# Exploration of Mechanisms for Resistance and Their Impact On Performance in Nematode Infected Lambs

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## Introduction

Gastro-intestinal parasitism is the major challenge to health, welfare and productivity of sheep worldwide. Due to the reduced efficacy of anthelmintics, there has been an increased interest in breeding for resistance to nematodes as an alternative. Sheep can be bred for improved resistance to gastro-intestinal nematodes using the indicator trait faecal worm egg count (Bishop and Morris, 2007). There are several examples of such selection working in practice, for example sheep bred in such programmes have been shown to display a faecal worm egg count which is approximately 20% that of non-selected control animals after 15 years of selection (Kemper et al., 2010). Of particular practical importance are the implications of selection such as this on animal performance, under differing environmental circumstances. Interpreting host-parasite interactions, their impact on performance traits and underlying mechanisms pertaining to selection may be aided by mathematical simulation models. Adapting and enhancing a previously published simulation model (Vagenas et al., 2007), this paper explores the plausible mechanisms of genetic resistance that may feasibly explain the findings of Kemper et al., and identifies the possible impacts such mechanisms may have on performance of contrasting breeds under differing feed regimes.

## Material and methods

Adapting the parasite simulation model of Vagenas et al. (2007) we investigated the effect of different nematode resistance mechanisms, nutritional environment and level of challenge with the most significant nematode in temperate climates, *Teladorsagia circumcincta*, on the performance of two different breeds of sheep, growing from 2 to 6 months of age. We simulated different genotypes with respect to growth, corresponding to the Suffolk and (Scottish) Blackface breeds. These were assumed to differ in initial fleece-free empty body weight and expected mature body protein and lipid weight (Table 1). Daily trickle challenges of either 1000 or 5000 *T. circumcincta* $L_3$ per day, were chosen to correspond to challenge levels that lead to sub-clinical *T. circumcincta* infections (e.g. Coop et al., 1985). Lambs were offered *in silico* either good or poor quality grasses *ad libitum* (AFRC, 1993).

Three resistance mechanisms were created; (a) absolute level resistance to infestation, (b) rate of acquisition of resistance and (c) ability to inhibit worm development and fecundity

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('worm development resistance') and compared to non-selected controls. The three resistance selected genotypes were parameterized by altering: (a) worm mortality and establishment absolute levels, (b) rate of acquisition of ability to control worm mortality and establishment and (c) worm development and fecundity rate, respectively. Relevant parameters were altered equally to obtain a 20% worm burden in resistance-selected animals in comparison to non-selected animals for the resistance to infestation and acquisition of resistance mechanisms at the day of maximum worm burden. For the worm development resistance mechanism the model was parameterised for worm mass rather than worm burden. The model was parameterised for the scenario where animals were offered good quality feed *ad libitum.* Maximum worm burden and worm mass occurred on day 38 and day 29 for non-resistance selected lambs given larval challenges of 1000 or 5000 $L_3$ per day respectively. Outputs investigated the impacts of parasite resistance mechanisms, challenge level, breed and their interactions on lamb growth, food intake and faecal worm egg count (FEC).

We assessed (a) the effects of the three resistance genotypes and two contrasting diets on Blackface-type lambs and (b) whether the results observed for (a) are predicted to differ between the two breeds. In all cases lambs were challenged with either 1000 or 5000 *T. circumcincta* $L_3$ per day from day one of the simulation, and offered either good or poor quality feeds *ad libitum,* corresponding to good and poor quality grass diets.

**Table 1. Body composition characteristics of the two breed types**

| | **Blackface** | **Suffolk** |
|---|---|---|
| **Initial fleece-free empty body weight (kg)** | 12.73 | 21.45 |
| **Expected mature body protein content (kg)** | 9.53 | 12.03 |
| **Expected mature body lipid content (kg)** | 40.11 | 65.60 |

## Results and discussion

Daily predictions were obtained for food intake (FI) and empty body weight (EBW) as the production traits of interest, and worm mass (WM) and faecal worm egg count (FEC) as the parasite resistance traits. Predictions obtained are reported at 28 days, 56 days and 84 days post initial larval challenge, to provide a summary of the trends predicted over the course of the 4 month experiments.

Predictions for Blackface type lambs are summarised in Table 2. Shown are trait means for selected animals expressed as proportions of the same traits observed in non-selected animals. These predictions would indicate that the absolute resistance to infestation mechanism has greater effect upon faecal worm egg count than the mechanism for rate of acquisition of resistance. Reductions acheived depended on the level of daily $L_3$ challenge. The resistance to infestation mechanism displayed the 18% FEC observed in the Kemper *et al.* (2010) studies for animals challenged with 5000 $L_3$ per day. The worm development resistance mechanism showed greater reduction in worm mass and FEC than expected, at the time points reported. This is due to the model being parameterised for a 20% level on the maximum worm mass rather than fixing a 20% level throughout the course of the simulation. The worm development resistance mechanism does, however, display a greater efficacy in reducing the FEC and may therefore have greater impact upon the severity of infection in field studies. These predictions would suggest that when comparing mechanisms of resistance that could plausibly lead to reductions in FEC similar to those observed by Kemper *et al.* (2010), it is the decreased worm development mechanism that would have the largest impact upon subsequent FEC. Detailed necropsy data from Kemper *et al.* (2010) suggested that each of these mechanisms is plausible, although different mechanisms appeared to apply to different worm species.

