Lecture 13: Genetics of Disease Resistance

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Learning objectives

On completion of this topic you should be able to:

- identify sheep diseases of importance to the Australian sheep flock that can be controlled by genetic means and define measures of resistance to these diseases
- describe the heritability of resistance to some major sheep diseases in Australia: nematode parasites, flystrike, fleece rot and footrot
- describe the genetic relationships among disease resistance traits and between the disease resistance traits and production traits
- understand the considerations involved in incorporating disease resistance traits into a breeding objective
- describe the potential to use variation in disease resistance between strains and bloodlines within the Merino breed and between breeds
- explain the potential benefits of using SNP markers and genomic selection to breed disease resistant sheep

Key terms and concepts

Disease resistance, resilience, nematode parasites, flystrike, fleece rot, footrot, heritability, genetic correlation, SNP marker.

Introduction to the topic

This topic describes the genetics of the major diseases that affect sheep production in Australia and approaches to breeding for resistance to these diseases: nematodiasis (the effects of gastrointestinal nematode parasites), flystrike, fleece rot (the major precursor of flystrike) and footrot. These diseases are among the diseases which are the most costly to the Australian sheep industry (Sackett *et al.* 2006). Other diseases are economically significant, such as perinatal mortality, post weaning mortality, plant toxicity, bacterial enteritis, arthritis and ovine Johne's disease. Although these diseases may cause substantial effects in individual sheep flocks and restrict movement and trade in livestock and their products, breeding for resistance has not been considered as a control strategy for these diseases, except in the cases of lamb mortality during the perinatal period and post weaning. These diseases are not covered in this lecture, with the reader referred to Raadsma *et al.* (1997) and Besier *et al.* (2010).

Background

Any sheep production system will need to consider the risk of diseases and subsequent losses. The importance of a disease will vary with the climate, the standard of sheep husbandry and management and the ability of the manager to prevent, control and treat a disease occurrence (Raadsma *et al.* 1997). More particularly, the relative importance of diseases for a sheep flock will be influenced by their impact on welfare and production. For some sheep diseases, control measures such as vaccination, chemical prevention and treatment and physical and biological intervention measures are effective and economic. For example, effective prevention of several clostridial diseases and anthrax can be achieved by the use of inexpensive vaccines.

However, for other sheep diseases these forms of control have become ineffective, uneconomic and/or potentially unacceptable in terms of animal welfare, occupational exposure of people to pesticides and accumulation of chemicals in the environment and sheep products. For some diseases, limitations on the use of chemicals by sheep producers have occurred due to the parasites developing resistance to the chemicals e.g. anthelmintic resistance in gastrointestinal nematodes. For other diseases such as blowfly strike, the use of some preventative or curative measures highlights additional issues. These issues include animal welfare (the use of surgical mulesing when performed without pain relief applied to lambs and conducted by untrained operators) and chemical residues in wool (residues from pesticide applications entering the environment following early stage processing of wool in overseas plants). Also, effective vaccines have yet to be developed against some diseases e.g. blowfly strike.

For these reasons, genetic approaches continue to be researched as a strategy for control of diseases of sheep. Research has shown that there is genetic variation in resistance between animals to many sheep diseases. The research has established the levels of inheritance of resistance to different sheep diseases and relationships with economically important production traits and other diseases. This will allow sheep producers to develop and implement breeding programs that incorporate disease resistance and to integrate these programs with other disease control strategies.

13.1 Disease resistance

To consider disease resistance in a breeding program and allow selection of disease resistant animals, it is necessary to define the most relevant measure of resistance. Disease resistance, as defined most often by sheep breeders and researchers, is usually taken to consist of both the sheep's ability to modify the life cycle of a pathogen or parasite and resist the consequences of the disease (Bishop and Morris 2007). Another definition is disease resilience, which consists of the sheep's ability to maintain production during a disease challenge. These definitions could be applied to any disease that affects sheep production, incurs preventative and treatment costs and can be measured on a linear scale. Each of these approaches has its advantages and disadvantages, as discussed in detail by Raadsma *et al.* (1997, 1998). However, it is important to note that all definitions require that the animal must be challenged with the disease before its ability to respond to the disease can be assessed.

Resistance

'Disease resistance' can be defined as absence of observable signs of disease in an animal after challenge (Raadsma *et al.* 1997). Under the same level of disease challenge, resistant sheep are unaffected by clinical signs of disease while susceptible sheep become affected. This means that disease resistance is often expressed on a discontinuous basis or as a binomial trait (0, 1 scale), e.g. blowfly strike where sheep show 'absence' (unaffected) or 'presence' (affected) of the condition. In some instances, the relative scale of susceptibility is expanded from 'absence/presence' by using a linear score describing increasing severity of the disease e.g. scoring of fleece rot on a 1-5 scale. In other cases, the relative scale of susceptibility can be expressed on a continuous basis where an indicator of resistance can be measured rather than scored, e.g. resistance to gastrointestinal nematodes, where resistant sheep carry fewer worms as indicated by a lower faecal worm egg count.

As will be shown, disease resistance in sheep is inherited. However, a major disadvantage of this definition is that it is very difficult to place an economic value on reducing the proportion of diseased animals in a flock or the concentration of disease-causing organisms relative to the value of genetic change in other production traits (e.g. fleece weight, reproduction rate). There is also the risk of selection pressure influencing the pathogen or parasite to adapt genetically to the higher proportions of resistant sheep in a flock. This risk should be minimised by combining genetic control strategies with other complementary control strategies in an overall animal health program. Advantages of breeding for disease resistance are: the trait indicating resistance usually is easy to measure and measurement protocols can be designed to reduce the period of infection and adverse effects on animals; there will be fewer sheep in the flock that are diseased and adversely affected by pathogens or parasites; and resistant sheep will transmit fewer pathogens or parasites, where in the case of gastrointestinal nematode parasites for example lower levels of pasture contamination will occur.

Resilience

'Resilience' can be defined as hosts suffering little or no adverse effects on production during infection or disease challenge. Measurement of resilience requires measurement of production under conditions of a disease challenge, which may not be cost- or time-effective in practice. Resilience does not require direct measures of the relative pathogen load of animals when part of the breeding objective. Information on production levels, with and without a disease challenge, is then needed to determine how an animal superior in production during challenge would produce in the absence of a disease challenge.

The heritability of resilience to internal parasites is estimated to be low, within the range of 0.03-0.14 (Albers *et al.* 1987; Morris and Bisset 1996; Morris *et al.* 2004). Selection for resilience may not be practical, as assessment of resilience to internal parasites usually requires a lengthy period of infection, which would be unacceptable to breeders of elite rams. Selection for resilience to blowfly strike, similarly, is likely to be impractical, as all affected sheep require treatment to minimise production losses. However, selection for resilience to footrot may be beneficial in that resilient sheep exposed to virulent strains of *Dichelobacter nodosus* would cope similarly to unselected sheep exposed to benign isolates of the bacteria (Egerton and Raadsma 1991).

13.2 Genetics of disease resistance in sheep

Resistance to Gastrointestinal Nematodes

Substantial between-sheep variation exists within a mob of sheep in responses to gastrointestinal nematodes or worms (Figure 13.1) as assessed by faecal egg count (FEC). FEC is expressed as the number of worm eggs per gram of faeces and provides a measure of the total worm burden of an animal at the time of sampling. If resistance is defined as the ability of the host animal to reduce the number of parasites that establish, reproduce and survive, then an animal with a low FEC reading as compared to its contemporaries could be considered more resistant to an infestation of worms.

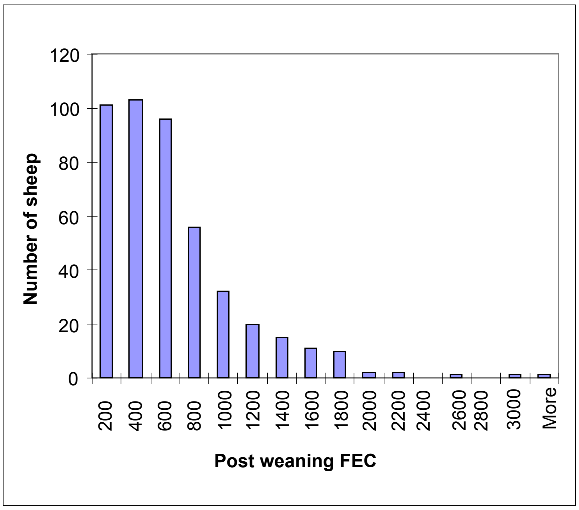

Figure 13.1: Between-sheep variation in post weaning faecal egg counts (FEC, worm eggs per gram of faeces) of 2010 drop Information Nucleus flock progeny at Trangie (S.I. Mortimer Unpubl. data).

