BREEDING FOR RESISTANCE TO FOOTROT IN SHEEP

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SUMMARY and PRACTICAL RECOMMENDATIONS

- Resistance to severe (virulent) and also moderate (intermediate) footrot in sheep is a heritable characteristic. In a flock of sheep exposed to virulent footrot, some will remain free from footrot(resistant), whereas others maybe extremely severely affected (susceptible). Selecting only those animals as breeding replacements which show the greatest resistance, will gradually improve resistance of the whole flock in future generations.

- Resistant sheep will express exposure to severe (virulent) footrot in a similar fashion as non-selected flocks express moderate or mild (benign) footrot.

- Selection for increased resistance will reduce production losses associated with exposure to virulent footrot, and reduce recurrent costs associated with control.

- Selection for increased resistance does not have undesirable genetic effects on other economically production traits. However, selection for increased resistance will most likely reduce the selection intensity and hence gain for other important production traits.

- Selection for increased resistance is a long and slow process, but gains will be permanent and cumulative.

- Selection of resistant breeds or strains within a breed, may be the most rapid means to improve resistance. However if genetic improvement within a specific flock is aimed at, there are no options for instant rapid genetic gain.

- There are no known DNA markers that allow selection for resistance without exposure to footrot. Selection for resistance based on selection for high antibody response to footrot vaccination will not be effective, since the genes controlling each trait are not the same.

- In a selection programme additional control options may be required until resistance is sufficiently high to decrease reliance on routine control.

- If eradication of intermediate or severe footrot is aimed for, selection for increased resistance may not be worthwhile. Selection for resistance to moderate (intermediate) footrot may have immediate impact without need for further control inputs. In the case of benign (mild) footrot, selection for resistance is not worthwhile, neither is control or eradication in this case.

I INTRODUCTION

It is not within the scope of this paper to provide a detailed account of all aspects related to footrot. The reader is referred to an excellent overview of footrot in ruminants by EGERTON *et al.* (1989), and in particular the comprehensive and detailed chapter on footrot of sheep by STEWART (1989). For those with a specific interest in footrot, the benchmark publication by BEVERIDGE (1941) is compulsory reading, and the recent reviews by ALLWORTH (1995), and ABBOTT (2000) also provide excellent overviews of the subject. The companion chapter by EGERTON and RAADSMA (2000, these proceedings), provides detailed background on the aetiology and methods available for control and eradication.

This review largely draws on work conducted by the author and co-workers and has recently been detailed in the text "Breeding for Disease Resistance in Farm Animals" 2000 (Chapter 10 Genetic Aspects of Resistance to Ovine Footrot) CAB (RTAADSMA 2000). The following text largely describes our understanding of genetic resistance to footrot. Where appropriate relevant practical recommendations have been included.

FOOTROT OF SHEEP

Footrot of sheep is an infectious and, on specific occasions, an exceptionally contagious disease resulting from invasion of epidermal tissue of the hooves by a mixed group of bacteria (EGERTON *et al.*, 1969; ROBERTS and EGERTON, 1969). An essential component of this mixture is *Dichelobacter nodosus,* formerly *Fusiformis nodosus* (BEVERIDGE, 1941) or *Bacteroides nodosus* (DEWHIRST *et al.,* 1990). *D. nodosus* is a Gram-negative anaerobic bacterium which, so far as is known, occurs naturally only in the feet of ruminants affected by footrot. The disease is characterised by infection of the interdigital skin (IDS), and may under certain conditions progress to separation of the sole, soft and hard horn from the underlying hoof matrix.

Infection of normal, dry healthy interdigital skin of sheep with *D. nodosus* alone is insufficient for the development of footrot. Predisposition of feet through water maceration and activity of normal environmental skin microflora, including *Corynebacterium pyogenes* and various surface located diphtheroid bacteria, is an essential prerequisite for the development of footrot. Footrot is therefore a mixed bacterial infection, and *Fusiformis necrophorum*, a faecal organism, is essential to the disease. *F. necrophorum* is often considered the main pathogen in the pre-disposition and early stages of initiation of footrot. Predisposition causes sufficient inflammation and damage of the *stratum corneum* for infection to proceed. The synergistic relationship between *F. necrophorum* and *D. nodosus* leads to progressive and destructive infection of the epidermis of the hoof, causing in severe cases a separation of the horn from the dermis. The underlying dermis may become inflamed but is not invaded, and the *stratum germinativum* is not destroyed. The extent of tissue damage is dependent on bacterial and host-resistance factors described further on.

Transmission of the disease is facilitated directly by transfer of infected material containing *D. nodosus*, from exposed lesions into the environment and thereby contaminating the feet of other sheep. Successful transmission is only possible under wet and warm conditions, in sheep which have been sufficiently predisposed. *D. nodosus*, as the obligate parasite, is thus considered the essential transmitting agent of footrot, but development of footrot requires the symbiotic relationship with *F. necrophorum*, as a normal environmental inhabitant, and the action of prolonged wetting of feet..

