Nutrition and Parasite Interaction

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Abstract—Coop R. L. & Holmes P. H. 1996. Nutrition and parasite interaction. International Journal for Parasitology 26: 951-962. This overview focuses on the interaction between nutritional status and gastrointestinal nematode infection in ruminants and considers: (i) the influence of the parasite on host metabolism; and (ii) the effect of host nutrition on the establishment and survival of parasite populations, the development of the host-immune response and the pathophysiology of infection. Gastrointestinal nematodes reduce voluntary feed intake and efficiency of feed utilisation, a key feature being an increased endogenous loss of protein into the gastrointestinal tract. Overall there is movement of protein from productive processes into repair of the gastrointestinal tract, synthesis of plasma proteins and mucoprotein production. Although reduction in feed intake is a major factor contributing to the reduced performance of parasitised ruminants, the underlying mechanisms of the anorexia are poorly understood. Supplementation of the diet with additional protein does not appear to affect initial establishment of nematode infections but the pathophysiological consequences are generally more severe on lower planes of protein nutrition. The main effect of protein supplementation is to increase the rate of acquisition of immunity and increase resistance to reinfection and this has been associated with an enhanced cellular immune response in the gastrointestinal mucosa. The unresponsiveness of the young lamb can be improved by dietary protein supplementation. Recent trials have shown that growing sheep offered a free choice between a low and a high protein ration are able to modify their diet selection in order to alleviate the increase in protein requirements which result from gastrointestinal nematode infection. Studies on the influence of nutrition on the expression of genotype have shown that the benefits of a superior genotype are not lost on a low protein diet whereas a high protein diet can partially ameliorate the disadvantages of an inferior genotype. In addition to dietary protein both macro-minerals and trace elements can influence the host-parasite relationship. Copyright © 1996 Australian Society for Parasitology. Published by Elsevier Science Ltd.

Key words: Gastrointestinal nematodes; dietary protein; ruminants; feed intake; parasite establishment; genotype; feed selection; immune response; resistance; pathophysiology.

INTRODUCTION

This overview primarily focuses on the interaction between nutritional status and gastrointestinal nematode infection in ruminants drawing attention to recent areas of research and future directions. Regulation of nematode populations in ruminants is complex and is influenced by host age, breed, immunological and nutritional status. This interaction between parasitism and nutrition can be considered from 2 inter-related aspects, firstly the influence of the parasite on metabolism of the host and secondly the effect of host nutrition on the parasite populations and the ability of the host to withstand the pathophysiological disturbances of infection.

INFLUENCE OF INFECTION ON THE NUTRITIONAL STATUS OF THE HOST

Over the last 20 years considerable research has been directed towards investigation of the overall and specific effects of parasitism and the mechanisms of impaired productivity in both cattle and sheep. Using trickle-infections of abomasal and intestinal nematodes or concurrent infections it has been established that parasitism can impair live-weight gain, soft-tissue deposition, skeletal growth, milk and wool production (Parkins & Holmes, 1989; Poppi et al., 1990; Holmes, 1993; Sykes, 1983, 1994). The carcases

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of parasitised ruminants generally contain less protein than uninfected controls (Sykes, 1983; Entrocasso et al., 1986). The use of pair-fed and ad-libitum fed controls has shown that reductions in feed intake and in the efficiency of feed utilisation are responsible for the reduced productivity, the relative importance of each being dependent upon the species of nematode, the rate of intake of larvae and the site of infection.

Detailed experiments investigating the underlying mechanisms of host dysfunction have shown a key feature to be the increased endogenous loss of protein into the gastrointestinal tract, partly as a result of leakage of plasma protein but also from increased exfoliation of gut epithelial cells and mucoprotein secretion (Poppi et al., 1986; Bown et al., 1991a). The leakage of plasma protein has been quantified (Parkins & Holmes, 1989) but due to technical difficulties the protein losses arising from increased turnover of the gastrointestinal tract in parasitised ruminants are unknown. Symons & Jones (1983), showed increased protein synthesis of the gastrointestinal tract of guinea-pigs infected with *Trichostrongylus colubriformis* and more recently MacRae (1993) has calculated protein turnover rates for different body components in sheep.

