Improving the diagnosis and control of gastrointestinal nematode infections

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Hypothesis – Gastrointestinal nematodes cause disease and death in both humans and livestock. In the UK, nematodes cost the sheep industry ~£100 million per year. The severity of infection is difficult to determine because the commonly used parasitological measurements, such as faecal egg counts (FEC), are not very accurate. We propose that the protective immune response will provide better markers for diagnosis and control than the current parasitological outcomes. We chose the sheep - *T. circumcincta* model for investigation because it is one of the best understood of all host – parasite systems.

Nematode Life-cycle

T. circumcincta adults live in the fourth stomach (abomasum). The eggs are carried in the faeces into the field, where the larvae develop to third stage (L3) and become infective. The ingested L3s travel to the abomasum where they become established, and develop further into L4 larvae and adults.

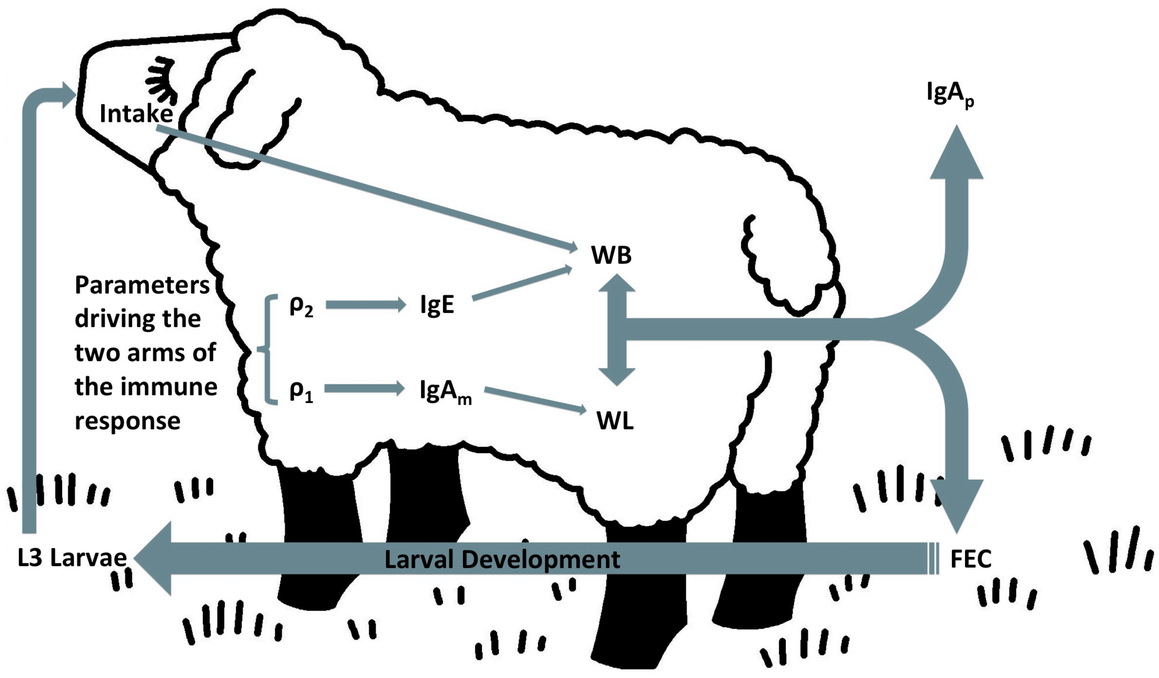

Figure 1. Schematic representation of the Model

WB: Worm Burden
WL: Worm Length
IgE: Anti-establishment response
IgA: Anti-fecundity response (m, mucosal; p, plasma)
FEC: Faecal egg counts
ρ_1 & ρ_2: immune potential

Model Description

The model reproduces the nematode life-cycle in a flock of sheep each with two drivers of the immune response ρ_1 and ρ_2 that differentiate the animals (Fig. 1). These responses are heritable and determine the heritability of observed parasitological variables, including FEC, plasma IgA and worm length, to which the model is fitted. The flock is created yearly by breeding 500 ewes with 25 rams, and ensuring a stable population of 1000. Two scenarios are run: the rams are selected either on low faecal egg counts or on high plasma IgA levels.

IgA is a potentially important marker because it regulates worm growth and fecundity, but has not been viewed as a useful marker because of uncertainty in the relationship between plasma IgA, which is easily measured, and mucosal IgA which acts at the site of infection and cannot be easily measured in live animals. Using a Bayesian regression analysis we related parasite specific plasma IgA (from the bloodstream) with local IgA and worm biomass:

Transfer Equation: $$IgAp = 3.98 \cdot IgAm - 1.02 \cdot log_{10}(WM + 1) \cdot IgAm$$

By including this relationship in our model, we can compare plasma IgA with FEC as an indicator of resistance to infection by simulating the impact of 10 generations of selection on key parasitological outcomes (FEC, WB, WL).

