RESPONSES TO SELECTION FOR DISEASE RESISTANCE IN SHEEP AND CATTLE IN NEW ZEALAND AND AUSTRALIA

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SUMMARY
Direct responses to selection are reviewed from 12 sheep and 3 cattle experiments in New Zealand and Australia, where the primary trait was resistance (R) or susceptibility (S) to "disease". Apart from three single generation experiments, the life of the remaining experiments averaged 14.9 years to 1997 inclusive. Single-record heritability, from the base population or from a restricted maximum likelihood analysis of all years and all flocks/herds in each experiment, averaged 0.28. This was no lower than for production traits such as milk yield, body weight or fleece weight. Direct responses (on a transformed scale) between R and control lines, or between S and control lines, averaged 0.085 phenotypic standard deviations per year, higher than corresponding responses (0.065 units) in cattle selection studies of weight or gain or efficiency, reviewed by Mrode (1988). Absolute rates of direct response may depend on the mean incidence of disease in the control, and on overall fitness. The ultimate rate of response in an R line may diminish as the line reaches fixation or as phenotypic variation is reduced, or both. Major genes have been implicated for resistance or susceptibility to three different disease traits. In most cases the disease selection lines are also providing a resource for studies of the underlying causes of resistance/susceptibility.

Keywords: Selection-response, resistance, disease, sheep, cattle

INTRODUCTION
Studies of the genetics of disease resistance have become more common in the last decade, usually beginning with paternal half-sib estimates of heritability ($h^2$), then followed by estimates of genetic correlations or by selection studies using single traits or selection indices. This review summarises responses to selection for disease resistance in sheep and cattle in New Zealand and Australia. The "diseases" include endo- and ecto-parasitic challenges, bacterial and mycotoxic challenges, and a metabolic challenge (in the case of bloat). For nematode parasites the contrast in this review is made between faecal egg count (resistance to infection) and productive ability whilst parasitised (resilience).

Background. In practice, incentives to apply genetic principles to disease traits result from - 1. a realisation that the breeding objective is often incomplete without a disease trait(s), 2. the increasing cost or the decreasing availability of effective management strategies and drug therapies, 3. ethical concerns about continuing to treat animals with drugs, although with perhaps equal ethical concerns to minimise the suffering experienced by diseased animals, and 4. increasing consumer preferences for food products from animals maintained in 'chemical free' or minimal drug environments.
Previously, Morris (1991) reviewed 23 $h^2$ estimates for resistance to 15 diseases of sheep and cattle in New Zealand and Australia, and found an average value of 0.31, which is no lower than for, say, milk yield or body weight. This report concentrates mainly on realised heritability estimates and also examines both the symmetry and persistence of the response.

RESULTS

Challenge methodology. For a heritable disease trait, planning a selection experiment is more complicated than selecting for a trait such as body weight, for a number of reasons:

1. a challenge test has to be set up, and planned in such a way that all animals under test receive an equivalent challenge;
2. use of a natural or artificial challenge? The former can be less predictable in terms of the severity of challenge, but with it the experimenter does not need to demonstrate that the artificial challenge provides a reasonable simulation of the natural challenge;
3. there are ethical concerns about knowingly challenging animals with a disease; these concerns have to be balanced against the good which potentially will follow in the rest of the animal population after the resistance genes are multiplied or the selection practice is widely adopted;
4. finding a method of ranking the challenged animals on a continuous scale, so as to increase the effective heritability, rather than on a binomial scale (i.e. affected or not);
5. if a divergent pair of selection lines is established (which is expected to provide double the rate of divergence of a resistant line from a control), a method of treating affected susceptible-line animals must be found, sufficient to allay ethical concerns, and sufficient to enable the most susceptible animals to breed and produce viable offspring. With an artificial challenge, it may also be necessary to protect susceptible-flock animals from unintended natural challenge, before and after the experimental test.