In abomasal infections the majority of the endogenous losses will be reassimilated (Rowe et al., 1982) although they may be absorbed partly as non-protein nitrogen (Rowe et al., 1988). In intestinal parasitism a greater proportion may be lost to the animal (Poppi et al., 1981; Bown et al., 1984) although compensatory increases in absorption can occur (Poppi et al., 1986). The increased flow of protein N at the ileum is largely responsible for the reduction in protein retention seen in parasitised ruminants (Poppi et al., 1986; Kimambo et al., 1988; Rowe et al., 1988). This recycling of protein has an energy cost and it has been shown using pair-feeding studies that the gross efficiency of use of ME for energy deposition is decreased by both abomasal and intestinal infections (Sykes & Coop, 1976; 1977; Sykes, 1983). Overall, there is a net movement of protein from productive processes such as meat, bone, milk and wool production into the synthesis of plasma proteins and repair of the gastrointestinal tract and mucus secretion (Steel et al., 1982; Symons, 1985; Bown et al., 1986).

It is well established that a reduction in voluntary feed intake is one of the major factors contributing to the reduced performance of parasitised ruminants (Sykes & Coop, 1976; Symons & Hennessy, 1981; Coop et al., 1982; Sykes et al., 1988), although very little is known about the mechanisms involved in the induced depression of intake (Sykes, 1983; Symons, 1985). Several hypotheses have been postulated for this reduction in voluntary feed intake, such as alterations in availability of amino acids, changes in flow rates and pH of digesta, alteration in gut peptides or hormones or direct neural effects on the central nervous system. Recently, 2 of these aspects have been investigated in greater detail.

Studies in cattle experimentally infected with *Ostertagia ostertagi* have shown associations between reduced feed intake, elevated blood gastrin concentrations and reductions in the rate of passage of digesta (Fox et al., 1989b, 1989c). They suggested that the increase in gastrin may reduce reticulorumen motility, inducing stasis of ingesta, thus leading to a reduction in feed intake. Subsequently, these authors (Fox et al., 1989a) showed that when endogenous blood gastrin levels were raised indirectly in worm-free calves by the administration of a gastric acid secretion inhibitor, omeprazole, a marked reduction in feed intake was induced. This association between elevated gastrin and depression of appetite needs to be confirmed in other nematode infections. One suggestion has been to block/inhibit the action of gastrin and observe whether feed intake increases (Poppi et al., 1990).

Dynes et al., 1990 examined the role of 2 factors which may affect depression of feed intake by antagonising various pathways and monitoring eating patterns. The addition of a potent competitive antagonist of peripheral cholecystokinin (CCK) action had no effect on short-term intake suggesting that peripheral CCK is not directly involved in parasite-induced depression of appetite. When the satiety effect at the hypothalamus was blocked through the diazepam receptor with a benzodiazepine drug short-term feed intake increased significantly in both control and in *T. colubriformis*-infected sheep, suggesting that reduction of feed intake may involve central satiety signals. The hypothalamus is an important site for the integration of peripheral and central signals involved in the regulation of food intake. Several hypothalamic neuropeptides are considered to play a role in central control of appetite including neuropeptide Y (a stimulator of appetite) and corticotropin-releasing factor (an inhibitor of food intake). Recent studies in rats infected with the intestinal nematode *Nippostrongylus brasiliensis* (Horbury et al., 1995) have shown that anorexia was accompanied by increases in neuropeptide Y gene expression in the hypothalamic arcuate nucleus. However, the animals did not feed in response to activation of the neuropeptide Y-ergic system and there were no significant differences in corticotropin releasing factor gene expression in the anorexic animals. Clearly, further research is required to
establish the role of neuropeptides and also investigation of the potential involvement of cytokines in nematode-induced anorexia in ruminants needs to be undertaken.