EXPRESSION OF FOOTROT

Clinical signs in individual sheep

Following infection with *D. nodosus* and in the successful development of footrot, a range of clinical signs may be evident. Inflammation, characterised by diffuse superficial necrosis and erythema of the interdigital skin, is evident during predisposition and initial onset of footrot. In more severe cases, a break at the skin-horn junction is visible approximately a week after infection. Extensive separation, which commences at the heel and the posterior region of the sole, may progress along the sole to the toe. In extremely severe cases, separation will extend to the abaxial wall of the hoof.

Chronic infection will cause the horn to be overgrown and misshapen, with extensive necrotising damage to underlying soft tissues. Apparent self-cure is possible under dry conditions, particularly in cases where the infection has been confined to the interdigital skin.

In order to standardise the description of severity and progression of lesions, a number of scoring systems have been developed for the subjective assessment of footrot. EGERTON and ROBERTS (1971) were the first to propose a scoring system for footrot lesions as follows:

Score 0: normal dry or wet foot.
Score 1: limited interdigital dermatitis.
Score 2: more extensive interdigital dermatitis.
Score 3: severe interdigital dermatitis and under-running (separation) of the horn of the heel and sole.
Score 4: as for 3, but with under-running extended to the walls of the hoof.

Other scoring systems have evolved from this system in an attempt to more clearly differentiate between various levels of progression of footrot infection, but generally do not contribute additional information in diagnosis or assessment of disease status.

The prevalence of sheep affected with footrot in different environments exposed to agents of varying virulence can range from negligible (<5%) to extremely high (>95%). This was illustrated by EGERTON and RAADSMA (1991). For convenience, footrot at the flock level can be classified as described by RAADSMA et al(1990, 1991), EGERTON and RAADSMA (1991):

Severe footrot - high proportion (>10%) of animals with severe lesions (score 3 or score 4); rapid development; severe production losses; little evidence of self-cure. This is a severe and debilitating disease with significant lameness and welfare implications.

Moderate footrot - disease expressed at a severity in between severe and mild footrot. A low proportion of sheep may express severe lesions which are usually confined to underrunning of the sole of the hoof (score 3); self-cure is evident; few sheep remain chronically infected. Fewer sheep show lameness, although the few sheep with severe lesions may show acute lameness, and may remain chronically infected.

Mild footrot – very low proportion (<1%) of animals with severe lesions, with most lesions confined to the interdigital skin (score 1 or score 2). Most lesions resolve spontaneously with onset of dry conditions. Little effect on production. Associated lameness is less than in severe or moderate footrot. Expression of mild footrot is further complicated in that it closely resembles Ovine Interdigital Dermatitis (OID).

It should be noted that these categories are subjective, and a wide range of expression of footrot is usually recognised in the field. The expression of footrot based on the severity and economic impact of the disease in a flock is, in fact, a continuum.

Factors affecting expression of footrot

The expression of footrot in a flock of sheep is governed by three factors: a) virulence of *D. nodosus,* b) the suitability of the environment for predisposition of the host and transmission of the organism, c) inherent susceptibility of the host. These factors have been described in detail by EGERTON AND RAADSMA (1991,2000). Their influence on the expression of the disease is shown in Fig 1. It should be recognised that control of the disease is feasible through direct manipulation of any of the three 'windows' of opportunity. This chapter will focus on those factors which affect host susceptibility only.

