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Ramguard – Increasing the Tolerance to Facial Eczema in New Zealand Sheep

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Abstract

Facial eczema (FE) is a metabolic disease resulting primarily from damage to the liver and bile ducts. It is caused in ruminants by the effects of a mycotoxin, sporidesmin, produced by the fungus Pithomyces chartarum. The disease causes significant loss in agricultural production mainly in northern New Zealand. Sporidesmin toxin is produced in a laboratory and made available to those sheep breeders who wish to increase the level of FE tolerance in their flocks. The sheep industry in NZ has made steady progress towards increasing genetic tolerance to FE by testing potential future sires in ram-breeding flocks with an artificial challenge of sporidesmin. Ramguard provides the sporidesmin to breeders to dose their sheep at a specified dose-rate which is dependent on the level of tolerance already obtained. The Ramguard service has operated from August 1988 and has 60 clients dosing a total of 800 to 1100 rams each year. Most of the long-term-testing flocks are now using a dose rate six times higher than at the outset, which indicates animals in these flocks are tolerant to all but the severest outbreaks of FE. The heritability estimate for resistance to facial eczema is high at 0.45 ± 0.03.

Keywords: Ramguard; facial eczema; sporidesmin; GGT; sheep

Introduction

Facial eczema (FE) is a metabolic disease resulting primarily from damage to the liver and bile ducts. It is caused in susceptible ruminants by the effects of a mycotoxin produced by the fungus Pithomyces chartarum. The main toxin is sporidesmin A, though other sporidesmins are produced in minor amounts. Toxin-containing spores produced by the fungus are present in pastures in most of the North Island and the very northern regions of the South Island and are released during periods of warm, humid weather over summer through to autumn. The disease causes significant loss in agricultural production mainly in the North Island of New Zealand. Severe and widespread outbreaks in the autumns of 1935 and 1938 led to the establishment of the Ruakura Research Station in 1939 (di Menna et al. 2009).

While sporidesmin can affect many organs, liver damage and thickening of the bile duct were identified early on as the major effects. Liver dysfunction causes the secondary photosensitivity and the subsequent tissue damage to the exposed areas of the face (and other bare skin), hence the name facial eczema. Not all animals affected with FE show physical symptoms (i.e., clinical FE) although liver damage has occurred. Clinical FE results in production losses and deaths while subclinical FE leads to depressed ewe fertility with fewer ewes ovolating and fewer ovulations per ewe.

Serum gamma-glutamyltransferase (GGT), measured 2-3 weeks after dosing of sheep with sporidesmin, was found to be positively correlated with liver damage scores on post-mortem examination and is used as the proxy for susceptibility (liver and bile-duct damage) today (Towers & Stratton 1978).

Ramguard is a commercial service run by AgResearch for the benefit of sheep breeders. AgResearch produces the toxin sporidesmin which is made available to sheep breeders where facial eczema (FE) is an issue on their farms.

Genetic progress can be made since the heritability estimates for resistance to this disease is high at 0.45 (Morris et al. 1999b, 2012). One group of Romney breeder’s genetic trend is showing a 2% gain per year.

Materials and methods

Industry testing

The early work in 1974 involved progeny testing a number of rams using mean liver-injury score from the euthanized rams and this identified variation in the proportion of lambs affected by FE in each sire group when they were orally dosed with sporidesmin.

A long-term breeding project was initiated at AgResearch Ruakura, to breed a FE-resistant and a FE-susceptible line of Romney sheep. Performance testing using GGT was first introduced for the 1981-born lambs and a performance-test line was set up in 1982 along with a control line (Morris et al. 1989). The design was used to demonstrate to ram breeders that progress in selection for increased FE resistance could be achieved.

The heritability estimate for resistance to this disease is high at 0.45 ± 0.03, and there are no significant genetic correlations with other production traits (Morris et al. 1999b, 2012).