The question now arises as to whether one can manipulate nutrition to the advantage of the host by increasing the supply of protein to assist the repair of the gastrointestinal tract and provide an effective immune response. As considered above, although the gastrointestinal tract may be locally damaged there appears to be little effect on protein digestion and absorption per se and therefore it may be beneficial to provide additional protein at the duodenum. This could be achieved by increasing overall feed intake or by increasing the proportion of rumen undegradable protein in the diet. As the mechanisms of appetite depression are not known, manipulation of feed intake is currently not possible. The second option has been the centre of considerable research over the last 5 years and is considered below.

**INFLUENCE OF NUTRITION ON PARASITE ESTABLISHMENT**

The nature of the immune response to gastrointestinal nematodes varies considerably at different stages of infection. The stages include effectors against parasite establishment, effectors against existing mature infections and effectors against reinfecction. There is evidence to suggest that the influence of nutrition varies with these different stages. To date, much of this evidence has been obtained from experimental studies in housed animals where the diet and level and type of infection can be controlled. This section considers the effects of diet on parasite establishment in naive animals. This can be determined most easily in studies in which a single infection is given to animals which have already been established on specific diets. In other situations in which trickle (continuous or repeated) infections are given it is more difficult to distinguish between the effects on initial infection and the responses to mature and new infections, although it is recognised that trickle infections more closely resemble the situation in the field.

Early studies to investigate the influence of protein intake on parasite establishment were conducted by Bawden (1969) and Dobson & Bawden (1974) in sheep given either a low protein (60g CP/kg DM) or a high protein (190g CP/kg DM) diet and later infected with *Oesophagostomum columbianum*. Their studies showed that initial establishment was not affected by the protein content of the diet although the number of adult parasites present at slaughter on day 56 post-infection was higher in lambs on the low protein diet. Abbott, Parkins and Holmes conducted a number of such studies in the 1980s in lambs infected with *Haemonchus contortus*. In an early experiment (Abbott, Parkins & Holmes, 1985a) 14 3-month old Scottish Blackface worm-free female lambs were divided into 2 groups and established on a low protein (LP; 88g CP/kg DM) or a high protein (HP; 170g CP/kg DM) diet and later infected with 125 *H. contortus* larvae/kg body weight. The lambs were killed 5 and 14 weeks after infection and the worm burdens assessed. Faecal egg counts increased rapidly in both dietary groups to maximum values of 15,000 epg in the high protein group and 12,000 epg in the low protein group 6 weeks after infection. The mean worm burden in the 3 HP lambs killed 5 weeks after infection was higher (816 range 750–850) than in the LP group (550 range 350–700) but the difference was not significant. In a later experiment similar diets were given but a different breed and higher parasite challenge were used. In the experiment (Abbott et al., 1986a, 1986b) Finn-Dorset/Dorset-Horn castrated male lambs were introduced to a high protein (HP; 169g CP/kg DM) or low protein (LP; 88g CP/kg DM) diet at 3-months of age. The LP diet supplied adequate energy but a sub-optimal amount of protein for growth of about 120 g/d; while the HP diet supplied more protein than is required for that daily weight gain. At 4-months of age 4 lambs from each group were infected with 350 larvae/kg body weight of *H. contortus* and 4 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. Various pathophysiological parameters also were measured during the 6-week study. The diet had no apparent effect on either the faecal egg counts or the worm burdens, which were similar in both groups of sheep. However, the diet did appear to affect the ability of the lambs to withstand the pathophysiological consequences of infection with *H. contortus*. Adverse clinical signs including anorexia were observed more frequently in the infected lambs on the poorer plane of nutrition (Abbott et al., 1986a).