Direct responses. Estimates of direct responses to selection for disease resistance/susceptibility are given in Table 1, with results standardised in phenotypic standard deviation units ($\sigma_p$). For 12 multigeneration studies, selection was applied for an average of 14.9 years, and all but two are still continuing. Flock/herd sizes were most commonly around 100 females per line. Three other experiments, selection for resistance to facial eczema in dairy cattle, to dermatophilosis in sheep and to ticks in beef cattle, were run for one generation each. It is notable how little work is being done in dairy cattle. The $h^2$ estimates for single records ranged from 0.13 to 0.45, with an unweighted mean of 0.28. Some of the traits and animal resources were the same as those cited by Morris (1991) where the average value was 0.31. Generally the estimates in Table 1 were animal model values whereas in the earlier review they were sire model estimates. Average divergences in selection response achieved between the resistant (R) and susceptible (S) lines, or between the R and control (C) lines are also given in Table 1, with the number of years of data analysed shown in brackets. For the New Zealand experiments, this involved including the 1995 or 1996 birth year, even though these results may have been later than the most recent published trial design and $h^2$ estimates. Results for 12 experiments (excluding single year/generation experiments)
Table 1 Summary of direct selection responses in New Zealand (NZ) and Australian (AUS) sheep and cattle studies\(^A\)

<table>
<thead>
<tr>
<th>Trait</th>
<th>Species</th>
<th>Breed</th>
<th>Years</th>
<th>Lines</th>
<th>Size</th>
<th>Difference</th>
<th>(h^2)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faecal egg count</td>
<td>Sheep, NZ</td>
<td>Romney</td>
<td>1979-P</td>
<td>R,C,S</td>
<td>100</td>
<td>1.95(18)</td>
<td>0.28±0.05</td>
<td>Morris et al. (1997b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Romney</td>
<td>1985-92</td>
<td>R,C,S</td>
<td>100</td>
<td>0.86(8)</td>
<td>0.34±0.05</td>
<td>Morris et al. (1997b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perendale</td>
<td>1986-P</td>
<td>R,S</td>
<td>90</td>
<td>1.27(10)</td>
<td>0.28±0.05</td>
<td>Morris et al. (1997b)</td>
</tr>
<tr>
<td></td>
<td>Sheep, AUS</td>
<td>Merino H(^B)</td>
<td>1977-P</td>
<td>R,C,S</td>
<td>110</td>
<td>1.83(15)</td>
<td>0.29±0.03</td>
<td>Woolaston &amp; Piper (1996)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Merino T(^B)</td>
<td>1975-P</td>
<td>R,C,S</td>
<td>100</td>
<td>2.19(22)</td>
<td>0.38±0.04</td>
<td>Woolaston &amp; Eady (1995)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Merino</td>
<td>1988-92</td>
<td>R,S</td>
<td>100</td>
<td>0.82(5)</td>
<td>0.42±0.14</td>
<td>Cummins et al. (1991)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Merino</td>
<td>1988-P</td>
<td>R,C</td>
<td>700,100</td>
<td>0.40(8)</td>
<td>0.28±0.05</td>
<td>Greeff &amp; Bisset (1996)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Romney</td>
<td>1994-P</td>
<td>R,C</td>
<td>70</td>
<td>0.43(2)</td>
<td>0.14±0.03</td>
<td>Morris &amp; Bisset (1996)</td>
</tr>
<tr>
<td>Resilience(^C)</td>
<td>Sheep, NZ</td>
<td>Romney</td>
<td>1975-P</td>
<td>R,C,S</td>
<td>120</td>
<td>2.34(22)</td>
<td>0.45±0.05</td>
<td>Morris et al. (1995b)</td>
</tr>
<tr>
<td>Facial eczema</td>
<td>Sheep, NZ</td>
<td>Romney</td>
<td>1990</td>
<td>R,S</td>
<td>-</td>
<td>0.41</td>
<td>0.31±0.10</td>
<td>Morris et al. (1991a)</td>
</tr>
<tr>
<td>Ryegrass stagsE</td>
<td>Cattle, NZ</td>
<td>Jersey</td>
<td>1993-P</td>
<td>R,S</td>
<td>100</td>
<td>0.86(4)</td>
<td>0.13±0.05</td>
<td>Morris et al. (1995a)</td>
</tr>
<tr>
<td>Bluet</td>
<td>Sheep, NZ</td>
<td>Romney</td>
<td>1973-P</td>
<td>R,S</td>
<td>30</td>
<td>1.20(23)</td>
<td>0.19±0.04</td>
<td>Morris et al. (1997a)</td>
</tr>
<tr>
<td>Bodystrike(^E)</td>
<td>Sheep, AUS</td>
<td>Merino</td>
<td>1974-P</td>
<td>R,S</td>
<td>175-100</td>
<td>0.26(15)</td>
<td>0.26±0.12</td>
<td>Raadsma (1991)</td>
</tr>
<tr>
<td>Dermatophilosis</td>
<td>Sheep, AUS</td>
<td>Merino</td>
<td>1985-86</td>
<td>R,S</td>
<td>-</td>
<td>0.25</td>
<td>0.13±0.05</td>
<td>Lewer et al. (1987)</td>
</tr>
<tr>
<td>Cattle ticks</td>
<td>Cattle, AUS</td>
<td>AIS(^D)</td>
<td>1967-70</td>
<td>R,S</td>
<td>-</td>
<td>0.83</td>
<td>0.39</td>
<td>Utech et al. (1978)</td>
</tr>
</tbody>
</table>