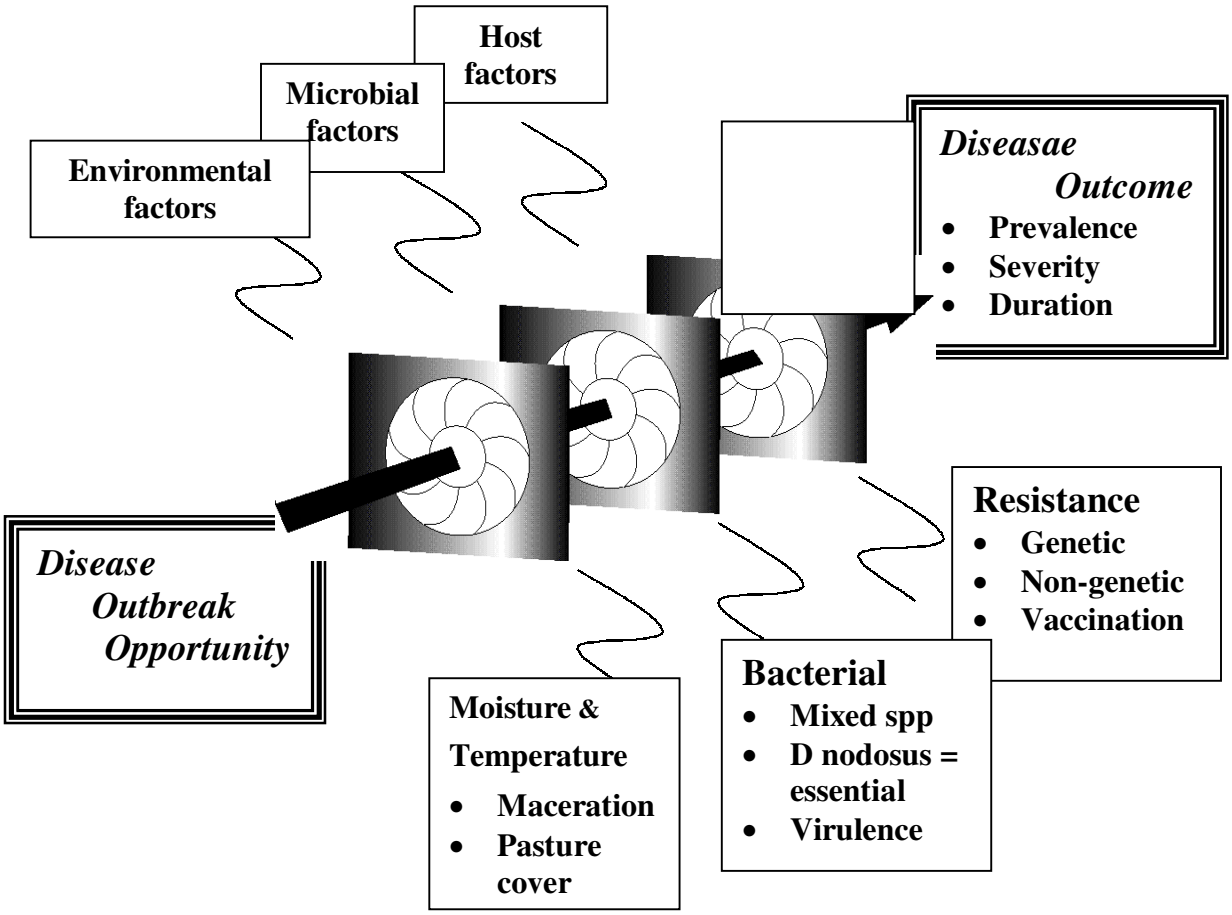

Figure 1 The three major factors (Environmental, microbial, and host) that influence the prevalence, severity and duration of footrot shown as windows of opportunity. The windows which allows for the lowest opportunity will determine the overall expression of footrot.

Variation in resistance to infectious disease is the consequence of a combination of innate and acquired resistance. In the case of footrot, innate resistance may be responsible for preventing invasion of the epidermis by the bacteria responsible for the disease. O'MEARA and RAADSMA (1995) provide an

overview of the physical and immunological factors of the host which aid or arrest the development of footrot.

The influence of non-genetic effects such as age, birth/rearing type, age of dam, and sex of sheep on susceptibility to footrot has been reported. Adult sheep are more susceptible than lambs, and rams more susceptible than ewes (BEVERIDGE, 1941; LITTLEJOHN, 1961; RAADSMA *et al.,* 1993,1995; WOOLASTON, 1993).

In general terms, acquired resistance is a sequel either to naturally-acquired infection, colostral transfer of immunity, or immunisation. The identification of the principal causative bacterial agent, *D. nodosus*, and the immunogenic properties of *D. nodosus* fimbriae, have made it possible to use vaccination as a method to control footrot. Following the initial development of whole-cell vaccines (EGERTON and BURRELL, 1970; EGERTON and ROBERTS, 1971), recombinant DNA techniques have now made it possible to produce effective vaccines comprised largely of *D. nodosus* fimbrial antigens (EGERTON *et al*., 1987; O'MEARA *et al.,* 1993). To establish the importance of these antigens in vaccine formulations, the measurement of K-agglutinating antibody titres can be used as an indication of the ability of the vaccine to protect against infection with *D. nodosus* (RAADSMA et al., 1994b).

Vaccines need to induce antibody titres against fimbrial antigens from each of the 9 major serogroups of *D. nodosus,* since there is little or no cross-protection between serogroups, and field infections often involve infection with more than one serogroup. The problem of reduced titres, possibly due to antigenic competition in the host immune response (RAADSMA *et al.*, 1994b), limits the efficacy of multi-component footrot vaccines. The existence of genetic variation in response to active immunisation against footrot is reviewed later in this chapter.