Many studies have estimated heritability of FEC and for studies reviewed by Safari and Fogarty (2003), heritability estimates range from low to moderate, with an average estimate of 0.27 (Safari *et al.* 2005). Variation in FEC and its heritability increases with age (Huisman *et al.* 2008). Overall, at this moderate level of heritability and combined with the variable nature of the trait (coefficient of variation of about 30%), genetic improvement in resistance to gastrointestinal nematodes from direct selection on FEC can be relatively rapid. Estimates come form a number of sources: natural infections, where sheep have grazed a known contaminated pasture; artificial infections, usually involving a 'clean out' drench followed by a measured inoculation (delivered by a modified drenching gun) with third stage larvae; and multiple records of FEC, as a means of improving the reliability of estimates of the phenotype and increasing the accuracy of heritability estimates.

The use of alternative indicators for resistance to gastrointestinal nematodes, following challenge and without challenge, has been studied (Raadsma *et al.* 1998). The indicators of resistance considered include circulating eosinophil count, circulating antibody levels, faecal antigen test, packed cell volume, ovine lymphocyte antigen (OLA) type and components of the immune response (e.g. mucosal mast cell accumulation in the gastrointestinal tract). The indicator traits have been shown to be relatively inefficient predictors of FEC and resistance to gastrointestinal nematode infections.

Dags and scouring are indicators of intestinal infection and affect production through soiling of saleable wool and increasing predisposition of a sheep to blowfly strike. Dag score and faecal consistency score are poor indicators of FEC and would be ineffective in improving resistance to internal parasites in sheep (Pollott *et al.* 2004). While dag score is a moderately heritable trait across ages, faecal consistency score is of low heritability. Also, the genetic relationship of FEC with dag score is unclear, as available genetic correlation estimates are inconsistent. There is a low negative genetic correlation between FEC and faecal consistency score.

Consequences of Selection for Resistance to Gastrointestinal Nematodes

Several single trait selection flocks have been established in the past to demonstrate the effectiveness of selection aimed at improving resistance to gastrointestinal neamtodes. These include selection for resistance to each of Barber's Pole Worm (*Haemonchus contortus)*, Black Scour Worm (*Trichostrongylus* species*)* and Small Brown Stomach Worm (*Teladorsagia* species). In all cases, a change in FEC has been achieved in the desired direction.

In the 1970s, CSIRO commenced an experiment at Armidale, NSW, to evaluate the responses achieved following continued selection for resistance to *H. contortus*. Three lines were established at the same time: one selected for increased resistance, a randomly selected control line and a line selected for increased susceptibility to *H. contortus.* All lines were closed to outside introductions and replacement animals came from within each line. The selection criterion was FEC after artificial infection with a known quantity of infective *H. contortus* larvae. During the late 1980s, the Rylington Merino internal parasite resistant line was established in south-western Western Australia to demonstrate the feasibility of breeding worm-resistant sheep in a winter rainfall environment. This line was based on selecting animals for low FEC following a natural parasite challenge. A randomly selected control line also was established. After sampling both rams and ewes from a wide range of flocks to establish the lines, both lines were closed to outside introductions of genetics.

Significant divergence between the CSIRO lines in FEC has resulted over time, with the resistant line achieving lower FEC compared to the control (Figure 13.2). The changes achieved in the selection lines were lower than theoretical expectation because of relatively small numbers and reduced selection pressure due to the need to restrict inbreeding. From the Rylington lines, it is clear that selection for reduced FEC has achieved lower estimated breeding values for FEC at weaning and hogget ages in the selected line (annual rate of genetic reduction of FEC of 2.7% at hogget age), whereas estimated breeding values for FEC of the control line have remained reasonably stable (Figure 13.3).

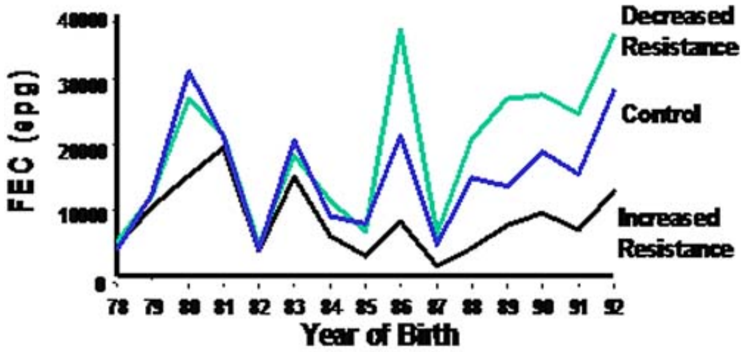

Figure 13.2: Faecal egg count (FEC) over time in the CSIRO lines selected for increased and decreased resistance to *H. contortus* and a randomly selected control line (R.R. Woolaston Unpubl. data).

The single trait selection lines have shown also if sheep selected for resistance to one type of internal parasite are resistant or otherwise to other types. Indirect evidence for favourable associations between resistances to different nematode species comes from the CSIRO *H. contortus* selection lines. When weaners from all three lines were run as a single mob, resistant line weaners showed lower FEC following natural infection with other worm species. These results indicated that resistance was expressed early in the animal's life and that selection for resistance to one worm species also conferred resistance to other worm species (Figure 13.4). Direct evidence that resistant sheep to one worm species are also resistant to another species has been reported by Windon *et al.* (1987), Woolaston *et al.* (1990) and Gray *et al.* (1992).

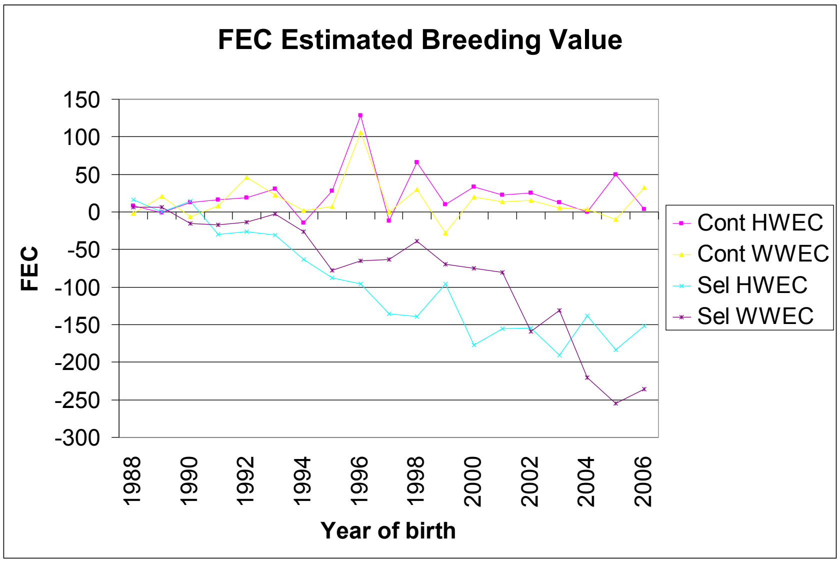

Figure 13.3: Estimated breeding values for faecal egg count (FEC, %) over time in the Rylington Merino line selected for increased resistance to gastrointestinal nematodes and its randomly selected control line. Sel WWEC, FEC at weaning in the selected line; Sel HWEC, FEC at hogget age in the selected line; Cont WWEC, FEC at weaning in the control line; Cont HWEC, FEC at hogget age in the control line (L.J.E. Karlsson Unpubl. data).

