AN INVESTIGATION INTO GENETIC ASPECTS OF RESISTANCE OF MERINO SHEEP TO FOOTROT

H.W. RAADSMA[a], J.R. EGERTON[a], P.M. OUTTERIDGE[b], F.W. NICHOLAS[c], S.C. BROWN[c], M. CURTIS[a] and A.M. LITCHFIELD[c]

[a] Department of Animal Health, University of Sydney, Camden NSW 2570
[b] McMaster Laboratories, CSIRO, Division of Animal Health, Glebe NSW 2037
[c] Department of Animal Husbandry, University of Sydney, Sydney NSW 2006

INTRODUCTION

Ovine footrot is a contagious disease of considerable economic significance in all major sheep production countries worldwide. The disease results from a chronic mixed bacterial infection which is confined to the epidermal tissues of the interdigital skin and horn of the hoof. The importance of the causal bacterium Bacteroides nodosus and the synergistic effect of Fusobacterium necrophorum in mixed infections is now well documented (Egerton et al 1989).

Despite progress in treatment, control and prevention measures, eradication of the disease is difficult on a large scale, and constant inputs are required to minimise the expression of the disease. Production losses and lost market opportunities make footrot the most serious contagious disease of sheep in Australia today.

One option which has not been described in the possible control of footrot in Merino sheep, a breed which is believed to be particularly susceptible, is the exploitation of genetic variation in resistance. In 1988 we designed and implemented an experiment which addressed the fundamental question of possible genetic variation in resistance of Merino sheep to virulent footrot.

EXPERIMENTAL OUTLINE

The main aims of the programme are to:

a) estimate the heritability of resistance to footrot,

b) determine whether there is a link between resistance to footrot and ovine lymphocyte antigen (OLA) markers,

c) evaluate potential indirect selection criteria for resistance to footrot,

d) estimate the correlations between resistance to footrot and all major production traits including other disease resistance traits.

Project design

To meet the major aims it is necessary to estimate the relevant genetic parameters, including genetic and phenotypic variances and co-variances for all traits of interest. We have implemented a basic core programme in which 3,600 ewes will be mated to 120 sires over a 3 year period, utilising a half-sib design for eventual analysis. Each year, 1,200 ewes are allocated at random to 40 non-selected sires in single sire mating groups. The rams and ewes are drawn from 4 major self-replacing flocks including 3 Medium Peppin bloodlines and one Superfine Merino bloodline. Approximately 900 fully pedigreed progeny will be available after weaning for experimental purposes. To optimise the efficient use of the design and minimise the impact of footrot on the main breeding flock, the progeny are allocated at random (stratified across sires) to 2 groups.

One group (n = 500) of both rams and ewes consists of potential breeding replacements which will remain free of footrot. The second group (n = 400 wethers and ewes) will be experimentally challenged with virulent footrot to study clinical, immunological and production parameters.

Resistance to footrot

The principal definition of innate resistance to footrot is the failure to develop clinical signs of the disease following challenge with B. nodosus under suitable environmental conditions. Because it was important to have all sheep exposed to the same conditions at the same time, it was therefore decided to use the experimental challenge technique developed by Egerton and Thorley (1981). This approach was primarily developed to monitor the efficacy of new vaccines and is phenotypically related to resistance under field conditions. It also allows for the expression of phenotypic variation in resistance.

Further definitions of resistance to footrot include the degree or severity of footrot which develops after challenge and whether sheep can overcome the disease through natural healing. We are monitoring the development of footrot on a graded severity system at +3, +6, +9 weeks after challenge to evaluate these responses. The response of sheep affected with footrot to therapeutic vaccination is an important tool in the control of the disease. It has been shown under field conditions that some sheep do not respond in a satisfactory manner to such a programme and remain chronically infected. To evaluate this component of resistance we are vaccinating the sheep twice with an experimental preparation of a recombinant DNA pilus vaccine of the same serogroup used in the challenge. Both clinical (healing) and serological responses (antibody titres) are measured at +12, +15 and +26 weeks after challenge.

Preliminary results of our first challenge in 1989 indicated a heritability of resistance to footrot following challenge in the range of 0.04 ± 0.10 to 0.31 ± 0.15 for different definitions of resistance to footrot.