\(\text{P} = \) Present year (1997); \(\text{R} = \) Resistant, \(\text{C} = \) Control, \(\text{S} = \) Susceptible; difference in selection response (on the transformed scale, if used) is between the extreme lines over the years shown in brackets, in phenotypic SD units; \(\text{size} = \) average flock/herd numbers per line (size is not given in single year or single generation tests); \(h^2 = \) single-record heritability, from the base population or from a REML analysis of all years and all flocks/herds in the experiment.

\(H = \) Haemonchus lines, where \(R = \) Increased resistance to \(Haemonchus\) (IRH), \(C = \) Control \(Haemonchus\) (CH) and \(S = \) Decreased resistance to \(Haemonchus\) (DRH); \(T = \) Trichostrongylus lines (data: Woolaston, R.R. & Windon, R.G. pers. comm. 1997).

\(B = \) High resilience = high productivity (post-weaning growth) and low dags, during extended period of parasitic challenge.

\(FJ = \) Friesian-Jersey synthetic; \(\text{AIS} = \) Australian Illawarra Shorthorn.

\(\text{Bodystrike and fleece rot: either or both traits in various years (artificial and/or natural challenge); } h^2 \text{ here was from a random-bred flock, and was on the observed scale, whereas } h^2 \text{ for liability on the underlying scale was } 0.54\pm0.25.\)
showed an average divergence (C-R, or S-C) accumulated over time of 0.71 $\sigma_p$, assuming symmetry between R and S responses. On an annual basis, the average divergence of selection line from control line was 0.085 $\sigma_p$/year, again assuming symmetry. For comparison Mrode's (1988) review of 29 growth-rate, weight-for-age and efficiency selection experiments in cattle found a mid-parent selection differential averaging 0.213 $\sigma_p$ per year. Combining this with realised $h^2$ estimates in cattle averaging 0.304 (Koch et al. 1982) led to a mean realised response of 0.065 $\sigma_p$/year. These estimates for both disease and growth traits do not necessarily indicate maximal achievable rates of response because the selection lines have generally been used at the same time as resource flocks for studies of the underlying biology. Parallel studies can affect selection intensities (especially among males) and also the numbers of females available for the next mating year. In many cases, flock or herd sizes were small, and mating restrictions were applied to reduce early inbreeding rates, which also meant reduced rates of progress. However, if selection intensity averaged 1.0 (about 2 in males and close to zero in females) and $h^2 = 0.28$, an expected annual response would be 0.08$\sigma_p$ if the generation interval was say 3.5 years, compared with 0.085$\sigma_p$ from Table 1 data.

The range of divergences across experiments also reflects the wide initial screening used in some experiments, whereas others used only a single flock/herd as the base. Absolute rates of direct response and $\sigma_p$ may both depend on the mean incidence of disease in the control. The ultimate rate of response in a resistance line may diminish as the line reaches fixation or as $\sigma_p$ declines, or both. Nevertheless, responses across experiments appear to have been encouragingly high. For the traits in Table 1, major genes have been implicated in three cases (out of eight “diseases”), i.e. FEC, bloat and cattle ticks, as detailed below.

**Symmetry.** In cases where there were R, C and S lines, the symmetry of response could be tested. For the New Zealand faecal egg count (FEC) lines measured on the log transformed scale, the S flocks diverged at 0.71 times the rate achieved in the R flocks (Morris et al. 1997b), and similar results have been observed in the Australian FEC (Haemonchus) lines (Eady, S.J. pers. comm. 1997). Asymmetry in the New Zealand Romney FEC lines was explained by a 9.8% higher net reproductive rate and by a 22% higher selection differential in the R than the S line (Morris et al. 1997c). Asymmetry, with the same probable explanations, also occurred in the facial eczema lines of sheep (Morris et al. 1991b, 1995b). Additionally, the $h^2$ estimates tended to be higher in the R than S facial eczema flocks. For the bloat herds, breeding value estimates in the absence of a control line showed that the responses were greater in the S herd than in the R herd; there was no difference in net reproductive rate (Morris et al. 1995c), but the presence of a putative major gene (recessive for susceptibility) and a lower $h^2$ in the R line led to the asymmetry (Morris et al. 1997a).