SCOPE FOR GENETIC IMPROVEMENT OF RESISTANCE TO FOOTROT

Incentive for genetic improvement in resistance to footrot

In the absence of regulatory control, the occurrence of footrot on a farm does not always justify treatment. EGERTON and RAADSMA (1991) presented estimates of losses likely to arise when owners take one of three options; (a) take no action, (b) implement control, (c) proceed through control to eradication. A number of important points were made:

- For mild footrot, the cost of control or eradication would exceed that which could be directly attributed to the disease if left untreated.

- The losses due to severe and moderate footrot could be halved through conventional control techniques, but the cost of control would be recurrent from season to season.

- The economic loss from severe or moderate footrot under a control management option is greater than that from uncontrolled mild footrot.

Breeding strategies could aim to reduce the impact of infection with virulent or intermediate isolates of footrot to that experienced with benign isolates of footrot, so that no specialised control strategies are warranted and the disease has minimum impact on production. An alternative strategy could be to improve the responsiveness of sheep to vaccination, so that footrot could be managed similarly to the clostridial diseases, with annual booster vaccinations offering effective protection.

Resistance to footrot defined in general terms

It is appropriate to think of resistance as a response to challenge. Clear clinical signs and diagnostic techniques have been established for bacterial diseases to classify animals according to their level of resistance after a disease outbreak.

a) Indicators based on clinical scores

Numerous measurement systems have been used to describe differences between sheep in their clinical response to footrot. Most of these systems are based on a simple binary scale indicating whether a foot or a sheep is affected or not. Sometimes the scale is extended beyond the two classes, in order to describe the severity of footrot as indicated by the extent of underrunning of soft and hard horn of the foot. A number of footrot severity indices have been derived from the individual foot scores. RAADSMA *et al*. (1993) evaluated 22 primary and derived indicators including footrot scores incorporating healing, for their utility to describe differences between feet, between sheep, and between flocks. For differences between sheep, all indicators were highly correlated (RAADSMA et al., 1993). Those traits with an ordered scale such as the number of feet affected or underrun, are inherently more useful than scores or grades which do not reflect incremental levels of severity.

Resistance is often measured as an all-or-none trait. However in reality, resistance is a multifactorial trait. The polygenic nature of the trait and all the non-genetic factors which influence expression of disease can be readily accommodated by adopting an underlying scale of liability as proposed by FALCONER (1965). This allows disease to be treated as a trait with quantitative characteristics similar to those of other production traits for which genetic parameters can be estimated. The genetic implication that all-or-none traits are due to single gene effects, where resistance behaves as a trait with Mendelian inheritance, is over simplistic and incorrect for most bacterial diseases.

Of particular interest is how traits with multiple categories, such as number of feet affected or underrun, fit a threshold model. Similarly, the relationship between the threshold for becoming affected, and the threshold for severe footrot (i.e. underrunning) can also be examined under a multi-threshold model of liability. RAADSMA *et al*. (1993) showed that for those indicators with several categories on an ordered scale (number of feet affected, or number of feet underrun), increasing grades of severity reflect a single underlying variable. On the basis of theiralysis, it is recommended to use ‘number of feet affected with underrun footrot’ as a simple indicator to describe differences between sheep in resistance to footrot after challenge.

c) Serological indicators of resistance to footrot

It has been shown that antibodies specific to *D. nodosus* are generated during chronic and severe footrot infection (EGERTON and ROBERTS, 1971; EGERTON and MERRITT, 1973; EMERY *et al.,* 1984c; FAHEY *et al.,* 1983; FERRIER *et al.,* 1986). Such antibodies may be directed to pilus or outer-membrane components. In addition, haemagglutination and protease-inhibiting antibodies have been detected following chronic infection (EGERTON and MERRITT, 1973). The results of these studies suggest that groups of sheep with more severe levels of infection develop higher antibody titres as a consequence of that infection. RAADSMA *et al*. (1993) were the first to report positive correlations between *D. nodosus*-specific antibodies generated during infection, and the susceptibility to footrot, on an individual sheep basis. Although antibody titre was correlated with severity and duration of infection, this relationship was not sufficiently strong (r=0.3-0.6) to replace clinical scores as a phenotypic indicator to describe resistance in individual sheep.

Acquired immunity following vaccination with native or recombinant pili preparations is an important tool in the control of footrot. Immunity in this case is reflected by the absence of footrot following challenge, and by the level of antibodies directed against the protective pilus antigen, which is traditionally measured by K-agglutination (EGERTON and MERRITT, 1973). RAADSMA *et al.* (1994b) showed a strong phenotypic relationship between K-agglutinating antibody titre following vaccination, and resistance following challenge. The value of K-agglutinating antibodies in genetic selection for innate resistance is limited given that responsiveness to vaccination is control is under separate genetic control from innate genetic resistance.