Progressive breeders, led by Colin Southey (South Auckland MAF Sheep & Beef Officer), initially used a performance-testing procedure based on field testing on toxic pastures and liver injury to score the progeny. Regular spore counting was essential to control toxin intakes and this was at the mercy of the weather conditions.
These problems led the breeders to form a company in 1985 to produce sporidesmin and conduct performance tests using dosing protocols developed at Ruakura. After four years, the company was acquired by the Ministry of Agriculture and Fisheries and the service has operated since August 1988 as Ramguard (Towers et al. 1990). The original breeders and their successors have now completed 29 years of FE testing. Ramguard produces sporidesmin at AgResearch Ruakura and provides sheep breeders with an ethical dosing strategy for ascertaining FE tolerance.

**Sporidesmin Production**

*Pithomyces chartarum*, the saprophytic fungus that produces the toxin sporidesmin, is grown on moistened, sterilised, whole-feed barley in aerated plastic culture bags at 20°C for five weeks (di Menna et al. 2009). During this incubation period, the fungus produces large quantities of toxin-containing black spores.

The culture-bag contents are repeatedly solvent extracted and filtered. The filtered extract is concentrated in a cyclone evaporator under vacuum to remove the solvent.

The concentrate is re-extracted with a second solvent and the resulting product is dried under vacuum to a brown semi-liquid with 10-20% sporidesmin content. This is redissolved and centrifuged to remove insoluble material to give a clear dark brown solution. The supernatant is dried under vacuum to a semi-liquid extract and stored at 4°C.

The extract is dissolved in solvent and analysed by High-Performance Liquid Chromatography (HPLC) to determine sporidesmin A, B, E (toxic), and D (non-toxic) levels (Miles et al. 1992). The concentrated solution is diluted in ethanol for preparation of animal doses based on the analysis by HPLC, and the required dose rate then dispatched to clients. Precise animal doses are prepared on-farm by adding a designated volume of water to form a pale-brown milky emulsion for gavage administration into the rumen.

**Breeders**

Dose rates are discussed with each breeder on the basis of the past results with small increases in the dose rate normally achieved each year. This is dependent on the sire team used, as sires used with no FE testing background will slow the FE tolerance progress of that flock. Conversely, sires purchased from flocks that are dosing at higher levels will increase the rate of progress and higher dose rates can be achieved more quickly.

The selection of rams is made using Sheep Improvement Ltd (SIL) indexes that contain FE tolerance and other production traits. Animal tags, current live weight and sire tags are sent by the breeder to Ramguard in the week prior to dosing. The prepared solution is couriered from Ruakura to the breeder’s veterinary practitioner. On dose day, the sporidesmin toxin is diluted with a set volume of water prior to dosing by veterinarians. Dosing is by intraruminal intubation and the dose is at a volume that is dependent on the animal’s live weight (mg per kg live weight). Blood samples for GGT testing at a veterinary pathology laboratory are taken prior to dosing for a base level and at 21 days after dosing (Day21). The rams are ranked on the Day21 GGT results and a summary of each year’s results is added into a breeder’s facial eczema certificate. The report of the year’s GGT results and the certificate are then sent to the breeders. The breeder’s FE certificate is a record of their Ramguard testing and lists the number of years dosing, number of rams dosed, number of rams that are tolerant to the dose and the dose rate for each year.

For new breeders using the Ramguard service, a conservative approach is taken with the initial dose rate. This is to ascertain the natural tolerance levels of that flock and sometimes a second dose round at a higher rate may be needed.

Because of the high cost of producing sporidesmin, this service is mainly useful to ram-breeding flocks. The cost is dependent on the animal live weight and the dose rate and can range from $120 to $300 per ram plus veterinary fees.

Most breeders using Ramguard are from the top half of the North Island but, as FE has become a problem further south, several lower-North Island breeders have recently started testing. The original breeds tested were Coopworth and Romney, whilst Perendale and other breeds have started testing more recently, and thus, will need some years of ram selection before reaching the higher dosing levels (Table 1).