**Table 2. Comparison of non selected and resistance selected genotypes at day 28 after initial infection in Blackface-type lambs**[α]

| | | Infestation | | Acquisition | | Worm development | |
|---|---|---|---|---|---|---|---|
| | | **1000** | **5000** | **1000** | **5000** | **1000** | **5000** |
| **Good** | **WM** | 0.34 | 0.22 | 0.41 | 0.31 | 0.11 | 0.19 |
| | **FEC** | 0.34 | 0.33 | 0.41 | 0.25 | 0.11 | 0.15 |
| **Poor** | **WM** | 0.35 | 0.24 | 0.46 | 0.26 | 0.10 | 0.13 |
| | **FEC** | 0.35 | 0.18 | 0.46 | 0.19 | 0.10 | 0.09 |

[α]Values presented are trait values in selected lambs expressed as a proportion of those in non-selected lambs.

Production trait values for the Suffolk-type animals were larger than the Blackface-type lambs (data not shown); this corresponds to increased growth attributes of the Suffolk-type animals that were input parameters to the model. When comparing the impacts of parasitism on resistance selected lambs with the non-selected lambs the same proportional changes were noted for all mechanisms of resistance upon both breeds offered the good quality feed (see Table 2 for parasite trait values). A 1.25-fold increase in food intake for resistance-selected lambs in comparison to non-selected lambs was noted on day 28 for lambs challenged with 5000 $L_3$ per day, this observation is due to the absence of parasite-induced anorexia in resistance-selected lambs. No further impacts upon performance were noted. However, for lambs offered poor quality feed, differences are predicted between the two breeds. Proportional changes in traits when comparing each resistance mechanism were similar to those described in Table 2 for each breed, and hence the results displayed in Table 3 are given as proportions of non-selected lambs averaged across all resistance mechanisms.

**Table 3. Comparison of non-selected and resistance selected genotypes for two breeds offered poor quality feed *ad lib.* given for days from initial larval challenge**[α]

| **Breed-type** | **Trait** | **Day 28** | | **Day 56** | | **Day 84** | |
|---|---|---|---|---|---|---|---|
| | | **1000** | **5000** | **1000** | **5000** | **1000** | **5000** |
| **Suffolk** | **EBW** | 1 | 1.02 | 1 | 1.08 | 1 | 1.06 |
| | **FI** | 1 | 1.40 | 1 | 1.08 | 1 | 1.02 |
| | **FEC** | 0.29 | 0.29 | 0.22 | 0.28 | 0.34 | 0.57 |
| **Blackface** | **EBW** | 1 | 1.02 | 1.13 | 1.16 | 1.16 | 1.19 |
| | **FI** | 1 | 2.10 | 1.57 | 1.61 | 1.16 | 1.19 |
| | **FEC** | 0.31 | 0.15 | 0.07 | 0.11 | 0.19 | 0.33 |

[α]Values presented are trait values in selected lambs expressed as a proportion of those in non-selected lambs.

Lambs selected for all resistance mechanisms, in both breed types, when evaluated on good and poor quality feed, showed no reduction in food intake due to parasite-induced anorexia, whereas non-selected animals did display a large albeit temporary reduction in food intake.

The consequence is that selected (i.e. resistant) animals are predicted to have lasting superiority in empty body weight at both challenge levels, with the effects being larger in the Blackface-type breed

The observed effects on food intake are due to the model currently assuming that parasite-induced anorexia is a function of worm presence, i.e. worm mass. Therefore, in this model, the reduced worm mass observed in resistance selected lambs is not sufficient to cause a reduction in food intake. The differences observed in the two breeds when offered poor quality feed can be explained after taking into account the absence of parasite-induced anorexia in resistance selected animals. With an absence of parasite-induced anorexia the predictions for all traits revert to those arising as a consequence of the next limiting factor, *viz.* maximum gut fill. In the model, maximum gut fill is assumed to be a function of animal live weight. Due to the Suffolk-type having greater growth rate than the Blackface-type its maximum gut fill is greater. The difference in growth rates, and the consequent impact on gut capacity, between the two breeds is therefore the reason behind the differences displayed in Table 3. This conclusion can only be drawn if the assumption that parasite-induced anorexia being a function of worm mass is correct. Greer *et al.* (2008) suggest that parasite-induced anorexia is a function of components of the immune response. If this is indeed the case then animals selected for resistance may be expected to have a greater reduction in food intake due to an increased immune response, hence the impact of selection for resistance may have the opposite effect upon production traits than that reported here. This, however, will be only for the period of acquisition of immunity and overall food intake might not differ.

## Conclusion

Results from our model suggest that the large responses to selection for nematode resistance seen under field conditions may plausibly be explained by a combination of reduced worm establishment, increased worm mortality, and decreased worm development. Decreased worm development is predicted to have a greater long-term impact upon faecal worm egg count than a reduction in worm establishment and an increase in worm mortality. Predictions made for production traits, in light of selection for resistance, are dependent upon the assumptions made about parasite-induced anorexia. However, under the assumptions made in this model and the resistance mechanisms explored, improved resistance is predicted to lead to increases in empty body weight under poor quality feeding regimens.

## References

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