The appropriate clinical indicators of resistance in individuals are clinical scores of footrot lesions and K-agglutinating antibody levels following vaccination.

d) Repeatability of resistance

For both clinical assessment of footrot and measurement of K-agglutinating antibody titres, repeatability between and within operators is very high (r>0.9, Raadsma unpublished), demonstrating that experienced operators can make consistent assessment of these two major indicators of resistance to footrot and response to vaccination respectively at any single time point.

As a consequence of the changes in footrot status of individuals following challenge and subsequent vaccination, clinical scores are moderately correlated when inspections are made at 2-3 week intervals (r=0.31-0.70 prior to vaccination, and r=0.02-0.31 after vaccination) (RAADSMA *et al.*, 1993; 1995, showing that timing of inspections are of critical importance in the assessment of footrot, and hence resistance. It is recommended to make a minimum of 2 inspections at least 3 weeks apart during an outbreak of footrot to get a better assessment of footrot in individual sheep.

Using repeated measures of footrot status during an outbreak in the assessment of resistance, has additional advantages in that repeatability models can be used in the estimation of genetic variation and prediction of breeding values. RAADSMA *et al.* (1994a) showed that genetic correlations between footrot status at consecutive inspections were almost unity, thus describing the same genetic trait. Genetic correlations between footrot assessed before and after vaccination within the same outbreak were slightly lower (0.8, RAADSMA *et al.*, 1994a). To adequately quantify resistance over time, repeated assessment of individual sheep may thus be necessary.

Of relevance is also the relationship between method of footrot challenge, and resistance among challenge with different serogroups. Unfortunately relevant data are scarce. RAADSMA *et al.* (1994a) obtained phenotypic, genetic and environmental correlations between resistance following induced and natural challenge, which was (through necessity of experimental design) confounded with serogroup of challenge strains. Phenotypic correlations between the responses to the two challenges were low (<0.10). Low negative environmental correlations (0.0 to –0.14) suggested that some carry-over effects may exist between sheep exposed to repeated challenge. Corresponding genetic correlations were moderate (0.37 to 0.67), suggesting that resistance under different challenge conditions may not be completely the same trait. Further data are necessary to determine if this is due to method of challenge, or if resistance is specific for different serogroups of *D. nodosus*.

Documented genetic variation in resistance to footrot

Although for most major production traits, the extent of genetic variation is reasonably well known, for footrot there is a paucity of information, except for Merinos (EGERTON and RAADSMA, 1991; RAADSMA, 2000).

a) Differences between breeds

Limitations of the available literature describing breed differences in resistance to footrot were identified by EGERTON and RAADSMA (1991), RAADSMA (2000) and will not be covered further. No further additional information of significance has become available since then.

b) Differences between strains and bloodlines

As detailed by EGERTON and RAADSMA (1991), within the Australian Merino breed there is a number of distinct strains and blood-lines within strains. These strains and bloodlines-within-strains vary considerably in major production characteristics (such as fleece weight, fleece length, body weight) and in resistance to fleece rot, and susceptibility to flystrike (ATKINS and McGUIRK, 1979; RAADSMA and ROGAN 1987; MORTIMER , 1987; RAADSMA, 1991a, b,2000). In contrast, there is relatively little variation between strains or between bloodlines within strains for resistance to internal parasites (EADY et al., 1996)

Estimates for differences between major industry bloodlines of Merinos in their susceptibility to footrot are limited (RAADSMA *et al.*, 1994a). One relatively small investigation conducted by Raadsma, Swan, and Purvis (Unpublished) involved 425 wethers from 11 fine- and medium-wool Merino bloodlines after separate exposure to an intermediate and then a virulent isolate of *D. nodosus.* Although no differences between the 11 flocks in resistance to the intermediate isolate was observed, substantial differences were observed following challenge with the virulent isolate. Repeated inspections over a 27-week period, following a challenge protocol similar to that used by RAADSMA *et al*. (1994a), showed that the most resistant flock had 34% of sheep affected with severe footrot (score 3 or score 4) compared with 79% for the most susceptible flock (Fig 4). These results are interesting in that they highlight potential differences between bloodlines in susceptibility to severe footrot, which has not been recorded previously, presumably because in most flocks, managers are actively trying to minimise the expression of footrot.