Results

Selection on plasma IgA gives a much faster reduction in FEC than selection on FEC itself (Fig. 2). This is because high levels of IgA reduce worm growth and fecundity, hence decreasing the egg output.

Because pasture contamination is reduced, the use of plasma IgA as a marker also indirectly controls worm biomass, the main source of pathology in lambs, and, over 10 generations of selection, it decreases by almost a half.

Conclusions

Plasma IgA is a better indicator of intensity of infection than FEC, and has a number of practical advantages. It is easier to sample, measures are more precise and there is reduced risk of contamination or infection. It has potential to be useful for both diagnosis and for control schemes such as selective breeding or targeted selective treatment (TST). In summary, it is cheaper, easier to use and provides a better marker than FEC for farmers, veterinarians and breeders.

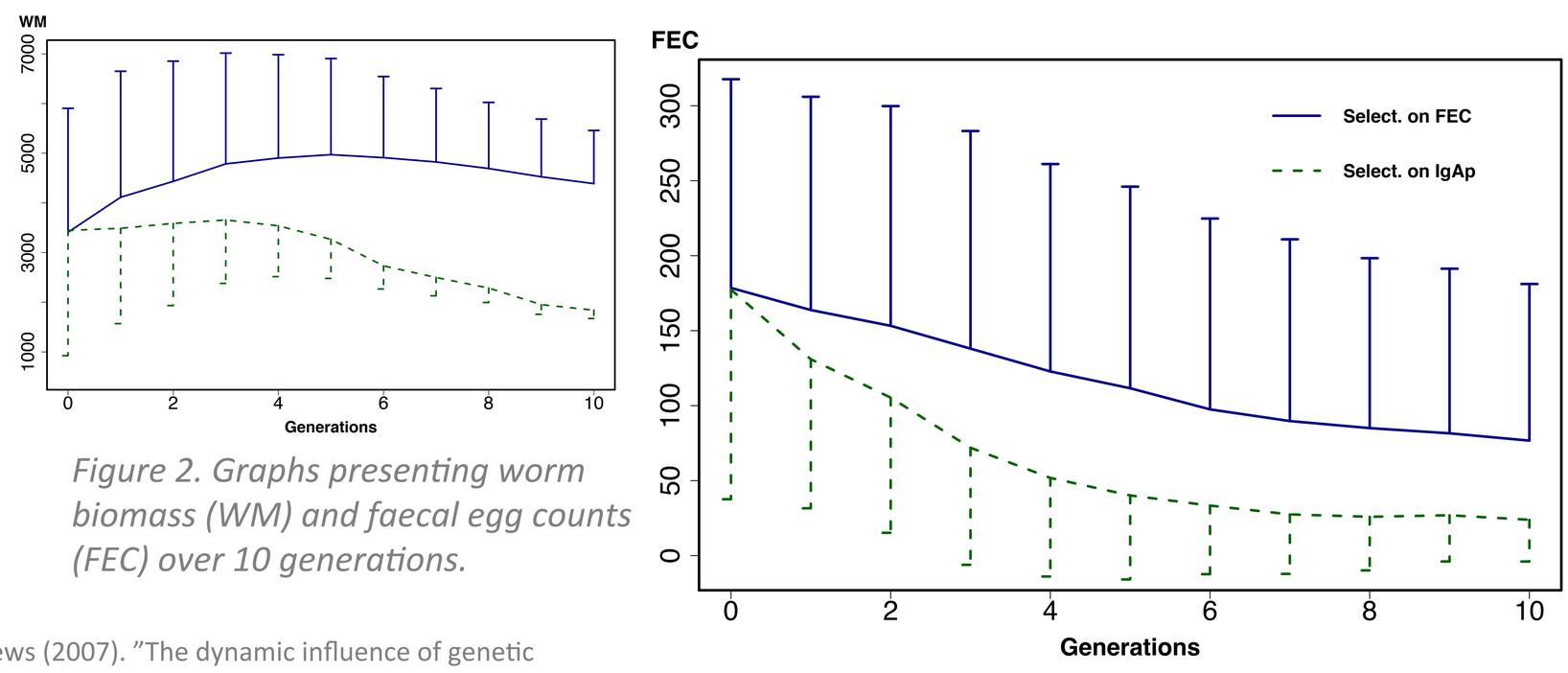

Figure 2. Graphs presenting worm biomass (WM) and faecal egg counts (FEC) over 10 generations.

References

M. J. Stear, L. Fitton, G. T. Innocent, L. Murphy, K. Rennie, L. Matthews (2007). "The dynamic influence of genetic variation on the susceptibility of sheep to gastrointestinal nematode infection" J. R. Soc. Interface 2007 4: 767-776.

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