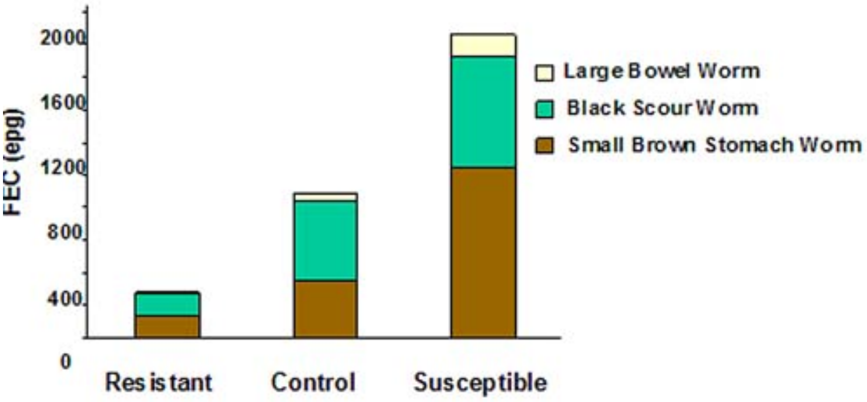

Figure 13.4: Faecal egg counts (FEC) associated with naturally-acquired infections of gastrointestinal nematode species other than *H. contortus* in Merino weaners selected for increased or decreased resistance to *H. contortus* and a randomly selected control line (R.R. Woolaston Unpubl. data).

When ewes approach lambing, their worm resistance decreases, referred to as the peri-parturient rise in FEC. In a study conducted during the 1990s, ewes from the CSIRO *H. contortus* selection lines were deliberately exposed to moderately contaminated pastures prior to lambing. All ewes were maintained together and were thus exposed to the same level of challenge. Resistant line ewes did not display as great a peri-parturient rise and were able to expel worms at a faster rate in the period following lambing, compared to control and susceptible ewes. These latter two lines required drenching at about 5 weeks after lambing due to extremely high FECs. Thus the resistance to gastrointestinal nematodes evident early in the life of the selected animals persisted through to older ages.

In winter rainfall environments, sheep typically show an increase in FEC over summer and autumn when a low larval challenge usually occurs. Using the Rylington lines, repeated measurements of FEC were obtained on adult ewes from September to March (Kemper *et al.* 2009). Although selected under conditions of high larval challenge, selected line ewes had lower FEC during the summer-autumn period (when low larval challenges occur) compared to the control line ewes, but the reduction in FEC was less than that under conditions of high larval challenge. This may be the basis of the benefits observed of lower winter pasture contamination and improved production from the running of resistant sheep in this environment.

In another study using the CSIRO *H. contortus* resistant and control lines, genetic and non-genetic approaches for worm control were compared from autumn to the next spring (Woolaston *et al.* 1997, Eady *et al.* 2003). The impact on FEC of selection for resistance was greater than that due to nutritional supplementation, vaccination (against *H. contortus*) or implementation of a strategic drenching program. When the experiment was completed, all sheep were drenched and combined into a single mob. Faecal samples were collected after 2 months. As expected, breeding for resistance conferred a permanent advantage to the host. In contrast, all other strategies had little residual benefits after the treatment had ceased (Figure 13.5a). The pastures were also grazed with new sheep after the experiment to provide a measure of worm contamination of the pastures. It was clearly evident that the resistant sheep left less contamination on the pasture compared to unselected sheep (Figure 13.5b).

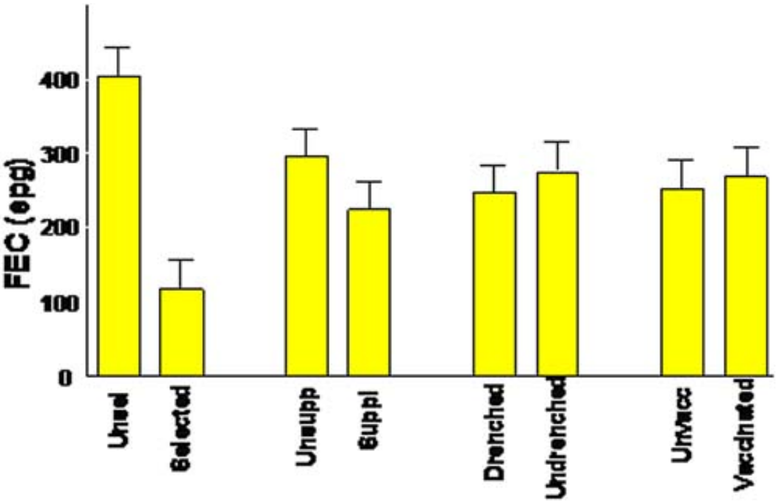

Figure 13.5a: Residual effects on faecal egg count (FEC) of genotype (unselected, selected), nutrition (unsupplemented, supplemented), strategic drenching (drenched, undrenched) and vaccination (unvaccinated, vaccinated) recorded 8 weeks after the experimental control strategies (Woolaston *et al.* 1997).

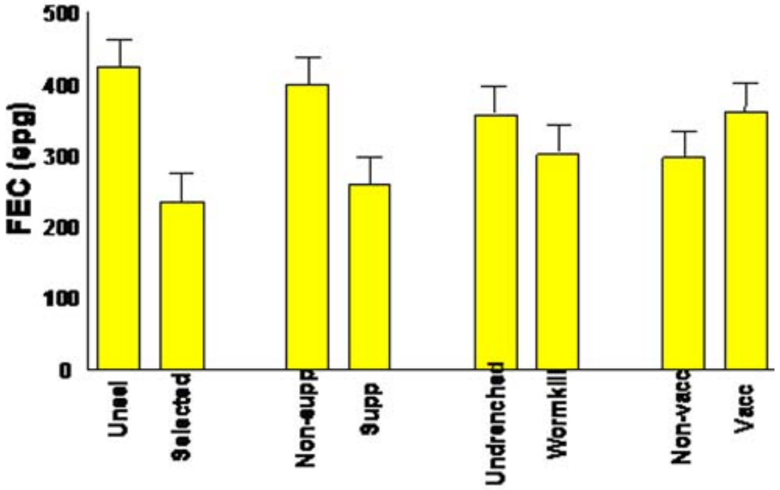

Figure 13.5b: Residual pasture contamination of various control strategies measured by faecal egg count (FEC) in new sheep grazing the pastures: genotype (unselected, selected), nutrition (unsupplemented, supplemented), strategic drenching (drenched, undrenched) and vaccination (unvaccinated, vaccinated) (Woolaston *et al.* 1997).

As few synergies and antagonisms between the various strategies for worm control were found, genetic and non-genetic approaches may be used effectively together in worm control programs, with each strategy contributing some value to the control of worms. The long-term benefits of selection for resistance on the frequency of drenches needed in a worm control program have been evaluated using simulation models. Across many runs, the simulation models show that selection for increased worm resistance could reduce drenching requirements from 3 to 0 per year after 11-18 years, depending on seasonal conditions (Eady *et al.* 1997).

Thus selection for resistance to gastrointestinal nematodes not only results in benefits to the individual arising from the permanent effects of reduced worm burdens, but resistant sheep also leave the pastures cleaner and, over the long-term, will reduce the reliance on anthelmintics and the costs associated with their application. Whole farm benefits of breeding resistant sheep have been shown in a winter rainfall environment, where the income from Rylington Merinos selected line sheep was about 10% greater than that of control line sheep when managed in separate commercial production groups (Table 13.1). As well as the resistant line having significantly lower FEC at weaning, the resistant line was consistently heavier, had a higher condition score than the control line and produced more (about 0.2 kg) and finer (0.4 micron) clean wool per hogget sheep of a higher yield (Geeff *et al.* 2006). There were no significant FEC differences at 14 months of age between the groups. The resistant sheep were more profitable than those not bred for resistance, even though there was no need to drench after weaning as FEC remained low during the period to hogget shearing. The greater profitability was due to the combined effects of resistance in the hogget progeny and lower pasture contamination with larvae by their dams. Drenching and labour costs were not included in estimating profitability.

Table 13.1: Differences in income ($) from wool and meat production in the Rylington Merinos selected (Resistant) and control lines (Greeff *et al.* 2006).