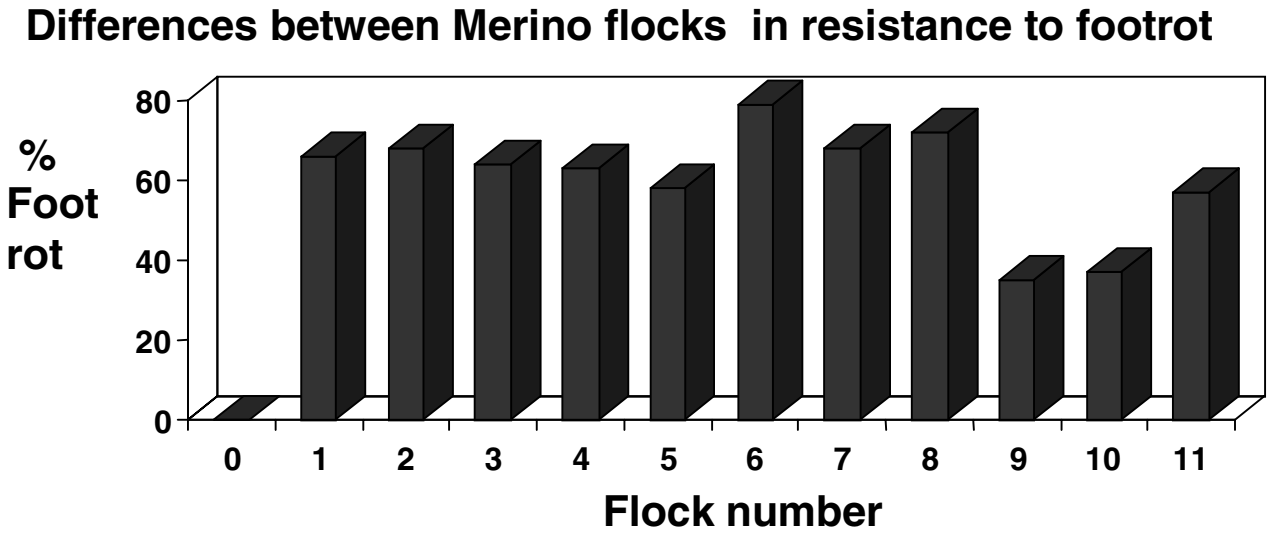

Fig 2. Difference between 11 flocks (1-11) of Merino sheep exposed to virulent footrot (n=425)

WOOLASTON (1993) observed no difference in resistance to footrot in single-trait selection flocks selected for different levels of resistance to *Haemonchus contortus*.

c) Differences between sheep within flocks

The estimation of additive genetic variance (heritability) of resistance to footrot has received relatively little scientific attention by comparison with other important traits in sheep. Early estimates of heritability of resistance to footrot in various breeds including the first major study by (SKERMAN *et al*, 1988) in Corriedale have been summarised by EGERTON and RAADSMA (1991), who also detailed some of the problems associated with traits describing resistance to footrot. Firstly, to diagnose 'footrot' only when underrunning of soft horn occurs, and 'footscald' when only interdigital skin inflammation has been recorded, is erroneous, unless individual intradigital lesions were specifically confirmed to be free from *D. nodosus* infection. Failure to recognise this mars some studies. Secondly, most of the early estimates are from binomial data. In such cases, heritability estimates are dependent on the prevalence of the condition, which means that differences in heritability estimates could reflect differences in prevalence, rather than differences in magnitude of genetic variation. However, it is possible to obtain estimates of the heritability of liability to footrot, independent of prevalence of the condition, through transformation of estimates on the observed scale (FALCONER, 1989) or directly on the underlying scale (GILMOUR *et al*., 1985). The difficulty in studying infectious diseases under uncontrolled conditions was highlighted by WOOLASTON (1993), who reported genetic differences between sire-lines in prevalence and severity of footrot in Merino lambs following natural challenge. However, sire effects were confounded with paddock effects, which were of the same magnitude as the paddock-effects in adult ewes allocated at random to sires.

RAADSMA *et al.* (1994a) reported heritability estimates for eight clinical indicators of resistance to footrot (five describing the extent of clinical signs, and three describing the extent of subsequent healing). Resistance was assessed in 1562 Merino sheep, representing the progeny from 162 sires in four major bloodlines, following exposure to virulent isolates of *D. nodosus* under both an experimental challenge in which footrot was induced, and a separate natural (field) challenge involving a different isolate of *D. nodosus.*. Resistance was assessed on seven occasions following induced challenge, and on five occasions following natural challenge. All sheep were vaccinated with primary and booster injections of an homologous rDNA pilus after initiation of the induced and natural challenge.

Table 1 Heritability estimates for resistance to virulent footrot under both induced and natural conditions based on single inspections or multiple observations during challenge, including observations before and after homologous vaccination.

Timing of inspection for assessment of resistance	Induced	Natural
Single inspections during challenge- before vaccination	0.20 (se 0.06)	0.18 (se 0.06)
Single inspections during challenge- after vaccination	0.07 (se 0.06)	0.09 (se 0.04)
Combined information from multiple observations- before vaccination	0.27 (se 0.07)	0.29 (se 0.07)
Combined information from multiple observations- after vaccination	0.16 (se 0.08)	0.28 (se 0.07)
Adoption of underlying scale of liability to footrot	0.28	0.30

Summarising observations made by RAADSMA et al (1994a) it was concluded:

- Heritability of resistance based on a single inspection were generally lower, then estimates based on multiple inspections during the same challenge.
- Heritability of resistance measured after vaccination is usually lower then heritability of resistance based on inspections before vaccination.
- Heritability for resistance to induced footrot and natural footrot were similar, but the genetic correlations between the two is not 1 (although the type of challenge was confounded with serotype of infection).

