MODELLING GENETIC AND EPIDEMIOLOGICAL RELATIONSHIPS BETWEEN PRODUCTIVITY AND NEMATODE INFECTION IN LAMBS

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SUMMARY
A model is presented which enables genetic relationships between productivity and resistance to nematode infection in lambs to be modelled, and epidemiological effects arising from the host genotype to be quantified. Moderate, favourable relationships between resistance and productivity are predicted, with the disease epidemiology affecting these relationships as well as responses to selection.
Keywords: Sheep, genetics, nematode infection, epidemiology, productivity

INTRODUCTION
Incorporating resistance to infectious diseases into breeding plans poses a unique challenge for animal breeders, as an interaction inevitably exists between the genetic resistance of the host population and the epidemiology of the disease. This interaction will affect the relative importance given to the disease resistance trait, which will change as the host genotype changes, as well as the expected responses to selection.

Demonstration of how responses to selection for resistance to an infectious disease may be greater than predicted by quantitative genetic theory is given by Bishop and Stear (1997) for nematode infection in lambs. Growing evidence (Woolaston *et al.* 1996; Bishop *et al.* 1996; Morris *et al.* 1997) suggests that genetic selection for resistance to this infection is a useful supplement to existing control strategies. However, effective incorporation of such selection into breeding schemes requires an understanding of epidemiological relationships between resistance and productivity, in addition to the genetic parameters describing these relationships. Currently, the epidemiological effects are unknown and published estimates of genetic relationships between resistance and productivity are variable.

This paper addresses genetic and epidemiological relationships between productivity and resistance to nematode infection in lambs. We incorporate productivity and production losses into the model described by Bishop and Stear (1997), giving a framework for predicting genetic relationships between resistance and productivity. This model is then used to explore epidemiological effects of host genotype for resistance on productivity.

MATERIALS AND METHODS
Consider an unselected flock of grazing lambs. Nematode infections will reduce the rate

of live weight gain, due to decreased appetite and decreased efficiency of utilisation of metabolisable energy and protein. Additionally, production losses are associated with the intake of larvae *per se* (McAnulty *et al.* 1982), presumably due to the consequences of the immune response. Therefore, observed growth rate is the sum of potential growth rate on uncontaminated pastures and production losses due to infection – a function of cumulative worm burden and cumulative larval challenge (Leathwick *et al.*1992).

Nematode infections in lambs were stochastically modelled by Bishop and Stear (1997), defining host/parasite interactions for individual animals. In this model, food intake varies between animals and increases with age, as does acquired immunity. Larval intake and faecal output are modelled as functions of food intake. *Establishment* of larvae, *fecundity* of adult female parasites and parasite *mortality* are defined as repeatable and heritable host traits. Additionally, density dependent control of *fecundity* is modelled.

The model of Bishop and Stear (1997) was extended to examine genetic and epidemiological relationships between resistance, growth rate and production losses. Individual animal growth rate and production losses were modelled as described above, with worm mass defined as the product of worm number and worm size. Production losses were estimated from Coop *et al.* (1985 and 1985), where continual infection reduced growth rate by 25%, and regular anthelmintic treatment restored 30% of this loss. Penalties applied to cumulative larval intake and cumulative worm mass were modified from those given by Leathwick *et al.* (1992) and rescaled so that the desired average production losses were achieved. Benchmark productivity values were 40 kg live weight at 6 months in the absence of infection, 33 kg for lambs grazed on infected pastures but drenched at 3, 4 and 5 months. This model implicitly creates genetic relationships between resistance and growth rate, without having to explicitly define such relationships.

The model was firstly run for unselected animals in one season. The parasitological parameters given by Bishop and Stear (1996) were assumed, except that the h^2 for worm fecundity was 0.5 (from Stear *et al.* 1997) and moderate density dependent effects were assumed. Food intake and growth rate, in the absence of infection, were given h^2s of 0.2, repeatabilities of 0.35, CVs of 0.2 and 0.1 and a correlation (rg and rp) of 0.5. Genetic and phenotypic correlations between faecal egg count (FEC) and productivity were then estimated from the output data across 10 replicates, assuming a population size of 10000 lambs. The effects of different combinations of input parameters and penalty functions on productivity were investigated by this means.

Epidemiological effects on productivity following selection were investigated by imposing selection for reduced FEC on a modelled flock of 1000 sheep over a 10 year period. Carry-over effects between years of pasture larval contamination were set to be zero or complete (Bishop and Stear, 1997). Twenty replicates were run for each scenario.

RESULTS AND DISCUSSION

For unselected animals, FEC and live weight at 6 months of age had a mean h^2 of 0.29 and 0.17, respectively, and genetic and phenotypic correlations of -0.27 (s.e. 0.07) and -0.10. Resilience, i.e. performance loss, had a mean h^2 of 0.38. The influence of the level of pasture contamination on some of these parameters is shown in Table 1. The upper limits to the genetic and phenotypic correlations are the values which would be observed if all the between-animal variation in live weight was due to the effects of the infection, i.e. they are the negative values of the correlations between performance loss and FEC. Increasing pasture contamination decreased live weight gain and it also strengthened the observed negative relationships between performance and FEC. Thus, altering the environment and the epidemiology of the infection alters the genetic relationships.