Income ($) from	Control	Resistant	Difference
Meat	58.82	64.68	5.86
Wool	18.07	19.51	1.43
Total income	76.89	84.18	7.29

Meat income calculated at $1.20/kg live weight after shearing.

Resistance to flystrike, fleece rot and dermatophilosis

Table 13.2 presents the range in published estimates of heritability for each of flystrike (in the form of both body and breech strike), fleece rot and dermatophilosis (also a precursor of flystrike in the form of body strike). These estimates indicate that all three diseases are low to moderately heritable and that breeding for resistance to these diseases could be accommodated within a practical breeding program.

Table 13.2: Heritability estimates of resistance to body strike, breech strike, fleece rot and dermatophilosis in Merinos (Raadsma *et al.* 1997, Greeff and Karlsson 2009, Li *et al.* 1999, Mortimer *et al.* 2009, Smith *et al.* 2009 and Brown *et al.* 2010).

Disease	Trait expression	Heritability
Body strike	Incidence	0.10-0.58
Breech strike	Incidence	0.32-0.57
Fleece rot	Severity, incidence	0.05-0.80
Dermatophilosis	Severity, incidence	0.27-0.44

There is a close genetic relationship between resistance to fleece rot and body strike in Merino sheep, indicated by the very strong positive genetic correlation reported by Atkins and McGuirk (1979), which allows breeders to make progress in body strike resistance by selection against fleece rot alone. Both the reduced production penalty associated with fleece rot and its ease of assessment make fleece rot the preferred selection trait for resistance to both diseases. It is likely that there is a similar genetic relationship between resistance to dermatophilosis and flystrike, and that selection against dermatophilosis will also reduce flystrike.

Many studies, reviewed by Norris *et al.* (2008), have investigated indicator traits for fleece rot as indirect selection criteria for resistance to fleece rot and body strike. As yet none have been identified for dermatophilosis, as genetic studies are lacking. For fleece rot and body strike, these include greasy wool colour, variability in fibre diameter, wax content and staple length. However, when direct and indirect selection strategies are considered in breeding programs that include other production traits, indirect selection has been shown to be no more useful than direct selection alone (Atkins 1987).

Immunological indicators of resistance to fleece rot have also been studied intensively to further understand the mechanisms underlying resistance to fleece rot and body strike (Norris *et al.* 2008). Although these studies have shown that the sheep’s immune response seems to contribute to the mechanism of resistance, no clear understanding of the mechanisms of resistance has become apparent. This suggests that several immunological mechanisms of resistance may be occurring. Among the more promising of the immunological traits identified as an indicator trait for fleece rot is a skin inflammatory test. However, there is inconclusive information on its heritability and the genetic relationship between the incidence of fleece rot and the skin inflammatory response to blowfly antigens (O’Meara and Raadsma 1995).

Research on the genetics of breech strike resistance is currently underway and indicator traits associated with breech strike that have been identified include breech wool cover, breech skin wrinkle, dags, wool colour and fleece rot (Brown *et al.* 2010; Greeff and Karlsson 2009; Smith *et al.* 2009). These indicator traits, apart from fleece rot, are at least moderately heritable (Table 13.3). Early evidence from the breech strike resistance flocks at Mount Barker, Western Australia (Department of Agriculture and Food Western Australia) and Armidale, New South Wales (CSIRO) show that breech strike has positive phenotypic and genetic correlations with the indicator traits, namely, breech wrinkle, breech cover, dags, wool colour and urine stain. In the winter rainfall environment of Mount Barker, dags followed by breech cover were the most important indicator traits, but the relationships between breech strike and the indicator traits appear to be complex as they varied across years (Greeff and Karlsson 2009). In the summer rainfall environment of Armidale, breech wrinkle and dags were the indicator traits with the strongest relationships to breech strike (Smith *et al.* 2009).

Table 13.3: Heritability estimates of breech strike indicator traits in Merinos (Greeff and Karlsson 2009, Smith *et al.* 2009 and Brown *et al.* 2010).

	Greeff and Karlsson (2009)	**Smith *et al.* (2009)**	**Brown *et al.* (2010)**
Breech wrinkle	0.45	0.36	0.39 (early), 0.69 (late)
Breech cover	0.42	0.23	0.27 (early), 0.30 (late)
Dag score	0.55	0.09	0.28 (late)
Crutch cover	-	0.47	-
Wool colour	0.49	-	0.56 (late)
Urine stain	0.49	0.30	-

Consequences of selection for resistance to flystrike and fleece rot

This has been demonstrated in long-term selection flocks selected for and against resistance to body strike and fleece rot, undertaken by NSW Department of Primary Industries at Trangie (Mortimer *et al.* 1998), while more recently the consequences of selection for breech strike resistance have been shown in linked flocks at Mount Barker (Greeff and Karlsson 2009) and Armidale (Smith *et al.* 2009).

For the Trangie selection lines, the selection criteria varied across years and included expressions of fleece rot and body strike following natural challenge between birth and 13 months of age and following fleece rot induction (i.e. challenge under simulated rainfall) at 14 months of age. Figure 13.5 shows the divergence in the incidence of natural fleece rot between the two selection lines over a 14 year period. This trend equates to a change in divergence of around 2.8% per year. Overall, the susceptible line had higher incidences of natural fleece rot (37% vs 10%), natural body strike (8% vs 3%), induced fleece rot (63% vs 38%) and induced body strike (5% vs 0%) than the resistant line. In terms of the incidence of natural body strike, the lines diverged at a rate of around 0.4% per year.

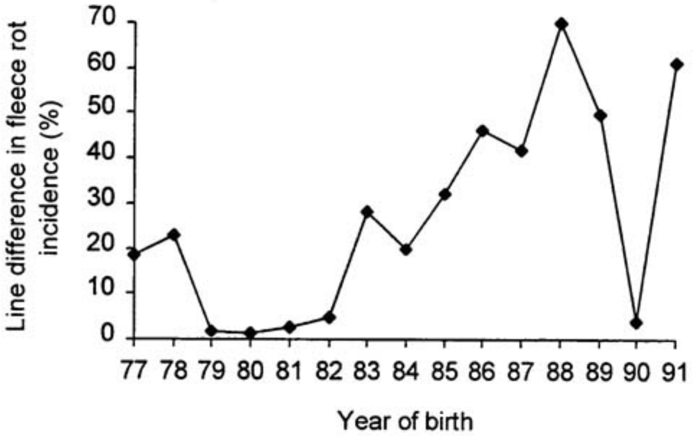

Figure 13.5: Annual differences in natural fleece rot incidence (%) between the fleece rot susceptible and resistant selection lines (Mortimer *et al.* 1998).

The breech strike resistance flock at Mount Barker includes a line where both rams and ewes are selected intensively using any information on breech strike and known indicator traits, another line where rams only are selected intensively and ewes are unselected and a control line. In this flock, the overall breech strike incidence was different between lines from post-weaning to hogget shearing. Although the selected lines had lower breech strike incidences between birth and hogget shearing than the control line, the difference between the lines was not significant. The resistant lines also had lower scores for breech wrinkle, breech cover, wool colour and urine stain. The Armidale breech strike resistance flock has lines selected similarly, except that the selection criteria used are plain breech characteristics (mainly breech cover, crutch cover and breech wrinkle). In the Armidale flock, breech strike rates were not different between the lines, whereas the selected lines had significantly lower scores for breech wrinkle, breech cover and crutch cover.

Resistance to footrot

The heritability of resistance to footrot is moderate, with estimates from 0.05 to 0.30 (Raadsma and Conington 2010), indicating that there is sufficient genetic variation to exploit through breeding for resistance to challenge from virulent isolates of *Dichelobacter nodusus* (the causative bacterium). Although heritability estimates are similar for natural and induced footrot, the heritability estimates varied with: number of foot inspections underpinning the estimate (single inspections provide generally lower estimates than many inspections during the same challenge); if foot inspections occurred after vaccination (estimates obtained from inspections post vaccination are lower than those from inspections before vaccination); and the prevalence of footrot (estimates are higher at higher prevalence). The advantages of selection for increased resistance to footrot are not clear. In the case of this contagious disease, eradication of *D. nodosus* from flocks of sheep under Australian conditions has been shown to be feasible. However the chance of successful eradication greatly decreases as the number of flocks and flock size increases. Egerton and Raadsma (1991) argued that under selective breeding for increased resistance to footrot, sheep exposed to virulent strains of *D. nodosus* would cope in a similar fashion to unselected sheep exposed to benign isolates. Under this scenario, the impact on production is minimal and sheep would not require any managerial input to control the disease. Breeding for resistance to footrot using conventional selection may not be practical.

