Interactions between parasites and animal nutrition: the veterinary consequences

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Parasites are a major constraint on animal productivity throughout the world. Gastrointestinal helminths are ubiquitous parasites of grazing ruminants and cause decreases in survival, live-weight gain, wool and milk production and reproduction performance. These losses can be particularly severe in developing countries where control measures are less readily available. In addition in many tropical countries protozoan diseases are of major importance. One protozoan disease in particular, trypanosomiasis, is the single most important constraint on animal production in sub-Saharan Africa.

The mechanisms by which parasites cause impaired productivity have become the subject of intense study and some of the findings will be discussed.

It has been frequently suggested that the nutritional status of the host can influence the pathogenesis of parasitic infections and it is generally accepted that well-nourished animals withstand parasitism better than those less adequately fed (Whitlock, 1949; Gibson, 1963). However, the mechanisms involved have rarely been elucidated. For example, the diet may not only influence host resistance to either the initial infection or reinfection but may also affect the ability of the host to withstand the pathophysiological consequences of infection. Unfortunately the few studies that have been conducted to examine these interactions in the past have often been unsatisfactory because of inadequate controls or poorly formulated diets. More recently attempts have been made to overcome these difficulties and a clearer picture has emerged of the interaction between host nutrition and the pathophysiological consequences of parasitic infections.

PATHOPHYSIOLOGY OF GASTROINTESTINAL (GI) HELMINTHIASIS

Domestic ruminants harbour a variety of pathogenic helminths and different species are associated with specific locations within the GI tract. The principal locations are the abomasum (*Haemonchus, Ostertagia*), small intestine (*Trichostrongylus, Cooperia, Bunostomum*), large intestine (*Oesophagostomum, Chabertia*) and liver (*Fasciola*).

An extensive series of experiments over the past two decades has established that a cardinal feature of all these infections is the loss of considerable quantities of host protein into the GI tract. The proteins represent plasma and frequently erythrocytes, exfoliated epithelial cells and mucus.

By the use of radioisotopic techniques it has been possible to quantify accurately the losses of blood proteins into the tract and these have been shown frequently to represent the equivalent of 10% of the total blood volume per d (Parkins & Holmes, 1989).

It is more difficult to quantify accurately the losses of epithelial cells and mucus but indirect evidence suggests that these are substantial (Poppi *et al.* 1981).

The fate of the endogenous protein lost into the GI tract has also been investigated and has been shown to be influenced by the site of the parasite infection. Thus, in sheep...
infected with the abomasal parasite *Haemonchus contortus* all the blood proteins lost could be accounted for by the increased N flow into the duodenum, and all was absorbed by the ileum (Rowe *et al.* 1982). However, in sheep infected with the small intestinal parasite *Trichostrongylus colubriformis* only about half the lost N was reabsorbed in the small intestine (Poppi *et al.* 1981).

Two subsequent studies extended these observations and their clinical significance. First, in a later study by Rowe *et al.* (1988) using sheep infected with *H. contortus* it was shown that much of the additional blood N found in the abomasum was converted to ammonia by the parasites, and metabolism of this NH$_3$ in the liver resulted in higher urea synthesis. Thus, in effect, the presence of the parasites increased the non-recoverable loss of amino acids into the gut and increased the protein requirement of the infected sheep.

Second, in abomasal infections, compensatory increases in digestion and absorption occur in the small intestine (Poppi *et al.* 1986). However, this may be prevented in the case of the common natural situation of mixed species infection affecting both the abomasum and intestine and the pathogenic effects are considerably exacerbated compared with mono-specific infections (e.g. Parkins *et al.* 1990) and this in part may be associated with reduced absorption of blood and other proteins. Certainly in such cases faecal losses of N are high and overall N retention greatly reduced.

Feed intake has been shown also to be significantly reduced in parasitized ruminants and by comparison of growth rates in parasitized animals with those of pair-fed and ad lib.-fed controls it has been possible to evaluate the relative influence of reduced feed intake on depressed growth rates in parasitized animals.