In most other reported studies trickle infections have been given on a daily or weekly basis over long periods to sheep on various nutrient intakes and it is not possible to distinguish clearly between the effects of diet on parasite establishment, persistence of adult parasites and the onset of immunity. However, in some experiments *post mortem* examinations have been performed on some of the sheep relatively early in the infection. In the study of Bown et al. (1991b) the effect of post-ruminal infusions of protein (50.4 g CP/day) or energy (in isocaloric amounts to the protein infusion) were compared with non-infused...
sheep infected daily with 3000 T. colubriformis larvae for 12 weeks. The protein infusion was calculated to replace the endogenous protein lost irreversibly beyond the terminal ileum. In lambs killed 6 weeks after the commencement of infection the worm burdens were similar in the protein-infused and non-infused groups. Similarly, in the recent studies of van Houtert et al. (1995) in which 2 levels of fish meal supplement (50 or 100g/day) were given to lambs infected thrice weekly with 1000 T. colubriformis larvae, the levels of protein intake did not affect mean faecal egg counts or mean worm burdens during the first 70 days of infection. Establishment rates of initial parasite establishment in naive sheep, although that protein intake does not appear to influence no effect on the rate of worm establishment.

Establishment rates of larvae in infected sheep, assessed by the presence of 9-day-old worms at slaughter, were unaffected by fish meal supplementation at any time. Changes in the mean worm burdens in lambs killed at days 105 and 140 showed that the supplemented animals were more able to expel established worms. A recent experiment (Coop & Jackson, unpublished) in which 4 month-old lambs were trickle-infected with Teladorsagia (formerly Ostertagia) circumcincta larvae (2000 L₃ daily for 10 weeks) and offered a basal ruminant ration supplemented (203 g CP/kg DM) or non-supplemented (143 g CP/kg DM) with 10 per cent fish meal has provided additional information. In this experiment the worm burdens in 2 groups of challenge controls (previously worm-free and offered the low or high protein diet) killed 10 days after receiving a single dose of 50,000 T. circumcincta L₃ were similar (20,250 vs 22,000), suggesting that the additional protein supplement had no effect on the rate of worm establishment.

The general consensus from these various studies is that protein intake does not appear to influence initial parasite establishment in naive sheep, although the pathophysiological consequences are usually more severe in animals on lower planes of protein intake. Early evidence that a high level of dietary protein may be beneficial to animals with established infections was provided by investigations into the influence of diet on the recovery of housed sheep with heavy mixed infections which were acquired whilst at grass. Although there were differences in the design of the various experiments, the main conclusions were that animals transferred to a higher protein diet generally showed an improvement in their clinical condition, a reduction in faecal egg counts and were more resistant to re-infection than the animals on a basal ration (Laurence et al., 1951; Brunsdon, 1964).

In addition, Clunies Ross & Gordon (1933) showed that acquired resistance to H. contortus infection in old sheep could be reduced by feeding a low protein diet. However, the diet had to be extremely low in protein (<30 g CP/kgDM) to cause weight loss before resistance was successfully overcome. Once again, these interesting observations have not been evaluated critically under controlled conditions.

In all the studies reported to date in which experimental trickle (continuous)-infections have been given over prolonged periods the plane of nutrition has been established prior to infection and maintained unchanged throughout the study, so it has not been possible to evaluate accurately the influence of nutrition on established infections. However, in such studies there is evidence that the level of dietary protein intake significantly affect the immune response and this is reflected in reduced faecal egg counts, reduced worm burdens and enhanced resistance to reinfection in animals receiving diets with higher levels (approximately >120 g CP/kg DM) of protein. We believe there is a need to examine, under controlled experimental conditions, the impact that changes in nutrient intake may have on established infections since seasonal changes in feed quality and quantity are likely to have significant influences on the responses of the host to its parasite burden and the epidemiology of the infection.
effect on the response to vaccination whereas a high protein diet (169 g CP/kg DM) has been shown to increase host resistance to infection with *H. contortus* in 4-month old lambs (Abbott *et al.*, 1988). Similarly, Kambara *et al.* (1993) investigated the effect of 2 levels of dietary protein (110 g CP/kg DM and 200 g CP/kg DM) on the acquisition of immunity in lambs infected with *T. colubriformis* and showed that dietary protein supplementation increased the resistance of lambs of 2–6 months of age but the effect was not apparent in sheep of 8–12 months of age. It is recognised that young growing lambs of less than about 6 months of age acquire immunity to gastrointestinal nematode infection at a slower rate than older sheep (Manton *et al.*, 1962; Urquhart *et al.*, 1966; Gibson & Parfitt, 1972; Dineen *et al.*, 1978).