**Table 1** Flock breed of sheep tested by Ramguard by region.

<table>
<thead>
<tr>
<th>Region</th>
<th>Coopworth</th>
<th>Romney</th>
<th>Perendale</th>
<th>Composite</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northland</td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>South Auckland</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Waikato/Bay of Plenty</td>
<td>6</td>
<td>11</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>28</td>
</tr>
<tr>
<td>Hawkes Bay</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Lower North Island</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>South Island</td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>25</td>
<td>10</td>
<td>6</td>
<td>4</td>
<td>58</td>
</tr>
</tbody>
</table>

The extract is dissolved in solvent and analysed by High-Performance Liquid Chromatography (HPLC) to determine sporidesmin A, B, E (toxic), and D (non-toxic) levels (Miles et al. 1992). The concentrated solution is diluted in ethanol for preparation of animal doses based on the analysis by HPLC, and the required dose rate then dispatched to clients. Precise animal doses are prepared on-farm by adding a designated volume of water to form a pale-brown milky emulsion for gavage administration into the rumen.
Results

Progress

Towers et al. (1990) reported that about 50 breeders had established facial eczema tolerance as one of their selection criteria. Currently, Ramguard has 58 clients and they are dosing a total of 800 to 1100 rams each year. There are 14 of the original 50 Ramguard breeders or successors who are still testing in 2013, and they have completed 27 to 29 years of testing. Another eight breeders have been testing for 15 or more years.

Most of these long-term flocks are now using a dose rate six times stronger than used originally, which indicates animals in these flocks are tolerant to all but the severest outbreaks of FE. Figure 1 includes data on dose rates from the original Ramguard flocks. The dose rate has been capped at 0.60 mg sporidesmin per kg live weight, with one breeding group capped at 0.65 mg per kg weight. The dose rate is capped to avoid the expense of ever-increasing dose rates.

Data for analysis

Most of the GGT data is sent to the national sheep performance-recording scheme managed by SIL (partially funded by Beef + Lamb New Zealand) for analysis to produce breeding values (eBVs) for the log-transformed Day21 GGT result (GGT21eBV). This FE goal trait was added to SIL in 2003. A facial eczema index with an economic value is also produced and this index can be added into the SIL Dual Purpose Overall index (DPO). Breeders get flock selection lists

Figure 1 Sporidesmin dose rates for the original 14 ram breeders over 28 years.

Figure 2 ARDG genetic trends for log GGT21 eBV and sporidesmin dose rate increases over 29 years.
from their SIL bureau which can list all the production trait BVs and indexes (Newman et al. 2009).

**Genetic progress**

Genetic-trends from SIL for the Auckland Romney Development Group (ARDG) for GGT21eBV in Figure 2 are used as an example of the genetic progress that can be made by selecting animals based on their eBVs. The ARDG group was one of the original breeders in Ramguard and currently has five breeders. Six breeders formed a central flock in 1984 where the FE testing was performed, rams selected and dispersed for ewe mating to the ARDG members. In 1993, the central flock was disbanded and the top ram hoggets were tested at each flock then shared around the group to maintain good genetic connectedness. In 1993, AgResearch started working with the ARDG group providing breeding values and ram-selection advice (Morris et al. 1999a). The genetic progress for this group is showing a 2% gain per year and the dose rate has been increased at a similar rate to enable animals to continue expressing genetic variation (Fig. 2).

**Discussion**

The sheep industry in NZ has made steady progress towards increasing genetic tolerance to FE by testing potential future sires in ram-breeding flocks with an artificial challenge of sporidesmin. Ramguard has produced and provided the sporidesmin to breeders to dose their sheep at a dose rate which is dependent on the level of tolerance already obtained through selection.

These Ramguard breeders are able to command a premium price for rams from their flocks. Although only a small number of the rams available for sale are FE tested, the breeders select their best FE tolerant tested rams for use in their own flocks.

Breeding tolerant rams is a long-term commitment that involves considerable expense. However, genetic progress is relatively rapid and significant permanent gains are made after a few years of concentrated selection.

Genetic progress is being made with the ARDG group showing an average 2% gain per year over the 29 years.

In terms of future developments, blood samples from the rams tested are being used in genomic selection looking for FE genetic markers, and some sporidesmin is being provided to the dairy industry for FE dosing work.

**Acknowledgements**

Kees Wesselink was the coordinator of Ramguard from its inception in 1988 through to 2009, and is thanked for his valuable input into maintaining an excellent liaison with breeders throughout his tenure. We thank John Kerby for his dedication to sporidesmin production at AgResearch and to the ARDG group for the use of their data for plotting genetic progress.

**References**


