weight gain, wool and ewe-milk production. Losses are most severe in higher rainfall zones (above 500 mm/year) and in irrigated pastures where moist conditions enable infective larvae to survive for long periods. Also, sheep are stocked at higher rates in wetter regions, contributing to greater concentrations of worm eggs in pastures.

In post-war years, graziers have sought to control the parasites with regular dosings of chemical drenches (anthelmintics), most of which kill worms by blocking their metabolism. At first this method worked a treat, but over time it has become less effective.

The key to this fall in efficacy is the worms' genetic variability. On average, anthelmintics kill 99.9% of worms in a given population. For every 1000 worms killed, one is sufficiently different to survive and pass its genes to successive generations. As long as the same drench is used, selection pressure in favour of the resistant worms continues. The resistance gene becomes more frequent, eventually becoming manifest to graziers when the sheep remain wormy after treatment. In this way, graziers' efforts to control the worms actually act to speed the evolution of worm populations with anthelmintic resistance.

The resistance of worms to anthelmintics is a classic example of the evolutionary consequence of drug use. Further examples exist in other kinds of agriculture, and in human medicine where the extreme mutability of microbes such as *Staphylococcus* and the malarial parasite *Plasmodium falciparum* compels continual drug development.

In the early 1970s, a pesticide-resistant strain of the moth *Helicoverpa armigera* drove the cotton industry out of Western Australia's Ord River scheme. The moths were able to breed year-round in the Ord's sub-topical climate and as insecticide use increased, resistant populations rapidly emerged.

Lining up against worms. Poll Merino rams at Panlatinga stud are selected for worm resistance as well as for production values.

Natural assassin runs rings around worms

The predatory fungi physically trap nematodes using sticky threads (mycelia) to catch them. The fungi then penetrate the cuticles of the worms and devour them.

FOUR years ago, two intrepid scientists from CSIRO's Division of Animal Production did the ultimate dirty work. They searched through 2000 samples of fresh dung, collected from sheep across Australia, for a fungus that would attack parasitic nematodes.

Fortunately, their search was triumphant, turning up 100 fungi with the right credentials. After a spot of performance-testing in the lab, one species, *Duddingtonia flagrans*, emerged with exactly the kind of killer instincts they required.

Because the fungus had to make its attack after passing through the belly of a sheep, a tough hide was also needed. Again, *D. flagrans* beat the field. Due to the relatively thick walls of its resting spores (chlamydospore), it was considered capable of passing through the sheep without being damaged. An added bonus was that the spores were produced in huge quantities.

Having selected their ruthless assassin, the scientists, Dr Peter Waller and Margaret Faedo, are devising a strategy for delivering *D. flagrans* inside sheep. One method involves capsules designed to release the fungus slowly in the stomach. The other involves growing the fungus on grain which is then compressed to form a block of feed.

After passing through the sheep unscathed, the fungus is expelled in the faeces along with the eggs of various stomach worms, attacking the larvae as they emerge. The result is that worm numbers are reduced to a level that can be tolerated by the sheep's own immune system, without significant production losses.

Waller says nematophagous fungi are at present the most promising of a range of biological control agents for animal parasitic worms. In future, however, other organisms such as mites, protozoa, other nematodes, bacteria or viruses could play a role. Another possibility is to genetically modify organisms to enhance their worm-attacking ability.

A commercial product incorporating *D. flagrans* and an effective system of delivery is expected to be available in two to four years. Used together with other methods of worm control, it should allow graziers to reduce their dependence on chemical worm treatments.

Short-term defence

Graziers employ a range of tactics to delay anthelmintic resistance. The simplest involves rotating drenches from three major chemical families, each acting on different metabolic pathways. Worms with gene-resistance to one chemical group may be susceptible to the other, so the evolution of resistant strains is slowed.

A more effective program requires regular testing to determine which drench is most effective; scheduling treatments to take advantage of the parasites' epidemiology; and providing 'clean' pastures for susceptible stock such as weaners. Given the complexity of this approach, however, many graziers rely on chemical treatments alone. As a result, more than 90% of Australian sheep farms show resistance to two of the drench families, and resistance to the third, (ivermectin), has been reported in some regions. Drench resistance is particularly serious in the New England region of NSW where a run of extremely wet summers has boosted worm populations.

With their weapons against worms wearing thin, graziers are eager to find a new one. But the discovery and production of effective drenches is expensive and slow, hopelessly outpaced by the worms' rapid evolution. A further consideration for graziers is the prospect of regulations limiting chemical use in food and fibre production. Even if a new drench were available, would it offer a sustainable solution, or just another dead-end road to resistance?

Fortunately, the answer to this question was apparent to CSIRO researchers back in the late 1970s, when anthelmintic-resistance first became widespread. Having noticed large differences in the ability of individual sheep to withstand worm infection, they decided to explore this variation as a fresh avenue of worm control.