Smith *et al.* (1985) investigated the response of 4½- and 10-month-old primed lambs to challenge with *T. circumcincta* and showed that the susceptibility of the younger lambs was associated with a reduced local immune response in the gastric lymph. The reason for these differences are unclear as very young lambs are capable of initiating an effective immune response against a range of viral and bacterial infections.

In the previous section, evidence has been presented which shows that the nutritional status of the host can influence the acquisition of immunity in ruminants as assessed by reductions in the number, size and fecundity of the worm populations. More recently, the influence of dietary supplementation on humoral and cellular responses to gastrointestinal nematode infection have been investigated. Kambara *et al.* (1993) studied the acquisition of resistance and associated immune responses to continuous *T. colubriformis* infection in lambs offered a low (110 g CP/kg DM) and a high (200 g CP/kg DM) level of dietary protein and at 2 different ages (2–6 months and 8–12 months). Although their data show that unresponsiveness of the young lamb can be improved by dietary supplementation lymphocyte responsiveness to T-cell mitogens and responses to L₃ antigens were not significant in the young lambs but were greatest in the older infected animals on the high protein diet. They concluded that these mechanisms are unlikely to play a major role in the acquisition of immunity in young lambs receiving a high dietary protein supplementation. Recently, van Houtert *et al.* (1995) have reported on the influence of 2 levels of dietary “protected” protein supplementation (50 or 100 g fish meal/day) on the immune responses of 3-month-old Merino lambs trickle-infected with *T. colubriformis*. The worm burden data from animals killed at 35, 70, 105 and 140 days of infection indicate that the apparent rate of worm expulsion increased with increasing levels of fish meal supplementation and that in the later stages of the experiment this expulsion correlated with the concentration of eosinophils in the peripheral blood. A significant increase (up to 13-fold) occurred in the concentration of mast cell proteases in the intestinal mucosa of the infected supplemented lambs compared to the uninfected controls. Mast cells and their secretory products and eosinophils are frequently associated with developing resistance to gastrointestinal nematodes (Huntley *et al.*, 1987; Rothwell, 1989; Rothwell *et al.*, 1993) although in this experiment worm expulsion appeared to precede the increase in sheep mast cell protease. Variable responses to protein supplementation were seen in the level of specific and non-specific circulating antibodies but in general the levels were unaffected by improved protein nutrition, a finding which contrasts with recent studies on fish meal supplementation in *Nematodirus battus*-infected lambs in which there was an enhancement of serum anti-worm IgG titres (Israf *et al.*, 1996). Similarly, the lymphocyte stimulation indices to a range of mitogens were generally unaffected although supplementation with the highest level of fish meal enhanced the stimulation index to *T. colubriformis* L₃ antigen in infected sheep. Recent studies (Coop *et al.*, 1995) on direct infusion of protein (45 g of crude protein/day) into the abomasum of lambs trickle infected with 2000 *T. circumcincta* L₃ per day for 8 weeks have shown an increased concentration of gastric mast cell protease (MCP) in lambs killed 10 days after a single challenge of 50,000 *T. circumcincta* L₃ (given 1 week after removal of the primary infection) when compared to the levels in naive challenge controls. This MCP response was significantly greater in protein-supplemented lambs and was correlated positively with the proportion of early 4th stage larvae in the gastric mucosa and negatively with the total worm burden. Using a similar *T. circumcincta* trickle infection (2000 L₃ daily for 10 weeks) and challenge regimen (50,000 L₃) but in lambs offered either a basal ruminant ration (143 g CP/kg DM) or the ration supplemented with fish meal (fish meal constituted 10% of the ration) it was shown that protein supplementation increased the number of mast cells (223 vs 42 cells/villus-crypt unit), the number of globule leucocytes (119 vs 18 cells/villus-crypt unit) and the concentration of MCP (219 vs 115 µg/g wet wt) in the gastric mucosa (Coop & Jackson, unpublished data). Mean worm burden was reduced by 58% in the protein supplemented previously infected challenged lambs and the area under the primary egg count curve was approximately 2.5-fold lower than that of the lambs which received the basal ration.
Recent experiments have been undertaken to see whether urea supplementation can produce the same beneficial effects as occur with dietary protein. Wallace et al. (1994) showed that the pathophysiology of H. contortus infection in a genetically susceptible breed (Hampshire Down sheep) can be reduced by the addition of urea (\(= 60 \text{ g CP/kg DM}\)) to the basal ration containing 88 g CP/kg DM but only if feed intake is sufficient for both growth and maintenance.