Attempts to evaluate protein deposition and tissue metabolism in parasitized hosts have been limited. One approach has been to examine food utilization in infected animals. For example, in lambs chronically infected with *Ostertagia circumcincta* Sykes & Coop (1977) and Coop *et al.* (1982) demonstrated a significant reduction in the deposition of fat and protein in infected animals compared with pair-fed controls. More recently, carcass evaluation studies have been conducted in cattle infected with mixed trichostrongyles (Entrocasso *et al.* 1986) and at slaughter various indices of protein deposition were found to be reduced in parasitized animals compared with parasite-free controls.

A controlled series of studies by Symons and his co-workers to examine tissue protein synthesis using L-[¹⁴C]leucine and L-[¹⁴C]tyrosine in parasitized animals is particularly relevant (for review, see Symons, 1985). These showed that protein synthesis was reduced in skeletal muscle of infected sheep, whilst protein synthesis by the liver was increased in such animals.

Measurements of protein synthesis in GI tissue have, for technical reasons, so far been restricted to guinea-pigs infected with *T. colubriformis*. In such animals the amount of protein synthesis per d was increased in both the small and large intestine (Symons & Jones, 1983). It is important that this finding is confirmed in ruminants as these sites of increased protein synthesis may be an important cause of reduced nutrient utilization by infected sheep and cattle.

As a result of such studies Symons (1985) concluded that, due to inappetence, GI losses of protein and increased rates of GI tissue protein metabolism, there is a net movement of amino acid-N from muscle and skin to the liver and GI tract which decreases the availability for growth and milk and wool production. However, it is still
not possible to construct accurate balance sheets of protein synthesis in parasitized animals nor is there any detailed information on the underlying mechanisms, including hormonal, which may be responsible for the changes in protein synthesis.

INFLUENCE OF DIETARY PROTEIN ON GASTROINTESTINAL HELMINTHIASIS

In the light of the pathophysiological changes associated with GI helminthiasis and especially the central role played by endogenous protein losses, host nutrition and especially dietary protein intake might be expected to influence the pathogenesis of such infections. One of the first indications that this indeed was the case was provided by observations of Allonby (1974) in Kenya. In his studies of the epidemiology of ovine haemonchosis he observed a distinctive chronic form of the disease during the dry season which was characterized by poor growth rates and a moderate anaemia, and which was associated with poor nutrition and low parasite burdens. Following these field observations our group examined the interaction between protein nutrition and the pathogenesis of ovine haemonchosis under controlled experimental conditions. In these studies a regimen using pair-fed controls was adopted and complete diets which only differed in protein content (88 or 169 g crude protein (N x 6.25)/kg dry matter).

Influence of protein nutrition on the pathogenicity of a single infection with H. contortus

In this initial experiment Finn-Dorset/Dorset Horn castrated male lambs were introduced to a high-protein (HP) or low-protein (LP) diet at 3 months of age. At 4 months, four lambs from each group were infected with 350 H. contortus larvae/kg body weight and four other lambs in each dietary group were maintained as uninfected pair-fed controls. The infected lambs were killed at 6 weeks post infection and the worm burdens assessed.

The results indicated that lambs on an LP diet were less able to withstand the pathophysiological consequences of infection with H. contortus than lambs given an HP diet. Adverse clinical signs such as dullness, weight loss, anorexia and oedema were more frequently observed in the infected lambs on the poorer plane of nutrition (Abbott et al. 1986a).

The haematological and biochemical indices showed that the anaemia and hypoalbuminaemia were also more pronounced in the LP groups, despite similar levels of gastric blood loss (measured by 51Cr-labelled erythrocytes) in both dietary groups. However, the infected lambs in both groups responded equally well to the gastric haemorrhage by increasing the rate of erythrocyte production (measured by 59Fe-labelled transferrin; Abbott et al. 1986b). The finding that total daily faecal egg outputs and worm burdens were similar in both groups showed that the diet had no apparent effect on parasite establishment. It would appear, therefore, that the LP diet, along with the anorexia induced by the infection in lambs on this diet, affected protein metabolism more severely than in lambs on a better diet and, as a result, the pathogenic effects of H. contortus were exacerbated.
Influence of protein nutrition on the pathogenicity of continuous infection with H. contortus

In many field situations, ruminants are exposed to continual low levels of infection; this study was designed, therefore, to investigate the effect of protein nutrition on lambs given repeated infections with small numbers of H. contortus larvae. An identical protocol to the previous experiment was adopted with the exception that the lambs were given an initial dose of 100 H. contortus larvae/kg body weight at 4 months of age followed by 200 larvae/lamb three times weekly for 17 weeks.