**DISCUSSION**

**Individual disease traits.** *Internal parasites.* Experimental selection to reduce FEC has been successful in New Zealand and Australia. However, this trait (resistance to nematode infection) is in reality only a component of host resistance to parasite-induced disease. Other factors include immunological responses to the parasites which succeed in infecting the host,
and the interplay between host infection and the subsequent pasture contamination, which continues the life cycle of the parasite. Bisset et al. (1996) have documented the immunological responses of the New Zealand Romney FEC lines. For production traits in the Romney and Perendale FEC lines, the R line had lower fleece weight, similar live weights of lambs and higher dag scores (breech soiling) than the corresponding S line (Morris et al. 1997b). In contrast the paternal half-sib genetic correlation estimates of FEC with live weight or with fleece weight were near zero for Merinos in Australia (Eady et al. 1994) and for Coopworths in New Zealand (McEwan et al. 1995). An alternative approach to selection for reduced FEC is now being tested in New Zealand, namely selecting for increased productivity under nematode challenge (formerly known as ‘resilience’). With low $h^2$ estimates for various traits contributing to productivity under challenge (0.10 to 0.19), initial screening from a large population and then progeny testing have been used for selection (Morris & Bisset 1996), and a response in the R over the C flock of 0.43 $\sigma_p$ has been achieved in the first two years. So far, a selection index has been used with equal weights for one genetic standard deviation of post-weaning gain and of dag score (with a minus sign between them). The breeding values for gain and dag score are based on heritability estimates of 0.16±0.02 and 0.32±0.02, respectively. ‘Resilience’ and FEC have a genetic correlation which is not significantly different from zero, under the New Zealand challenge conditions.

The selection-line differences in FEC (Table 1) were estimated from transformed data, using the loge or cube root values. Where FEC of one line was only reported as a percentage of that in the other line, the difference for Table 1 was calculated using logs, and assuming a $\sigma_p$ of 0.85. As selection response advanced, the percentage difference between lines in some experiments widened quickly; for example from the experiment of Greeff et al. (1995), the selection-line differences from controls were 0.12 and 0.40 $\sigma_p$ in 1994 and 1995 respectively. Selection for divergence in FEC has been equally successful using a natural mixed-species challenge on pasture (as is common in New Zealand) or following single-species artificial challenge (as is common in Australia). For the CSIRO Trichostrongylus lines, similar $h^2$ values have been obtained from artificial challenges applied under pasture conditions or to worm-free sheep in pens (Woolaston, R.R. & Windon, R.G., pers. comm. 1997).

Searches for a major gene for resistance/susceptibility to nematode infection in New Zealand sheep have led to the hypothesis that a major gene is segregating which is recessive for resistance or low FEC (McEwan et al. 1997). This was identified using a mixed inheritance model (Janss et al. 1995), applied independently to data from Romney, Perendale and Coopworth research flocks. The common ancestral breed is the Romney, which could account for the gene segregating in all three breeds.

**Facial eczema.** The facial eczema selection lines of sheep currently provide animal resources for attempting to understand the underlying biology of this type of resistance. The challenge involves a fungal toxin, sporidesmin, ingested from autumn pastures. Grazing cattle are more resistant than sheep, but they still show heritable variation in response to challenge, measured as log (serum gamma-glutamyltransferase). As with FEC in sheep,
there is no obvious sign of a selection plateau in R or S sheep facial eczema lines, after two decades of selection.

Ryegrass staggers. Another fungal toxin, lolitrem B, leading to metabolic disease in grazing ruminants, is the cause of ryegrass staggers in New Zealand. Some of the same metabolic pathways of detoxication in the ruminant may be common to ryegrass staggers and facial eczema, because a genetic correlation of 0.30 has been estimated between them (Morris et al. 1995a). Unlike facial eczema where an artificial challenge is used, natural challenge with a 0 to 5 or a binomial scoring system is used for ryegrass staggers with repeated measures. In Table 1, binomial scores were used for this trait, and $\sigma_p$ was calculated from the mean. On an absolute scale, there was a large apparent selection-line difference of 55.6 percentage points in incidence by year 4 ($P<0.001$), in spite of a low heritability.