Knox et al. (1994) investigated the effects of urea supplementation on gastrointestinal parasitism in 4-month-old Merino wethers fed low quality roughage diets in controlled pen studies. Lambs were offered either oaten chaff or oaten chaff containing 3% urea. Faecal egg counts were lower and worm burdens reduced in the lambs supplemented with urea. The effect of urea supplementation could be partly attributed to an increase in intake of the basal diet but also to increased availability of microbial protein. In contrast, similar studies in young goats (Knox & Steel, 1995) showed that T. colubriformis burdens and faecal egg counts were not reduced in animals fed a hay diet supplemented with 2% urea alone, whereas urea supplementation plus 100 g of cottonseed meal per day increased productivity. Singh et al. (1995) compared production and parasitological parameters in young goats infected with 1000 T. colubriformis larvae 3-times per week for 21 weeks and offered a basal ration (95% oaten chaff and 5% lucerne chaff) with either 3% urea–molasses blocks (UMB), 15% UMB or 15% UMB plus 100 g cottonseed meal per goat per day. Total worm burdens at week 21 were lowest in the goats which received the urea plus cottonseed meal. Antibody levels to T. colubriformis and peripheral eosinophil counts increased during infection, the greatest response occurring in the goats fed the UMB plus cottonseed meal. The results indicate that supplementation with urea–molasses blocks alone will not fully overcome the adverse effects of parasitism whereas protein supplementation plus UMB increases the resilience of the host.

To date, the majority of experiments have been conducted with penned animals trickle-infected with larvae and little information is available on the interactions between protein nutrition, the development of acquired immunity and the pathogenesis of gastrointestinal nematode infections in grazing ruminants. Recent studies have assessed the effects of additional protein supplementation on the development of resilience to gastrointestinal parasitism in grazing sheep (Shaw et al., 1995; van Houtert et al., 1995) and also the effect of improved dietary protein supply through grazing lambs on grass/clover pastures (Vipond et al., 1994) and this aspect is considered in more detail elsewhere in this volume of International Journal for Parasitology.

It is apparent from these studies that only limited information is available on the effects of supplementation on immune responses in parasitised ruminants. One might expect the level of protein nutrition to influence many components of the effector arm such as immunoglobulins, mucoproteins and cellular products such as leukotrienes, as they are proteinaceous in nature. Indeed, the data of Bown et al. (1991b) indicate a specific role of protein intake in the acquisition of resistance and resilience during larval challenge. It seems reasonable to suggest that there may be competition for available nutrients between the requirement to mount an effective immune response and the maintenance of growth in the young parasitised animal which has a high metabolisable protein requirement relative to energy demand. Once the animal’s rate of growth declines and it starts to attain a mature body weight, the demands of the immune response may be able to be more fully satisfied. This partitioning of available nutrients between growth and immune responses could in part explain the immune unresponsiveness of the young ruminant to gastrointestinal nematode infection. The addition of a “protected” protein would increase the availability of amino acids at the small intestine and possibly enable the young growing lamb to mount a more effective immune response. The acquisition of immunity will have a cost penalty but currently we have no quantitative estimates of this penalty where animals are maintaining their immune competence under continuous larval challenge.