- Resistance based on an underlying scale of liability (risk) to footrot shows a moderate heritability (0.25-0.30) indicating that this trait should respond to selection.
- Normal quantitative breeding practices could be adopted to exploit genetic variation in resistance to this disease based on conventional selection and breeding practices [provided that animals were exposed to direct challenge with footrot.

It was concluded that there is substantial genetic variation within flocks of Merino sheep in resistance to challenge with virulent isolates of *D. nodosus*, especially if resistance is assessed on the basis of preferably 3 inspections at 3-week intervals. However this required individuals to be exposed to direct challenge. To circumvent the direct exposure of valuable breeding animals to footrot (RAADSMA et al 1994a) The genetic variability amongst a group Merino sires was expressed as Estimated Breeding Values based on performance of progeny under direct challenge (ie the sires were not exposed, but rather their progeny).

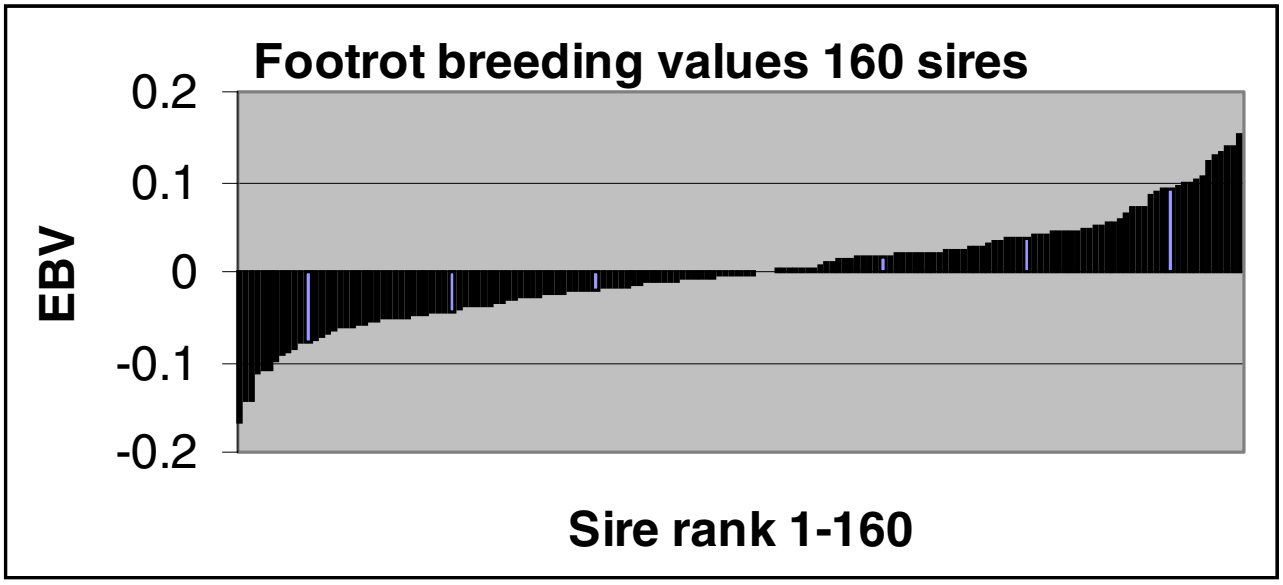

Fig 3 Distribution of estimated breeding values (EBV) for resistance to footrot in 160 sires based on progeny performance testing under direct challenge with virulent footrot. Negative EBV indicate sires with higher resistance, positive EBV indicate sires with lower resistance.

Based on these observations it was shown that sires showed genetic differences in resistance and it would possible to select breeding replacements with high resistance to footrot without direct exposure of valuable breeding individuals to footrot.

SKERMAN (1985) and SKERMAN and MOORHOUSE (1987) reported the development of a bloodline with increased resistance to footrot, in each of the Romney Marsh and Corriedale breeds. Both bloodlines evolved through direct selection under natural outbreaks of footrot and extensive use of sires whose progeny showed increased resistance over their contemporaries. Both studs claim now that footrot is an insignificant problem in their flocks (SKERMAN and MOORHOUSE, 1987; WARREN *et al*., 1990). Although reports of this nature highlight the potential for genetic control of this disease, formal genetic comparisons such as those described by SKERMAN and MOORHOUSE (1987) are needed, but are usually lacking, in on-property experiments. The follow-on benefit of increased usage of breeding stock from more resistant bloodlines in the Merino industry still awaits evaluation, but has already prompted certain stud breeders to place heavy selection pressure on resistance (PATTERSON and PATTERSON, 1989, 1991).

