THE MECHANISMS UNDERLYING GENETIC RESISTANCE TO *OSTERTAGIA CIRCUMCINCTA*

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SUMMARY

Lambs naturally infected with predominantly *Ostertagia circumcincta* show substantial variation in the concentration of nematode eggs in their faeces. The heritability increases with age indicating that genetic variation is due to an acquired and not an innate response. Necropsy analysis indicates that there is substantial genetic variation in mean adult female worm length but not in the number of larvae or adult worms. Variation in adult female worm length is associated with variation in fecundity. Therefore genetic resistance appears to operate through the control of worm fecundity. The only immunological responses that are consistently associated with differences in worm fecundity are the amount of parasite-specific IgA and the specificity of serum antibody. These two traits, together with density-dependent effects of worm number, account for the vast majority of variation in worm length and consequently of fecundity. In conclusion, in growing lambs resistance to infection with *O. circumcincta* appears to be remarkably simple; the major and perhaps the only mechanism is the IgA mediated control of worm fecundity.

Keywords: Sheep, *Ostertagia circumcincta*, nematodes, parasite fecundity, resistance.

INTRODUCTION

The abomasal nematode *O. circumcincta* is a major constraint on sheep production throughout the temperate areas of the world. The disease is particularly severe among growing lambs. The purpose of this project was to improve our understanding of the variation among lambs in resistance to natural infection and, subsequently, use the improved understanding to develop better and more sustainable methods of controlling the disease.

MATERIALS AND METHODS

A flock of Scottish Blackface sheep on a commercial farm in Southwest Strathclyde was studied. There is substantial variation in resistance to nematodes within the breed (Stear *et al.* 1995 a,b). On this farm over 80% of the worms recovered at necropsy and 80% of the worms recovered from larval culture were *O. circumcincta.* Each year for 5 years, 200 lambs, mostly twins, and their mothers were reared close to the farmhouse on two or three fields. After weaning at 3 or 4 months of age all lambs were kept together on one field until they were sold at 6 months of age. Every four weeks, each animal was sampled for blood and faeces, weighed and given anthelmintic treatment as well as any other medication required. Faecal egg counts, worm burdens, worm length and the number of eggs *in utero* were assessed by standard parasitological procedures (Stear *et al.* 1995b). Immunological responses were measured in the abomasal mucosa by ELISA and by cell counting (Stear *et al.* 1995b). The number of eggs, larvae and adult *O. circumcincta* were skewed to the right; the data were transformed prior to analysis by taking the logarithm of each variable plus one. The heritabilities and genetic correlations were estimated by residual maximum likelihood (REML) fitting an animal model that included all known pedigree relationships (Meyer, 1989). The standard errors were calculated from the second derivative of the log likelihood profile around the parameter estimate.

RESULTS AND DISCUSSION

Sources of variation in resistance to infection. There was substantial variation among lambs in faecal egg count and this variation increased as the lambs matured (Stear *et al.* 1995a).