Table 1. Effect of pasture larval contamination levels on genetic relationships between productivity, i.e. live weight (kg) and faecal egg count

Relative pasture contam.:	Quarter	Half	Benchmark	Double	Quadruple
Live weight mean	37.3	35.8	33.4	29.4	22.50
Observed rg	-0.16	-0.20	-0.27	-0.34	-0.40
Observed rp	-0.07	-0.08	-0.10	-0.12	-0.14
Upper limit: rg	-0.65	-0.60	-0.55	-0.48	-0.41
Upper limit: rp	-0.32	-0.28	-0.24	-0.20	-0.16

Shown in Table 2 are the effects of altering the relative balance of live weight gain penalties arising from worm mass and larval challenge, at a constant overall impact on performance. This has a dramatic effect on the observed and the upper limit correlations: the greater the relative penalty applied to worm mass the stronger the negative relationship between performance and FEC. If the parasite effect results mainly from the consequences of larval challenge then no correlation between FEC and performance is detectable, despite the fact that mean flock performance is considerably reduced.

Table 2. Effect of relative magnitudes of worm mass penalty compared to the larval intake penalty, on genetic relationships between productivity and faecal egg count

Relative worm mass penalty:	Zero	Half	Benchmark	x 1.5	Complete
Live weight mean	33.4	33.4	33.4	33.4	33.4
Observed rg	-0.02	-0.15	-0.27	-0.37	-0.46
Observed rp	-0.02	-0.06	-0.10	-0.13	-0.16
Upper limit: rg	-0.04	-0.28	-0.55	-0.71	-0.80
Upper limit: rp	-0.04	-0.13	-0.24	-0.30	-0.33

These results pertain to moderate density dependent effects. Increasing the density dependent effects buffers the worm population following anthelmintic treatment, increases weight loss and strengthens the correlation between FEC and performance.

Altering the correlation between food intake and gain has only a trivial effect on these relationships. Increasing the absolute penalties on worm mass and larval challenge, i.e. altering mean resilience, increases productivity loss and stengthens the observed correlations of performance and FEC, but does not alter the upper limit correlations.

The effects of selection for reduced FEC on liveweight are shown in Table 3, for cases of no carry-over and complete carry-over of pasture larval contamination between years. Selection results in immediate responses in live weight gain which are larger than those predicted by quantitative genetic theory – the predicted change in year 1 in live weight is 0.45kg, compared to an observed value of 0.66 (±0.04) kg. Subsequently, correlated responses in live weight depend on the assumptions made about how larval contamination relates to the previous year's contamination, i.e. grazing management and climate. Thus, the epidemiology of the infection profoundly affects correlated responses in performance.

Table 3. Effect of selection for reduced faecal egg count on 6 month live weight (kg)

Year:	0	1	2	5	10
Live weight (no larval carry-over)	33.4	34.0	34.3	35.1	35.8
Live weight (complete carry-over)	33.4	34.0	35.2	38.3	39.9

In summary, assuming an infinitessimal model and absence of pleitropy, the correlation between productivity and resistance (i.e. FEC) is expected to be moderate and favourable, with genetic correlations stronger than phenotypic. The correlations change as the level of infection or larval challenge changes, and the between-animal relationship is independent of the average effect of infection on productivity. Epidemiological effects ensure that responses in live weight, when selecting on FEC, are greater than expected. Incorporating these effects into practical breeding schemes remains a challenge.

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REFERENCES

Bishop, S.C., Bairden,K, McKellar,Q.A., Park,M., Stear,M.J.(1996)*Anim.Sci.* **63:**423-428.

Bishop, S.C and Stear, M.J. (1997) *Anim. Sci.* **64:**469-478.

Coop, R.L., Sykes, A.R. and Angus, K.W. (1982) *J.Agr. Sci.,Camb.* **98:**247-255.

Coop, R.L., Graham, R.B., Jackson, F., Wright, S.E. and Angus, K.W. (1985) *Res. Vet. Sci.* **38:**282-287.

Leathwick, D.M., Barlow, N.D. and Vlassof, A. (1992) *Int. J.Parasit.* **22:**789-799.

McAnulty, R.W., Clark, V.R., Sykes, A.R. (1982). Proc.N.Z.Soc.Anim.Prod. **42:**187-188.

Morris, C.A., Vlassoff, A., Bisset, S.A., Baker, R.L., West, C.J. and Hurford, A.P. (1997) *Anim. Sci.* **64:**319-329.

Stear, M.J., Bishop, S.C., Bairden, K., Dunca, J.L., Gettinby, G., Holmes, P.H., McKellar, Q.A., Park, M., Strain, S. and Murray, M. (1997) Nature, In Press.

Woolaston, R.R. and Piper, L.R. (1996) *Anim. Sci.* **62:**451-460.