In many respects the results from this study were similar to those observed in the earlier experiment, but several aspects were particularly noteworthy. First, weakness, inappetence and oedema were observed in the majority of the infected lambs on the LP diet. In contrast, the infected lambs on the HP diet remained alert throughout the experiment and none showed clinical signs. The degree of anaemia and hypoalbuminaemia was also more marked in the infected lambs on the LP diet. Second, there were marked differences in the faecal egg counts of the two infected groups. In the HP lambs the counts rose to a maximum of 13,900 eggs/g (epg) at 11 weeks and then slowly declined to 6000 epg at slaughter, whilst in the LP lambs the counts rose to 45,000 epg at week 11 and then continued to remain high until slaughter.

The worm burdens at slaughter reflected these findings, with the HP lambs having no worms or only low numbers of worms present. In the LP lambs, by contrast, large numbers of worms were present (Abbott et al. 1988).

The main conclusion from this experiment was that lambs repeatedly infected with small numbers of H. contortus and given an HP diet generally developed resistance to further infection. In contrast, lambs given an LP diet and subjected to an identical infection regimen all failed to develop resistance and showed signs of severe clinical haemonchosis.

Influence of post-rumen infusions of protein in parasitized sheep

The pivotal role of protein in the pathophysiology of GI helminthiasis has been further confirmed in a recent elegant study by Bown et al. (1991).

In the experiment the effect of post-rumen infusion of protein or energy on the pathophysiology of T. colubriformis infection and body composition in lambs was investigated using the comparative slaughter technique. Groups of twelve infected animals were given either a continuous infusion (via abomasal catheter) of 50 g crude protein/d as sodium caseinate, glucose in isoenergetic amounts to the caseinate or a solution containing P and Na at the same rate as the caseinate infusions. Uninfected controls were also infused with P and Na solution. Animals were slaughtered after 6 and 12 weeks for estimation of worm count and body composition. N retention in infected sheep was increased fourfold by protein infusion and twofold by energy infusion. The rate of energy retention was reduced by infection but increased by protein infusion. Protein infusion also reduced mean faecal egg output and mean total parasite count. However, endogenous plasma losses into the GI tract were similar in all infected groups. The authors concluded that parasite-induced protein deficiency is a major limiting factor in animals infected with GI helminths since their debilitating effect could be markedly reduced by increasing the protein supply to the duodenum.
INFLUENCE OF DIETARY PROTEIN ON GENETIC RESISTANCE TO GASTROINTESTINAL HELMINTHIASIS

Ruminants show considerable variation in susceptibility to parasitic infections even when maintained on similar planes of nutrition as a result of genetic variations. The use of genetically resistant livestock to control disease is being vigorously explored in several areas of the world as the limitations of current methods of control, e.g. regular drug therapy and strict grazing regimens, become increasingly apparent.

With the increasing interest in the development of genetically resistant livestock and our previous findings that low planes of nutrition can exacerbate the pathogenic effects of GI helminthiasis it is important to determine if the benefits of genetic resistance are easily lost when nutrition is sub-optimal. An initial experiment has indicated that diet can influence genetic resistance. In this study (Abbott et al. 1985a,b) the same HP and LP diets as used in our previous studies were fed to groups of lambs of two breeds (Finn-Dorset and Scottish Blackface) known to differ in their susceptibility to haemonchosis (Altaif & Dargie, 1978). The lambs were given a single infection of 125 larvae/kg body weight.

As in the other experiments the principal feature of the disease was the development of a moderately severe macrocytic anaemia, hypoproteinaemia and hypoalbuminaemia. However, both breed and diet influenced the severity of the pathophysiological changes associated with infection. The Finn-Dorset lambs had higher faecal egg counts and a more pronounced anaemia than the Blackface lambs. Diet influenced the degree of anaemia in both breeds but not the faecal egg count. Gastric blood losses were similar in the HP infected Finn-Dorset, HP infected Blackface and LP infected Blackface (16–18 ml erythrocytes/d) but considerably higher in the LP infected Finn-Dorset (30 ml erythrocytes/d). Erythropoiesis, as exemplified by the rate of 59Fe uptake by erythrocytes was most rapid in the LP infected Finn-Dorset and similar in the three other infected groups.