13.3 Genetic relationships among disease traits

The major diseases attracting research attention are all favoured by common environmental conditions: high rainfall, moderate temperatures and improved grazing conditions. It is then very likely that sheep grazed under such conditions would be exposed to internal parasite challenge, fleece rot and flystrike and footrot in infected flocks. Information on genetic associations between resistances to these diseases is of interest, not only to predict the indirect consequences of selecting for resistance to one disease, but also allows the consideration of the potential for ‘broad-based’ disease resistance. Little information is available on this. Where preliminary information is available, multiple diseases have been monitored on the same animals, and results may therefore have been biased by the influence of one disease on the expression of the other. Results from Australian studies indicate that, at best, the genetic associations between internal parasite resistance and resistance to other diseases are neutral or slightly favourable (Table 13.4).

Similarly genetic relationships among resistance to fleece rot, dermatophilosis and footrot (essentially all diseases of the skin) appear to be essentially neutral. It is unlikely that there are strong favourable or unfavourable genetic relationships between resistances to the important sheep diseases, but more reliable information is required to refine selection programs that aim to include resistance to more than one disease. It seems that breeding programs will need to consider separately individual diseases if resistance to a number of diseases is the objective (Raadsma and Conington 2010).

Table 13.4: Predicted changes in resistance to gastrointestinal (GI) nematodes, fleece rot, dermatophilosis and footrot following selection for resistance to a range of diseases (Raadsma *et al.* 1997, Pollott *et al.* 2004 and Brown *et al.* 2010).

Selection for	**Predicted change in resistance to:**			
resistance to:	**GI nematodes**	**Fleece rot**	**Dermatophilosis**	**Footrot**
GI nematodes	-	No change	Slight increase	Slight increase
Fleece rot	No change	-	No change	Slight decrease
Dermatopihilosis	Slight increase	No change	-	No change
Footrot	Slight increase		No change	-
Dags	No change			

13.4 Genetic markers

Genetic markers would allow information to be collected for selection purposes even when expression of the disease trait is limited by environmental conditions (e.g. insufficient rainfall to allow prolonged wetting of a sheep’s skin for the development of fleece rot). Information for assessment of disease resistance would also be available for environments where disease incidences vary across years (e.g. gastrointestinal nematode challenges) and at any age. Where indicator traits are difficult, time consuming and/or expensive to measure, genetic markers may be able to provide information for use in the breeding program. Genetic markers could then be used by ram breeders who breed rams, which are rarely challenged or not challenged by the diseases, to be sold and used in flocks in environments of greater disease challenge.

A genetic marker is a sequence of DNA that differs between animals and is located near to or within a gene. The search for genetic markers for disease resistance in sheep has been occurring for more than a decade. The recent availability of higher density single nucleotide polymorphism (SNP) chips in livestock species, containing SNPs from across the whole genome, has stimulated further the search for DNA mutations underlying the variation in sheep disease traits through genome wide association studies (Goddard and Hayes 2009). From these studies, the estimated SNP marker effects are used to derive a prediction equation that is used to predict genomic breeding values for animals in other populations. Selection of animals based on these breeding values is known as genomic selection.

In relation to disease resistance in Australian sheep populations, SNP marker effects have been associated with fleece rot scores (Smith *et al.* 2010) and FEC (Kemper *et al.* 2011), where the many individual SNP marker effects for FEC were found to be small. As part of the Information Nucleus Program (van der Werf *et al.* 2010), genome association analyses will be undertaken that will allow the prediction of genomic breeding values for indicator traits for resistance to gastrointestinal nematodes and flystrike.

13.5 Including disease resistance into a breeding program

Some implications of the inclusion of disease resistance into a breeding program are:

1. Selection pressure applied to other traits in the breeding objective will be reduced, which will affect subsequently genetic change in these traits, depending on the size and direction of the genetic correlations involving disease resistance traits.
2. Little is known of the physiological impact of selection for disease resistance on other traits that are in the breeding objective. An animal's ability to mount a continued immune response (i.e. resistance) may compromise the utilisation of nutrients and energy for wool and meat production.
3. Expression of resistance to a disease usually requires that animals be exposed to a disease challenge.
4. Economic values of disease resistance traits are difficult to quantify.

No breeding program should have disease resistance as its only objective. Realistic programs will include disease resistance with other important production traits. Therefore genetic relationships of resistance with other traits targeted for improvement (such as live weight gain, fleece weight, fleece quality and resistance to other diseases) all need to be considered. At present, estimates of such relationships are scarce. Table 13.5 provides an indication of the likely genetic relationships between disease resistance and important production traits.

For improvement programs that do not consider disease resistance, preliminary predictions can be made on the likely consequences on resistance to the major diseases. Programs with a strong emphasis on clean fleece weight may lead to a small increase in susceptibility to disease. Programs with a strong emphasis on reducing fibre diameter are likely to see no changes in resistance to gastrointestinal nematodes, a slight improvement in resistance to fleece rot and flystrike, and no major change in resistance to footrot. Selection for increased body weight is likely to lead to a favourable effect on nematode resistance, a small decrease in resistance to fleece rot and flystrike, and an unknown effect on resistance to footrot. It should be noted that in all cases the likely changes in resistance / susceptibility are small.

Table 13.5: Summary of available information of likely genetic relationships between disease resistance in young animals and production traits (Khusro *et al.* 2004, Pollott and Greeff 2004, Pollott *et al.* 2004, Safari *et al.* 2005, Ingham *et al.* 2007, Afolayan *et al.* 2009, Huisman and Brown 2008, 2009, Mortimer *et al.* 2009, Brown *et al.* 2010 and Abdelsayed *et al.* 2011).

Trait	**Disease Resistance**		
	Worms	**Fleece Rot and Flystrike**	**Footrot**
Clean fleece weight	Neutral to slightly unfavourable	Neutral to slightly unfavourable	Neutral to slightly favourable
Fibre diameter	Neutral	Neutral to slightly favourable	Neutral to slightly unfavourable
Body weight	Neutral to slightly favourable	Neutral to slightly unfavourable	Unknown
Eye muscle depth	Slightly favourable	Unknown	Unknown
Fat depth	Slightly favourable	Unknown	Unknown
Reproduction	Neutral	Unknown	Unknown

For the Australian sheep industry, selection indexes for a range of breeding objectives are available from Sheep Genetics, through LAMBPLAN and MERINOSELECT that provide national genetic evaluation services (http://www.sheepgenetics.org.au/). A number of indexes consider resistance to gastrointestinal nematodes in the breeding objective. Through LAMBPLAN, these indexes include: the LAMB2020 Index for terminal sire selection (predicted to yield a 30% reduction in FEC over 10 years); Maternal $ Index for selection of maternal sires (predicted to yield a reduction in FEC of 24% over 10 years); Dual Purpose $ Index for selection of dual purpose sires (predicted to yield a reduction in FEC 0f 17% over 10 years); and the Self-replacing Carcase $ Index for selection of sires for use in self-replacing flocks (predicted to yield a reduction in FEC of 17% over 10 years). For Merinos, in addition to a MERINOSELECT index being available for a fine wool production system (Merino F10%+SS), a variation of this index is offered that also aims to improve worm resistance (Merino 10%+SS+W). As well as predicted to achieve moderate decreases in fibre diameter, moderate increases in clean fleece weight and staple strength and small increases in body weight, this index is predicted to reduce FEC by 20% over the same 10 year period. Including FEC in this index will lead to not greatly smaller responses in clean fleece weight and fibre diameter.