The first step was to find out whether the sheep's resistance to worms was heritable. In 1977, at the Division of Animal Production at Armidale in NSW, a trial was set up to compare over time the worm burden of flocks selected for worm-resistance with control flocks of 'normal' unselected sheep. The results showed that breeding for worm-resistance was indeed feasible. In flocks selected for resistance to barber's pole worm, the number of eggs passed by sheep was halved in 10 years. Also, weaners selected for resistance to one worm species showed cross-resistance to other species, and females retained their resistance later in life as lambing ewes.

According to the division's Dr Sandra Eady, worm resistance can be built up relatively quickly in a breeding program because the variation in sheep for this characteristic is much higher than for most production traits. While the average variation in fleece weight is 10-12%, levels of worm-resistance vary by more than 100%. This greater variability offers scope for faster genetic gain.

Eady says sheep bred for resistance have a stronger immune response to worms, suppressing egg production to a greater extent, and at a much earlier age than unselected sheep. (The cause of this difference – such as whether the sheep have more antibodies of a specific type – is not yet known.)

'This is particularly significant for Merino sheep which are notorious for their poor immune response to worms, especially when young,' Eady says. 'Also, Merino ewes not selected for resistance lose immunity when in late pregnancy and lactating, becoming a source of pasture contamination for their lambs as worm-egg output rises.'

Turning the tables

Here at last was good news for graziers: a chance to use the genetic variability of their sheep to turn the tables on those wily worms. By the early 1990s, Merino studs in Australia's high-rainfall regions, mindful of growing worm-resistance on their properties and those of their clients, were itching to try the new breeding strategy. In 1994, a national technology-transfer project was begun to help them.

Project Nemesis is a three-year joint venture between CSIRO, the University of New England and Agriculture WA, with added funding from Australian woolgrowers provided through the International Wool Secretariat. It aims to help breeders select rams with a high natural resistance to parasites, potentially halving the worm burden in their flocks over three to four generations of breeding.

The time taken by each breeder to achieve this reduction depends on how heavily they select for worm resistance. Strong resistance does not necessarily occur in with the best fleece weight, fibre diameter, body weight and fertility. As a result,

Michael and Lisa Pocock (right) and Grazing Properties manager, GH Mitchell & Sons, David Jupp, overlook rams tested for worm resistance at Panlatinga.

heavy selection for worm-resistant rams reduces the production gains that could have been made were selection based on these traditional selection traits alone. A compromise between the two goals is therefore needed.

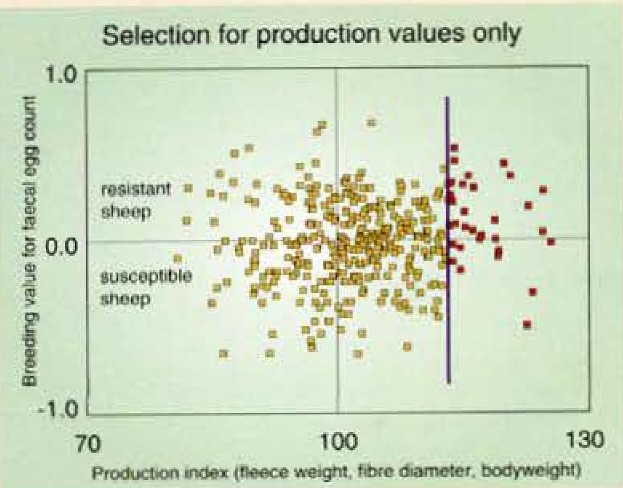
During 1994 and 1995, a field trial at Panlatinga measured the outcome of two different levels of selection emphasis. The trial found that when 50% of the possible selection emphasis for worm resistance was applied, a 9% sacrifice in production gain was the result. When 70% selection emphasis for resistance was used, the production sacrifice was 19.7%. Results of this and other studies are now helping other breeders to tailor their selection programs.

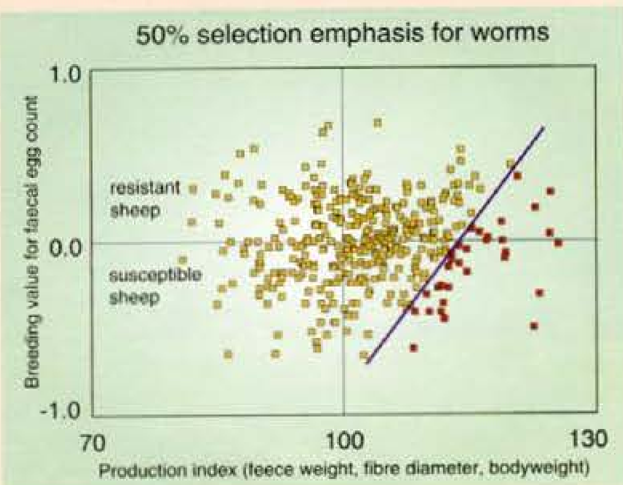
At Panlatinga, Michael Pocock decided to opt for 50% selection emphasis. 'It's taking a "best bet",' he says. 'We're making about half the theoretical gain that we could, yet we're still making progress in other traits as well.