The results clearly indicate an additive detrimental effect of genetic susceptibility and poor diet but also show that genetic superiority in terms of disease resistance was not compromised by poor nutrition.

Thus, at this level of challenge, providing an HP diet significantly improved the pathophysiological changes in the genetically susceptible sheep to the same level as that observed in the genetically superior animals whilst diet did not influence the pathophysiological changes in the genetically superior animals. This indicates that the benefits of a superior genetic background are not lost on an LP diet whilst an HP diet can overcome the disadvantages of an inferior genetic background, at least in sheep exposed to moderate parasite challenge.

These preliminary results, if confirmed in larger studies, have important implications for future programmes using genetically resistant livestock.

INFLUENCE OF DIETARY PROTEIN ON THE PATHOGENESIS OF TRYPANOSOMIASIS

There have been numerous anecdotal accounts from Africa of the importance that host nutrition plays in the pathogenesis of trypanosomiasis in African ruminants, although until very recently these have remained unsubstantiated. Thus, it has been frequently reported from the field that during the dry season trypanosomiasis becomes more severe
when the quality and quantity of nutrition is particularly low. This has recently been investigated in The Gambia by offering supplementary feeding during the dry season to trypanosome-infected N’dama cattle (Agyemang et al. 1990; Little et al. 1990). As a result of the supplementary feeding it was found that the severity of the disease, as judged by the degree of anaemia, was significantly reduced. However, no nutritional evaluations of the diets were reported, with the result that the relative influence of protein intake could not be evaluated. A recent study conducted in Glasgow in trypanosome-infected sheep was designed to investigate this aspect of host nutrition on the pathogenesis of trypanosomiasis (Katunguka-Rwakishaya et al. 1993). In the experiment sheep were offered either an HP or an LP diet and then infected with Trypanosoma congoense. The diets were the same as those used in our earlier studies in sheep infected with helminths.

It was observed that both groups of infected sheep developed a similar degree of anaemia but the erythropoietic response, as judged by the increase in mean corpuscular volume and the appearance of normoblasts in the circulation was greater in the animals on the HP diet. The infected animals on the HP diet also gained weight at a similar rate to uninfected controls on the same diet, whilst the infected sheep on the LP diet gained significantly less weight than their uninfected controls. Finally, following treatment with a trypanocidal drug at 10 weeks post infection, the sheep on the HP diet showed a more rapid resolution of the anaemia than infected sheep given the LP diet.

These studies in trypanosome-infected ruminants indicate that, as is the case in helminth infections, the quality of the diet, and in particular the protein level, can markedly influence the pathogenicity of this important parasitic disease. Furthermore with the growing interest in the use of genetically resistant (or trypanotolerant) breeds of livestock it is important to determine the influence and level of interaction of host nutrition on trypanotolerance for the planning of future sustainable control programmes for African trypanosomiasis.

CONCLUSIONS

Many aspects of the pathophysiology of parasitic infections have been elucidated and GI helminthiasis has been the subject of particular study. It is now clear that the cardinal feature of such infections is the loss of considerable quantities of host protein into the GI tract and consequent changes in protein synthesis in host tissues.

Experiments with sheep given diets of varying protein content and infected with H. contortus have shown that although dietary protein does not influence initial parasite establishment animals on an LP diet (70 g crude protein/kg) exhibit more severe clinical signs in terms of retarded growth rates, degree of anaemia and mortality than those offered an HP diet (160 g crude protein/kg). Furthermore, sheep given an HP diet and subjected to repeated infection are more likely to develop resistance to reinfection than animals on an LP diet.

The level of protein intake has also been shown to influence the genetic susceptibility of sheep to haemonchosis. Preliminary studies have indicated that the benefits of a superior genetic background are not lost on an LP diet whilst an HP diet can overcome the disadvantages of an inferior genetic background, at least in sheep exposed to moderate parasite challenge.

The influence of diet on the pathogenesis of African trypanosomiasis has also been
recently examined. Field studies indicate that supplementation during the dry season can reduce losses from this disease and experiments under controlled conditions have shown that the level of protein intake can have a striking effect on the growth rates and erythropoietic responses of infected animals. Future studies are expected to examine the influence of diet on genetic resistance to this major African disease.

REFERENCES