For some disease traits though, the impact of including selection for disease resistance in the breeding objective is greater. In the case of an objective that includes breech wrinkle, as an indicator of flystrike resistance, Brown *et al.* (2010) have shown that selection using an index is the best means to reduce breech wrinkle and simultaneously improve production traits in Merinos. Responses in the traits were greater also when sires were selected across flocks and within flocks, rather than using within-flock selection alone. Table 13.6 shows the predicted changes in breech wrinkle, clean fleece weight, fibre diameter and body weight associated with varying levels of emphasis on breech wrinkle when included in the MERINOSELECT F10%+SS index for across-flock and within-flock selection scenarios. With no emphasis given to breech wrinkle (F10%+SS), gains in clean fleece weight and fibre diameter are optimal, but breech wrinkle score increased by 0.7 units (across-flock selection) and 0.1 units (within-flock selection). Adding breech wrinkle to the index resulted in changes to breech wrinkle of -0.4 to -0.9 units (across-flock selection) and -0.7 to -1.1 units (within-flock selection) as emphasis on breech wrinkle increased from 25 to 66% of the overall gain. However, responses in clean fleece weight and fibre diameter were reduced (both traits unfavourably correlated with breech wrinkle) while responses in body weight were increased (favourably correlated with breech wrinkle). Responses from the across-flock scenario in yearling clean fleece weight and fibre diameter were reduced by 11-34% and 31-69% respectively as emphasis on breech wrinkle increased, versus reductions in response of 42-90% in yearling clean fleece weight and 0-19% in yearling fibre diameter from within-flock selection. Although wool production is compromised as more emphasis in the index is placed on breech wrinkle, there are some benefits due to greater responses in body weight.

Importantly, even where slight genetic antagonisms exist between production traits and disease resistance, the breeding program must be appropriately designed to optimise improvement in all traits in the breeding objective. One of the major difficulties, though, is the derivation of the economic weights required for formal inclusion of disease resistance traits into the breeding objective. Some attempts have been made to include resistance to individual diseases in the breeding objective, but only for a few diseases. The relevant issues have been addressed by Ponzoni (1984), Atkins (1987), Richards and Atkins (2010) and Brown *et al.* (2010) with respect to fleece rot, body strike and breech strike in breeding programs, while the issues relevant to including resistance to gastrointestinal nematodes have been discussed by Woolaston and Eady (1995) and Woolaston and Baker (1996) and issues for the inclusion of footrot resistance have been discussed by Raadsma and Conington (2010).

Table 13.6: Predicted ten-year responses to selection using the MERINOSELECT F10%+SS index when breech wrinkle is excluded or included with varying levels of emphasis (Brown *et al.* 2010).

	Across-flock scenario				**Within-flock scenario**			
Trait	**F10%+SS**	**+25%**	**+50%**	**+66%**	**F10%+SS**	**+25%**	**+50%**	**+66%**
ycfw (%)	9.2	8.2	7.0	6.1	9.2	5.3	2.6	0.9
yfd (μm)	-1.6	-1.1	-0.7	-0.5	-1.6	-1.6	-1.4	-1.3
ywt (kg)	2.9	4.2	4.2	4.0	2.9	3.8	3.9	3.8
acfw (%)	4.6	3.4	2.6	2.0	4.6	1.4	-0.5	-1.7
afd (μm)	-1.6	-0.9	-0.6	-0.3	-1.6	-1.6	-1.4	-1.3
awt (kg)	1.7	3.0	3.2	3.2	1.7	2.8	3.2	3.3
bwr	0.7	-0.4	-0.7	-0.9	0.1	-0.7	-0.9	-1.1

ycfw, yearling clean fleece weight; yfd, yearling fibre diameter; ywt, yearling body weight; acfw, adult clean fleece weight; afd, adult fibre diameter; awt, adult body weight; bwr, breech wrinkle score (1-5).

Choice of bloodline, strain and breed

Considerable variation in resistance to fleece rot and body strike exists between strains and bloodlines within the Merino breed (Table 13.7). Bloodline differences in fleece rot resistance have been shown also in data from wether comparisons for a limited number of bloodlines (Mortimer and Atkins 2001). Differences between bloodlines in resistance to dermatophilosis also exist, though to a lesser extent (Woolaston *et al.* 1995). This provides breeders with the option of changing Merino strain or bloodline to make relatively large and rapid changes in resistance to these diseases, as well as exploiting within-flock genetic variation. The implications on all other production traits obviously need to be considered before making such changes.

Table 13.7: Average incidence of fleece rot between Merino strains and average range for bloodlines within strain (Atkins and McGuirk 1979).

	Average incidence (%)	
	Strain	**Bloodline within strain range**
Fine (n=2)	9	3-14
Medium non-Peppin (n=2)	28	20-36
Medium Peppin (n=10)	23	13-39
Strong (n=1)	38	38

Preliminary data also suggest differences between Merino bloodlines within the fine-wool spectrum in resistance to footrot (Raadsma and Conington 2010). Resistance to gastrointestinal nematodes, in contrast, has shown very little variation between strains and bloodlines of the Merino breed, with most of the genetic variation occurring between animals within flocks (Eady *et al.* 1996). Variation in worm resistance between bloodlines may change in the future as individual studs are now including this trait in their breeding programs.

While breed differences have been documented for some of the diseases considered in this topic, e.g. gastrointestinal nematode resistance as reviewed by Stear (2010), breed substitution is seldom used as a control strategy due to potentially unfavourable impacts on overall productivity. Nonetheless, it is possible that some of the superior production gained from production systems that use crossbreeding may be due to improved disease control (Stear 2010).

Choice of individuals across flocks

Identification of resistant individuals, rather than resistant flocks, is the major genetic option available to breeders looking to improve resistance to disease. To assess the genetic performance of individual sheep across flocks, Sheep Genetics reports estimates of breeding values, known as Australian Sheep Breeding Values (ASBVs). ASBVs indicate the across-flock performance of a sheep. ASBVs are available for early breech wrinkle (EBWR) of Merino sires and FEC of sires of various breeds from genetic evaluations done by MERINOSELECT and LAMBPLAN and from genetic evaluations conducted by central test sire evaluation (Table 13.8). The table shows the large range in genetic performance in FEC and EBWR of Merino sires available for use within the Australian sheep industry. Many sires show high levels of performance in these disease resistance traits. In Table 13.8, sires having a negative ASBV for HFEC or EBWR have greater genetic resistance to the diseases, whereas sires having a positive ASBV have greater genetic susceptibility.

Table 13.8: Percentile bands of Australian Sheep Breeding Values for hogget faecal egg count (HFEC, %) and early breech wrinkle (EBWR, score unit) for sires published in Merino Superior Sires 16 (Swan *et al.* 2010).

Band	**0**	**1**	**2**	**3**	**4**	**5**	**10**	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**
HFEC	-99	-85	-79	-74	-68	-68	-49	-30	-14	2	12	23	41	59	99	319
EBWR	-1.2	-0.7	-0.7	-0.6	-0.5	-0.5	-0.3	-0.2	-0.1	-0.0	0.1	0.1	0.2	0.3	0.4	1.0

Using ASBVs, sheep breeders can identify the current level of performance in FEC and EBWR and monitor the rates of genetic improvement in individual traits and the overall breeding objectives of their flocks, as well as using the ASBVs in selection of animals. A commercial producer can use ASBVs, either individually or combined in selection indexes, to compare rams and identify those rams that are best suited to the objective of their flock and for use in their production system. Summaries of the average ASBV within years for a breed can be obtained from Sheep Genetics to provide the genetic trend over time for a trait that has arisen due to selection. Genetic trends for EBWR and FEC in the Merino, Border Leicester and terminal breeds over the period 2000-2010 are shown in Figure 13.6. Overall, the genetic trends for FEC at the various ages show that FEC has been reduced, particularly in the Merino and terminal breeds. A small reduction in EBWR in Merinos is also shown. These genetic trends indicate that sheep breeders are breeding sheep that are more disease resistant. In the case of the decrease in early breech wrinkle, this has been in response to sheep breeders recognising in recent years the need to breed sheep that do not require mulesing.