Bloat. Susceptibility to (clover-dominant) pasture bloat is scored on a 0 to 4 scale, with successive records obtained during repeated days of natural pasture challenge (and with days of non-potent challenge excluded by setting a lower threshold mean score for animals from the high susceptibility herd) (Morris et al. 1997a). Using this system, bloat score has a single-record $h^2$ in Friesian-Jersey crosses of 0.19±0.04 and a repeatability of 0.44±0.02. Response in the susceptible direction is still continuing after 23 years, with the within-line $h^2$ remaining similar and repeatability only falling to 0.32±0.05. However, the response to selection for reduced susceptibility plateaued in about 1984, with low $h^2$ and $\sigma_p$, suggestive of a major gene which is recessive for susceptibility. A two-allele autosomal mixed inheritance model (Janss et al. 1995) was able to account for 80% of the genetic variance. Using an alternative trait, maximal bloat score per animal, we were led to similar conclusions, with 83% of the genetic variance accounted for by the major gene.

Bodystrike. Susceptibility to flystrike, particularly body strike, is a major problem under extensive grazing in Australia. Dermatophilosis and fleece rot are intimately linked to its development. In experimental work, providing animals with a uniform challenge for body strike is difficult because, under natural conditions, it depends on weather conditions and fly populations. Raadsma (1991) has estimated a value of 0.26±0.12 for $h^2$ from a random-bred multiple-bloodline Merino flock. A pair of divergent lines of sheep was established at Trangie in 1974 and has continued until now under the control of various scientists, who have taken a variety of approaches. This includes natural or artificial challenge, and direct or indirect selection (body strike or fleece rot), so that the response recorded is the result of a combination of selection processes. Analyses of realised response and $h^2$ for natural body strike are currently being made for 15 years of divergent selection, with a preliminary divergence estimate of 0.26o (Mortimer, S.I. pers. comm. 1997). The related disease, dermatophilosis, which results from an invasion of the skin of sheep by a bacterium Dermatophilosis congolensis, causes scabby inflamed areas and leads to solid, lumpy projections in the wool. A Western Australian study involved screening ewe and ram lambs from 8 farms, artificial challenge, and a one-generation (2-year) breeding programme for divergence in dermatophilosis susceptibility. This led to an 11% difference ($P<0.01$) in
progeny response to one form of artificial challenge, although the $h^2$ was low at $0.11 \pm 0.05$ to $0.14 \pm 0.05$ on days 5 to 9 after challenge (Lewer et al. 1987). Some of the same analytical problems were encountered in this project as with ryegrass staggers (described above), with a binary trait, an apparent low $h^2$ when measured on this scale, but a significant response.

**Cattle ticks.** Genetic resistance of cattle to the tick, *Boophilus microplus*, was demonstrated in the 1970s and a direct selection response to artificial challenge was achieved in Australian Illawarra Shorthorns by Utech et al. (1978). The one-generation response shown in Table 1 was calculated assuming an $h^2$ of 0.39 for log (tick count). Assuming also a repeatability of 0.5 or 0.6 to derive $\sigma_p$ from the error mean square, the response was 0.83 or 0.91 $\sigma_p$ units, respectively. Further work in Queensland in other breeds and crosses at CSIRO (Belmont) has now culminated with the demonstration in interbred *Bos taurus* cattle (Hereford-Shorthorns) that a major gene is segregating (Kerr et al. 1994). The gene is dominant for resistance, expressed early in life, and leads to absolute or extremely high resistance to ticks.

**Footrot.** Egerton & Raadsma (1991) have reported a paternal half-sib $h^2$ estimate of $0.18 \pm 0.10$ for footrot in Australian Merinos, based on response to a vaccine challenge. They also found genetic variation in subsequent response to the disease. In New Zealand Romneys Skerman et al. (1988) reported $h^2$ estimates of footrot score ($0.14 \pm 0.03$) and liability to footrot (0.28). Selection lines (125 ewes per line) were established in 1993 with Merinos by Raadsma (pers. comm. 1997), i.e. R and C lines based on semi-natural challenge, and two lines (alongside a Control) for response to vaccination. Response estimates have yet to be reported.

**Conclusions.** Large direct responses to experimental selection have generally been found for disease traits. Percentage response depends somewhat on the control mean, and thus on the degree of artificial challenge applied (or on the length and degree of natural challenge applied). In industry, actual responses will depend on relative emphases on disease and production. A major gene has been hypothesised for three diseases. Identifying a marker on the gene in these cases would provide sire breeders with opportunities to screen their flock/ herd for presence of the desirable allele, if indeed the major gene segregation is widespread.

**REFERENCES**