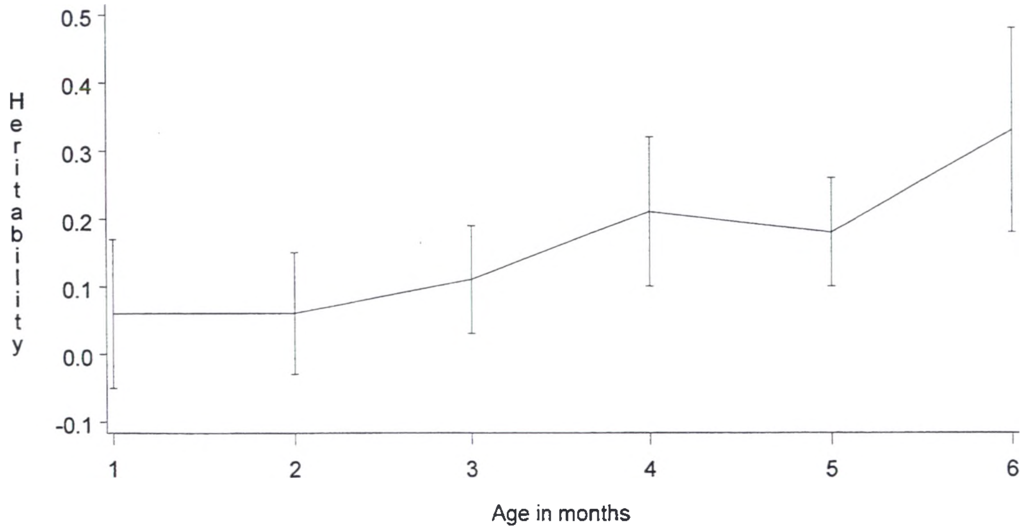

Figure 1. The heritability of faecal egg counts increases with age.

Variance analysis indicated that 4 major and 4 minor components were responsible for the observed variation among lambs in faecal egg count (Bishop *et al.* 1996; Stear *et al.* 1996). The minor effects were type of birth (single or twin), sex (castrated male or intact female), date of birth (all animals lambed within a three-week interval in late April and early May) and early exposure (egg counts at two months of age were negatively correlated with subsequent egg counts). The major components were additive genetic effects, maternal common environmental effects, measurement variation and effects specific to each individual. The influence of these components varied with age. For example, the heritabilities increased from 0.06 ± 0.11 at 1 month of age to 0.33 ± 0.15 at six months of age (Figure 1). The increase in heritability from essentially zero to 0.33 indicates that genetic resistance is an acquired and not an innate phenomenon.

Parasitological traits influenced by resistance. A total of 501 lambs were necropsied over 4 years (1992-1995). Table 1 shows that the heritabilities for the number of fourth-stage larvae, fifth-stage larvae and adult worms were all very low and not significantly different from zero. In contrast, the heritabilities for adult female worm length and the number of eggs *in utero* were extremely high. Adult female worm length is highly correlated with the number of eggs *in utero* (Stear *et al.* 1997) and both traits are markers of worm fecundity (Stear and Bishop, manuscript in preparation). The necropsy results strongly suggest that the major manifestation of genetic resistance is the control of worm fecundity. Reducing worm burdens by prevention of larval establishment or by rejection of adult worms plays at most a minor role in genetic resistance to natural infection in growing lambs.

Table 1. Heritabilities and standard errors of parasitological traits at necropsy

Faecal egg count	Number of fourth-stage larvae	Number of fifth-stage larvae	Number of adult worms	Mean length of adult female worms	Number of eggs per adult female worm
0.33 ± 0.14	0	0.08 ± 0.09	0.14 ± 0.10	0.62 ± 0.20	0.55 ± 0.19

Mechanisms of resistance to infection. For *O. circumcincta*, there are no consistent phenotypic relationships of worm length or fecundity with parasite-specific local IgG1, IgG2 and IgM responses to L3, L4 or adult parasite antigen, or the number of mast cells, globule leucocytes or eosinophils in the abomasal mucosa. The only immunological traits that are consistently associated with differences in worm length and worm fecundity are the local IgA response to fourth-stage larvae and the specificity of serum antibody (Stear *et al.* 1995b; McCririe et al. 1997; Strain *et al.* unpublished observations). Together with the influence of worm burden on worm fecundity (density-dependence), these traits account for the vast majority of variation among lambs in parasite length and hence fecundity. At best, all other mechanisms account for only a trivial proportion (< 10%) of the observed variation in resistance to infection.

Relationship between parasitism and productivity. The genetic correlation between faecal egg count and body weight was estimated from approximately 1,000 lambs at 4, 5 and 6 months of age. It was -0.8 (Bishop *et al.* 1996; Unpublished observations). This result confirms that infection with *O. circumcincta* is a major constraint on production, even under conditions of regular anthelmintic treatment. The major genetic differences among lambs are in worm length and not in worm number, therefore the detrimental influence of parasitism on growth rate may be less influenced by worm number than by traits associated with worm length, such as size or activity.

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