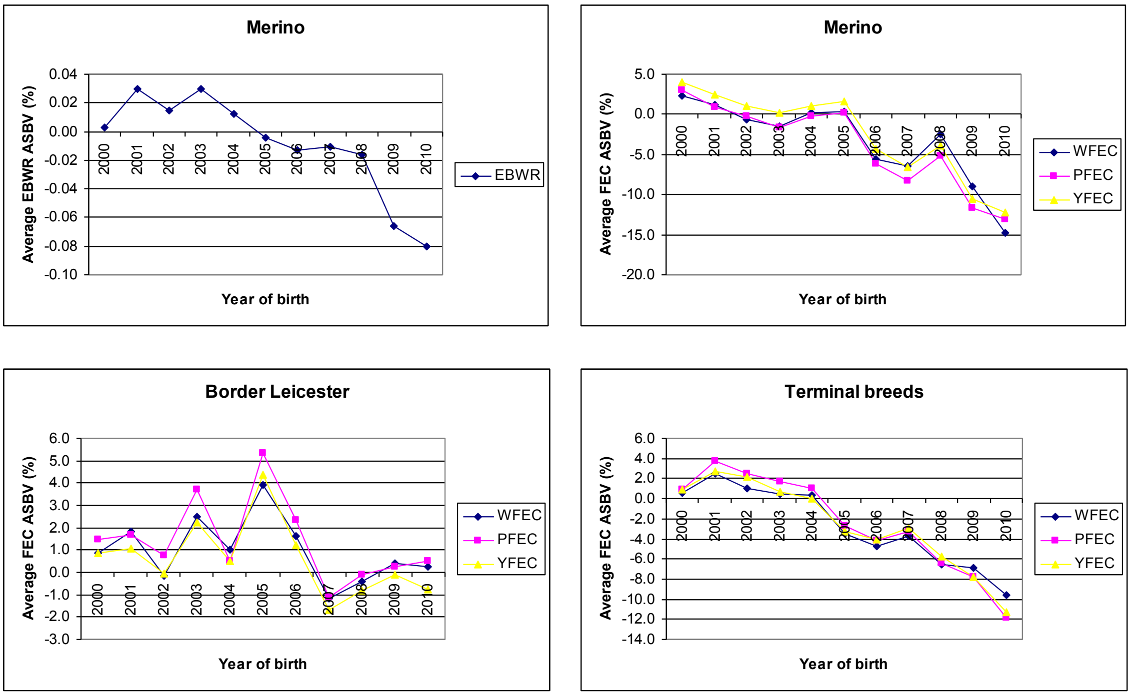

Figure 13.6: Genetic trends in Australian Sheep Breeding Values (ASBV) of the Merino, Border Leicester and terminal breeds (Sheep Genetics (Unpubl. data). NB: EBWR, early breech wrinkle; WFEC, faecal egg counts (FEC) at weaning; PFEC, FEC at post weaning; YFEC, FEC at yearling age

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Readings

The following readings are available on web learning management systems

1. Eady, S.J., Woolaston, R.R. and Barger, I.A. 2003, 'Comparison of genetic and non-genetic strategies for control of gastrointestinal nematodes of sheep', *Livestock Production Science,* vol. 81, pp. 11.
2. Greeff, J., Kinghorn, B.P. and Brown, D. 2010, 'Breeding and selection' in *International Sheep and Wool Handbook* (ed. D.J. Cottle) pp. 165-188. This book available in library.
3. Woolaston, R.R. and Baker, R.L. 1996, 'Prospects of breeding small ruminants for resistance to internal parasites', *International Journal Parasitology,* vol. 26, pp. 845.

References

Abdelsayed, M., Thomson, P.C. and Raadsma, H.W. 2011, 'Genetic, phenotypic, and environmental correlations between footrot and fleece traits in sheep' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 19, pp. 411-418.

Afolayan, R.A., Fogarty, N.M., Gilmour, A.R., Ingham, V.M., Gaunt, G.M., and Cummins, L.J. 2009. 'Genetic correlations between early growth and wool production of crossbred ewes and their subsequent reproduction' in *Animal Production Science* vol. 49, pp. 17-23.

Albers, G.A.A., Gray, G.D., Piper, L.R., Barker, J.S.F., Le Jambre, L.F. and Barger, I.A. 1987, 'The genetics of resistance and resilience to *Haemonchus contortus* infection in young Merino sheep' in *International Journal Parasitology,* vol. 17, pp. 1355-1363.

Atkins, K.D. 1987, 'Resistance to fleece rot and body strike: its role in a breeding objective for Merino sheep', in *Proceedings of a Sheep Blowfly and Management Workshop*, NSW Department of Primary Industries, Orange, NSW.

Atkins, K.D. and McGuirk, B.J. 1979, 'Selection of Merino sheep for resistence to fleece-rot and body strike' in *Wool Technology and Sheep Breeding,* vol. 27, pp. 15-19.

Besier, B., Jacobson, C., Woodgate, R. and Bell, K. 2010, in *International Sheep and Wool Handbook,* (ed. D.J. Cottle), pp. 471-488.

Bishop, S.C. and Morris, C.A. 2007, 'Genetics of disease resistance in sheep and goats' in *Small Ruminant Research*, vol. 70, pp. 48-59.

Brown, D.J., Swan, A.A. and Gill, J.S. 2010, 'Within- and across- flock genetic relationships for breech flystrike resistance indicators traits' in *Animal Production Science*, vol. 50, pp. 1060-1068.

Eady, S.J., Dobson, R.J. and Barnes, E.H. 1997, 'Impact of improved host resistance on worm control in Merinos - a computer simulated study' in *Proceedings of the 4th International Congress for Sheep Veterinarians,* p. 341.

Eady, S.J., Woolaston, R.R. and Barger, I.A. 2003, 'Comparison of genetic and non genetic strategies for control of gastrointestinal nematodes of sheep' in *Livestock Production Science,* vol. 81, pp. 11.

Eady, S.J., Woolaston, R.R., Mortimer, S.I., Lewer, R.P., Raadsma, H.W., Swan, A.A. and Ponzoni, R.W. 1996, 'Resistance to nematode parasites in Merino sheep: sources of genetic variation' in *Australian Journal Agricultural Research,* vol. 47, pp. 895-898.

Egerton, J.R. and Raadsma, H.W. 1991, in *Breeding for Disease Resistance in Farm Animals,* (eds. R.F.E. Axford and J.B. Owen), p. 347-370.

Gray, R.R., Barger, I.A. and Piper, L.R. 1992, 'Parasitological and immunological responses of genetically resistant Merino sheep on pastures contaminated with parasitic nematodes' in *International Journal for Parasitology* vol. 22, pp.417-425.

Greeff, J.C. and Karlsson, L.J.E. 2009, 'Opportunities to breed for resistance to breech strike in Merino sheep in a Mediterranean environment' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 18, pp. 272-278.

Greef, J., Karlsson, L. and Underwood, N. 2006, 'Breeding Merino sheep for worm resistance increases profit in a Mediterranean environment' in *8th World Congress on Genetics Applied to Livestock Production,* Communication 15-08, pp. 1-4.

Goddard, M.E. and Hayes, B.J. 2009, 'Mapping genes for complex traits in domestic animals and their use in breeding programmes' in *Nature Reviews Genetics* vol. 10, pp. 381-391.

Huisman A.E. and Brown D.J. 2008, 'Genetic parameters for weight, wool, and disease resistance and reproduction traits in Merino sheep: 2. Genetic relationships between body weight traits and other traits' in *Australian Journal of Experimental Agriculture* vol. 48, pp. 1186–1193.

Huisman A.E. and Brown D.J. 2009, 'Genetic parameters for weight, wool, and disease resistance and reproduction traits in Merino sheep: 3. Genetic relationships between ultrasound traits and other traits' in *Animal Production Science* vol. 49, pp. 283-288.

Huisman A.E., Brown D.J., Ball A.J. and Graser H-U. 2008, 'Genetic parameters for weight, wool, and disease resistance and reproduction traits in Merino sheep: 1. Description of traits, model comparison, variances and their ratios' in *Australian Journal of Experimental Agriculture vol. 48,* pp. 1177–1185.