OLA typing

The role of the major histocompatibility complex (MHC) in modulating immune responses and subsequently disease resistance is well documented for a number of species. Ovine lymphocyte antigens (OLA) are glycoproteins which are present on the surface of most cells and are divisible into two types, Class I and Class II antigens, which are controlled by genes of the MHC. Class I OLA can now be serologically typed, utilising a panel of 17 typing sera as outlined by Outteridge et al 1985. Two particular antigens are of interest, namely SY1b and SY6, since they have been implicated in both resistance to footrot and responses following vaccination in previous studies utilizing different flocks(Outteridge et al 1989). Preliminary results in the present project confirmed the importance of SY1b in resistance to footrot.

Although Class II MHC genes are believed to have a key role in the regulation of immune responses, it has proven more difficult to type animals for Class II antigens with a serological assay. The use of cDNA probes for Class II genes from human, mouse and other species has opened the possibility of screening the sheep genome for corresponding Class II genes. The use of Restriction Fragment Length Polymorphisms (RFLPs) derived from a number of suitable restriction enzymes and a number of suitable Class II probes could yield valuable information on the role of Class II genes in the resistance of sheep to footrot. We have established the basic procedures of this potentially powerful screening technique in 90 progeny from 16 sires.

Immunological responsiveness

Potential indirect selection criteria are likely to be based on physiological processes which are linked with innate or acquired resistance. To evaluate the role of such selection criteria it is necessary to have information on the relevant genetic parameters. At present no information is available on the important immunological responses which reflect innate resistance of sheep to footrot. To cover the major arms of the immune system which have been implicated in the resistance of sheep to footrot, we are evaluating non-specific (neutrophil and complement activity) and specific (cell mediated) responses of sheep following a standard stimulus of footrot antigen.

The protection of sheep to footrot is feasible through vaccination with titres above a threshold level of 3,000 being indicative of protection against footrot. However, the fact that sheep need to be vaccinated against a range of antigens from all 9 serogroups of B. nodosus, and that

they differ considerably in their response to vaccination, is a possible limiting factor in vaccine efficacy. The ability of the host to respond better to a full range of footrot antigens is thought to be partly under genetic control and hence a heritable characteristic. To minimise the effect of challenge on vaccine responsiveness, we are monitoring serological responses in the non-challenged progeny group following a full course of vaccination with a decavalent vaccine. Routine serological procedures based on K-agglutination and ELISA techniques form the basis of this screen.

Production parameters

The major production traits which are being recommended as breeding objectives and/or selection criteria for fleece sheep are being measured in the programme. Additional traits which are of interest include resistance to fleece rot and body strike, susceptibility to yellow fleece discolouration and variation in fibre diameter within fleeces. All these traits are measured in both the non-challenged progeny group and twice in the challenged progeny group at 10 and 16 months of age, which includes a 6 month phase before challenge and a 6 month phase during challenge. Basic production and reproductive parameters are measured for all breeding ewes.

CONCLUDING REMARKS

Although the basic design of the programme outlined above is straightforward and relatively simple for half-sib estimates of genetic parameters, the biological constraints and range of traits examined are unique for this experiment. The power of the design to correlate a range of disease resistance traits, genetic markers and important production traits is a major feature of this design. The combination of expertise in veterinary epidemiology, immunology, immunogenetics, molecular biology and quantitative genetics make experiments in disease resistance at this scale possible and worthwhile.

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REFERENCES

EGERTON, J.R. and THORLEY, C.M. (1981). Res. Vet. Sci. 30:28.
EGERTON, J.R., YONG, W.K. and RIFFKIN, G.G. (1989). "Footrot and Foot Abscess of Ruminants" (Eds), 1st Ed. Boca Raton, Florida, CRC Press.
OUTTERIDGE, P.M., STEWART, D.J., SKERMAN, T.M., DUFTY, J.H., EGERTON, J.R., FERRIER, G. and MARSHALL, C. (1989). Aust. Vet. J. (In press).
OUTTERIDGE, P.M., WINDON, R.G., and DINEEN, J.K. (1985). Int. J. Parasitol. 15:121.