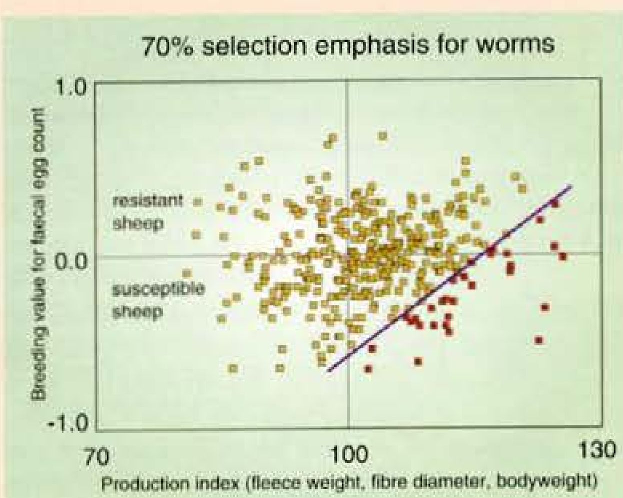
'At the moment we drench twice in summer. Our sights are set on 10 years' time when we should be able to drop a drench because fewer worms will be breeding in the gut of our resistant sheep. This will reduce contamination in the pastures. It won't be a big cost saving, but will represent a definite production increase. It also will cut our reliance on chemicals: we just can't keep using them as we have been.'

A CSIRO trial begun in 1977 compared over time the worm burden of flocks selected for worm-resistance with control flocks of 'normal' unselected sheep. The results showed that breeding for worm-resistance was feasible. (Faecal Egg Count is a measure of worm resistance.)

Panlatinga is one of 11 Merino studs in Victoria, NSW, WA and SA taking part in Project Nemesis, which also involves technical workshops for agriculture department advisors, vets, breeding consultants and researchers interested in sheep breeding and parasite control. A compelling reason for Panlatinga's participation was the high level of anthelmintic resistance on the property which receives 520 mm of rainfall a year. Pocock says effective drenches have been vital to his worm-control program, which







Deciding which rams to keep. These graphs show selection strategies available to breeders. They indicate which rams would be selected, according to the level of emphasis placed on worm resistance. (Faecal egg count is a measure of worm resistance.)

Top: The best 30 rams (coloured red) when selection is made on the basis of production values alone.

Centre: The best 30 rams when 50% of possible selection emphasis for worm resistance is used. The overall gain in production traits is less.

Above: The best 30 rams when 70% of possible selection emphasis for worm resistance is used. Faster gains will be made in worm-resistance, but advances in production will be further reduced.

in 1993 was only 83% effective. 'If we lost ivermectin (the third drench group) now, we'd have to switch from sheep to cattle production,' Pocock says. 'That's how dangerous it can be.'

Pocock estimates that half his 100 or so clients are concerned about anthelmintic resistance and 10-15% will pay a premium for rams bred to improve their flocks' resistance to worms. So it's well worth recording each rams' level of worm resistance in the stud's sale catalogue. With this pattern repeated among clients of each stud involved in Project Nemesis, the adoption by woolgrowers of this natural defence against worms is gaining momentum.

According to Eady, graziers who begin their selection programs now will be well rewarded in the medium to long term. 'Our computer modelling suggests that in 14 to 18 years, graziers may be able to stop drenching completely, provided their resistant sheep are kept separate. Even before this goal is reached, reduced reliance on drenching and improved host resistance offers a much more sustainable strategy for worm control.'

With all this pressure on worm populations through selection for resistant hosts, is there any chance of the worms overcoming the sheep's resistance? To test this possibility, the scientists at Armidale conducted an experiment in which resistant and non-resistant sheep were artificially infected with worms. After 30 generations, (the equivalent of 15 years in the paddock) the worm populations showed no changes in terms of infectivity and pathogenicity. They concluded it was unlikely that the worms will be able to circumvent the improved host resistance.

'Unlike anthelmintic treatment, the resistant host does allow some worms to survive, so the selection pressure on the worms is much lower,' Eady says. 'Also, the "control" the sheep exerts on its resident worm burden appears to be moderated through a large number of genes and gene products, so the worms have a much tougher barrage to penetrate.'

Further research at Armidale is fine-tuning selection strategies, assessing the drench requirements of resistant sheep and adding up the economics of breeding for worm resistance. Given the success of Project Nemesis to date, the technology may well be sought by other members of the sheep industry, such as prime lamb producers. It could also be exported to overseas regions experiencing drench resistance, such as Europe, the United States, South Africa and South America.

In the meantime, graziers have a swag of ideas about other types of resistance that might be improved through prudent selection. Sheep that resist flystrike and footrot, in addition to worms, would be good for starters. It may sound like a tall order, but Eady says there are diseases, not only of sheep, but also of other domestic livestock such as pigs and cattle, that may respond to similar strategies.

Of course it would mean adding a few more columns' worth of performance records to the Panlatinga sale catalogue. . . But by that time their rams should just about be able to sell themselves.

More about worm resistance

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