Ingham, V.M., Fogarty, N.M., Gilmour, A.R., Afolayan, R.A., Cummins, L.J., Gaunt, G.M., Stafford, J. and Hocking Edwards, J.E. 2007, 'Genetic evaluation of crossbred lamb production. 4. Genetic parameters for first-cross animal performance' in *Australian Journal of Agricultural Research* vol. 58, pp. 839-846.

Kemper, K.E., Emery, D.L., Bishop, S.C., Oddy, H., Hayes, B.J., Dominik, S., Henshall, J.M. and Goddard, M.E. 2011, 'The distribution of SNP marker effects for faecal worm egg count in sheep, and the feasibility of using these markers to predict genetic merit for resistance to worm infections' in *Genetics Research,* vol. 93, pp. 203-219.

Kemper, K.E., Larsen, J.W.A, Bishop, S.C., Anderson, N., Goddard, M.E., Greeff, J.C., Woodgate, R. and Karlsson, L.J.E. 2009, 'A comparison between sheep bred for worm resistance and unselected controls when exposed to low larval challenges during summer' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 18, pp. 596-599.

Khusro, M., van der Werf, J.H.J, Brown, D.J., and Ball, A. 2004, 'Across flock (co)variance components for faecal worm egg count, live weight, and fleece traits for Australian Merinos' in *Livestock Production Science*, vol. 91, pp. 35-43.

Li, Y., Swan, A.A. and Purvis, I. 1999, 'Genetic variation in resistance to fleece rot in CSIRO's fine wool flock' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 13, pp. 524-527.

Morris, C.A., Amyes, N.C., Bisset S.A. and Mackay, A.D. 2004, 'Resilience to nematode parasite challenge in industry and AgResearch selection flocks' in *Proceedings of the New Zealand Society of Animal Production, vol.* 64, pp. 300-303.

Morris, C.A. and Bisset, S.A. 1996, 'Progress on genetic studies of resilience to nematode parasites in sheep' in *Proceedings of the New Zealand Society of Animal Production* vol. 56, pp. 91-93.

Mortimer, S.I. and Atkins, K.D. 2001, 'Genetic differences among Merino bloodlines in fleece rot resistance from wether comparisons' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 14, pp. 183-186.

Mortimer, S.I., Atkins, K.D. and Raadsma, H.W. 1998, 'Responses to selection for resistance and susceptibility to fleece rot and body strike in Merino sheep' in *Proceedings World Congress on Genetics Applied to Livestock Production,* vol. 27, p. 283-286.

Mortimer, S.I., Robinson, D.L., Atkins, K.D., Brien, F.D., Swan, A.A., Taylor P.J., Fogarty, N.M. 2009, Genetic parameters for visually assessed traits and their relationships to wool production and liveweight in Australian Merino sheep' in *Animal Production Science* vol.49, pp. 32-42.

Norris, B.J., Colditz, I.G.. and Dixon, T.J. 2008, 'Fleece rot and dermatophilosis in sheep' in *Veterinary Microbiology* vol.128, pp. 217-230.

O'Meara, T.J. and Raadsma, H.W. 1995, in *Breeding for Resistance to Infectious Diseases in Small Ruminants*, (eds. G.D. Gray, R.R. Woolaston and B.T. Eaton), pp. 187-218.

Pollott G.E. and Greeff J.C. 2004, 'Genotype x environment interactions and genetic parameters for fecal egg count and production traits of Merino sheep' in *Journal of Animal Science* vol. 82, pp. 2840–2851.

Pollott G.E., Karlsson L.J..E, Eady S. and Greeff J.C. 2004, 'Genetic parameters for indicators of host resistance to parasites from weaning to hogget age in Merino sheep' in *Journal of Animal Science* vol. 82, pp. 2852–2864.

Ponzoni, R.W. 1984, 'The importance of resistance to fleece rot and body strike in the breeding objective of Australian Merino sheep' in *Wool Technology and Sheep Breeding,* vol. 32, pp. 20-40.

Raadsma, H.W. and Conington, J. 2010, in *Breeding for Disease Resistance in Farm Animals,* 3rd Edition (eds. S.C. Bishop, R.F.E. Axford, F.W. Nicholas and J.B. Owen), pp. 251-276.

Raadsma, H.W., Gray, G.D. and Woolaston, R.R. 1997, in *The Genetics of Sheep*, (eds. L.R. Piper and A. Ruvinsky), pp. 199-224.

Raadsma, H.W., Gray, G.D. and Woolaston, R.R. 1998, 'Breeding for disease resistance in Merino sheep in Australia' in *Revue Scientifique et Technique Office International des Epizooties* vol. 17, p.315-328.

Richards, J.S. and Atkins, K.D. 2010, 'Will genetics offer a permanent solution to breech strike?' in *Animal Production Science*, vol. 50, pp. 1053-1059.

Sackett, D. Holmes, P. and Abbott, K. 2006, 'Assessing the economic cost of endemic diseases on the profitability of Australian beef cattle and sheep producers' in *Final Report AHW.87*, Meat & Livestock Australia Limited.

Safari, A. and Fogarty, N.M. 2003, 'Genetic Parameters for Sheep Production Traits: Estimates from the Literature', Technical Bulletin 49, NSW Department of Primary Industries, Orange, NSW, pp 1-100.

Safari, E., Fogarty, N.M. and Gilmour, A.R. 2005, 'A review of genetic parameter estimates for wool, growth, meat and reproduction traits in sheep' in *Livestock Production Science*, vol. 92, pp. 271-289.

Smith, J.L., Brewer, H.G. and Dyall, T. 2009, 'Heritability and phenotypic correlations for breech strike and breech strike resistance indicators in Merinos' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 18, pp. 334-337.

Smith, W.J.M., Li, Y., Ingham, A., Collis, E., McWilliam, S.M., Dixon, T.J., Norris, B.J., Mortimer, S.I., Moore, R.J. and Reverter, A. 2010, 'A genomics-informed, SNP association study reveals FBLN1 and FABP4 as contributing to resistance to fleece rot in Australian Merino sheep ' in *BMC Veterinary Research,* vol. 6, pp. 27.

Stear, M.J. 2010, in *Breeding for Disease Resistance in Farm Animals,* 3rd Edition (eds. S.C. Bishop, R.F.E. Axford, F.W. Nicholas and J.B. Owen), pp. 279-294.

Swan A., Casey, A. and Swain, B. 2010, 'Merino Superior Sires Central Test Sire Evaluation Results Number 16 – 2010 – 1987-2009 Drops', Australian Wool Innovation Limited and Australian Merino Sire Evaluation Association.

van der Werf, J.H.J., Kinghorn, B.P. and Banks, R.,G. 2010, 'Design and role of an information nucleus in sheep breeding programs' in *Animal production Science,* vol. 50, pp. 998-1003.

Windon, R.C., Dineen,J.K. and Wagland, B.M. 1987, 'Genetic control of immune responses against the intestinal nematode *Trichostrongylus colubriformis* in lambs' in *Merino Improvement Programs in Australia* (ed. B.J. McGuirk), pp. 371-375.

Woolaston, R.R. and Baker, R.L. 1996, 'Prospects of breeding small ruminants for resistance to internal parasites' in *International Journal of Parasitology,* vol. 26, pp. 845-855.

Woolaston, R.R., Barger, I.A. and Eady, S.J. 1997, 'The relative effectiveness of alternative worm control measures and their interactions' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 12, pp. 45-49.

Woolaston, R.R., Barger, I.A. and Piper, L.R. 1990, 'Response to helminth infection of sheep selected for resistance to *Haemonchus contortus*' in *International Journal for Parasitology* vol. 20, pp.1015-1018.

Woolaston, R.R. and Eady, S.J. 1995, in *Breeding for Resistance to Infectious Diseases in Small Ruminants*. (eds. G.D. Gray, R.R. Woolaston and B.T. Eaton), pp. 53-75.

Woolaston, R.R., Eady, S.J., Ponzoni, R.W., Lewer, R.P., Gifford, D.R. and Ancel, P.M.C. 1995, 'Genetic variation in resistance to dermatophilosis in Merinos' in *Proceedings Association for the Advancement of Animal Breeding and Genetics,* vol. 11, pp. 126-129.