4 Genetic markers for resistance and vaccine responsiveness

The option of exploiting genetic differences in footrot resistance through direct selection is of limited practical value, as it requires challenging all animals before selection. The possibility of using indirect selection strategies is therefore appealing. The limited utility of serological responses as indirect selection traits was discussed above. No other physiological responses have been identified which show potential as indirect selection criteria (O'MEARA and RAADSMA, 1995). Other options for indirect selection strategies include the use of genetic markers linked to resistance genes. The role of the major histocompatibility complex (MHC) in modulating immune responses and subsequently disease resistance is well documented for a number of species. MHC gene products are glycoproteins which are present on the surface of some cells, and are divisible into two types, Class I and Class II histoglobulins. Genetic polymorphism within both the Class I and Class II regions has been investigated in relation to innate resistance to footrot, and response after vaccination with *D. nodosus* antigens (OUTTERIDGE *et al.,* 1989; LITCHFIELD *et al.,* 1993; ESCAYG *et al*., 1997; Raadsma and Stear, unpublished data). Overall, the conclusion is that associations between resistance/antibody-response and MHC polymorphism are not sufficiently strong or consistent to justify their application in the field. Obviously,, the search for suitable markers should be extended to other regions within (Class III) or outside the MHC. The use of genome-wide screens with high-density coverage of polymorphic microsatellite markers in crosses between resistant and susceptible populations (breeds or selection lines), as conducted by Crawford *et al*. (pers communication), may provide evidence for major genes which affect resistance to footrot. Identification of such major genes may then open the possibility to use marker-assisted introgression, or marker-assisted selection within flocks.

RAADSMA *et al*. (1998) reported preliminary findings from genome screens in resource flocks held by Crawford, McEwan, and colleagues at AgResearch (NZ), in relation to response to vaccination with *D. nodosus* antigens. The results suggested that a region in the MHC plays a role in regulating serogroup-specific responses, and a region within chromosome 1 contributes to variation in generalised vaccine response. Further studies will identify the chromosomal regions, and, where possible, specific genes, which affect vaccine responsiveness.

5 Resistance and other breeding objectives

Should it prove to be feasible to improve resistance to footrot through selective breeding, it is unlikely to be the sole breeding objective in any well-designed programmes. It is important, therefore, to have accurate information on the correlations between resistance to footrot and all the major production traits which are recommended as breeding objectives and/or selection criteria for sheep and wool production. In high-rainfall areas, resistance to other important diseases such as flystrike and internal parasites may also need to be considered.

No published estimates of phenotypic or genetic correlations between resistance to footrot and production traits are available. RAADSMA *et al*. (unpublished) obtained such estimates in the study described above (RAADSMA *et al*.,1993; 1994c). Estimates of genetic correlations between resistance and production were obtained for production traits both under challenged and non-challenged conditions, to account for the environmental influence of disease on production performance. The results indicate no strong undesirable genetic correlations. In fact, all estimates of correlations between the important production traits (clean fleece weight and mean fibre diameter) were neutral (range –0.1 to +0.2). These data suggest that selection for important production traits will have no adverse or desirable effect on resistance to footrot. Similarly, selection for increased resistance to footrot will not adversely affect important production traits, and there

should be sufficient scope to improve production and resistance simultaneously, albeit at slower rates than if either objective was taken as a sole breeding objective.

6 Resistance to other diseases

The question of broad-based resistance(resistance to multiple diseases) is relevant here, since the important diseases in sheep production are often influenced by common environmental factors. RAADSMA *et al*. (1997) reported a unique study, where resistance to all important diseases that affect production was examined in the same flock under the same environmental conditions. Genetic variation for resistance to each of the disease existed within the flock, but genes conferring resistance to one disease do not, in general, have any effect on resistance to another disease – the genetic correlations between resistance to different diseases were low. The only possible exception was a moderate (undesirable) genetic correlation between resistance to fleece rot (a major predisposing factor to blowfly strike) and resistance to footrot.

The observation on a neutral genetic correlation between resistance to footrot and resistance to internal parasites confirms earlier observations by WOOLASTON (1993) who reported a neutral genetic correlation (0.02 ±0.20) between resistance to footrot and resistance to a major internal parasite in sheep, namely *Haemonchus contortus*. Similarly, GRAY *et al.* (1991) did not observe significant differences in K-agglutinating antibody levels following vaccination with a whole-cell *D. nodosus* vaccine, in flocks with various levels of resistance to *Haemonchus contortus*.

It is likely that breeding programmes aimed at resistance to multiple diseases will need to consider each relevant disease separately. It may be feasible to exploit and combine resistance to multiple diseases, including footrot, from different flocks which have been selected specifically for resistance to just one disease. This type of breeding exercise would be greatly assisted by gene markers.

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