**INFLUENCE OF NUTRITION ON EXPRESSION OF GENOTYPE**

Even when maintained on similar planes of nutrition ruminants show considerable variation in susceptibility to parasitic infections as a result of genetic variation. With the increasing interest in the exploitation of genetically resistant livestock to control helminthiases and the findings that low planes of nutrition can exacerbate the pathogenic effects of gastrointestinal helminthiasis it is important to determine if the benefits of genetic resistance are easily lost when nutrition is sub-optimal. An initial experiment conducted at the Glasgow Veterinary School indicated that diet and expression of genotype are interactive. In this study Abbott et al. (1985a); Abbott et al. (1985b) the same HP and LP diets as used in their previous studies (170 g CP or 88 g CP/kg DM) were fed to groups of lambs of 2 breeds (Finn-Dorset and Scottish Blackface) known to differ in their
susceptibility to haemonchosis (Altaif & Dargie, 1978). The lambs were then given a single infection of 125 *H. contortus* larvae/kg body weight. 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. The results indicated an additive detrimental effect of genetic susceptibility and poor diet but also showed that the expression of genetic superiority in terms of disease resistance was not compromised by poor nutrition, at least at this level of a single moderate infection.

Subsequent studies in Glasgow using similar diets (173 g CP or 98 g CP/kg DM) have investigated the nutrition/genotype interaction in larger groups of sheep and using heavier parasite challenges. In a study using pedigree Hampshire lambs, a breed known to be relatively susceptible to haemonchosis (Preston & Allonby, 1979), an initial infecting dose of 100 *H. contortus* larvae/kg body weight was given and followed by a trickle-infection of 200 larvae 3-times per week for 10 weeks (Wallace et al., 1995). This infection regimen was designed to provide moderate establishment and a continuous low level exposure to parasites, leading to a sub-clinical infection. A similar study using lambs of a relatively resistant breed, Scottish Blackface, was conducted in parallel using an identical protocol (Wallace et al., 1996). As anticipated, the Scottish Blackface lambs had lower worm burdens (1367 vs 1795) and lower faecal egg counts (6000 vs 22000 epg at day 35) than the Hampshire lambs. The number of eggs per female worm were also lower. However, within the Scottish Blackface lambs diet did not influence these parasitological parameters whilst in the Hampshire lambs the higher protein diet (173 g CP/kg DM vs 98 g CP/kg DM) did reduce the faecal egg count between 30 and 70 days post-infection. The severity of the clinical and pathophysiological changes was also influenced by the breed with the Scottish Blackface lambs showing less anaemia than the Hampshire lambs on the same diets. However, within each breed diet did influence these parameters with animals on the lower protein diet being more anaemic, hypoproteinaemic and hypoalbuminaemic than animals receiving the higher protein diet. These dietary influences were more pronounced in the Hampshire lambs. These results, and the earlier ones of Abbott et al. (1985a,b), clearly show that protein supplemented diets can significantly reduce the pathophysiological changes associated with haemonchosis in genetically susceptible and genetically resistant animals. However, these effects are more pronounced in the former breeds and less critical in the latter breeds. This indicates that the benefits of a superior genotype are not lost on a low protein diet whilst a high protein diet can help overcome the disadvantages of an inferior genotype.

**EVIDENCE OF FEED SELECTION BY PARASITISED RUMINANTS**

It does not seem unreasonable to suggest that animals are able to monitor their nutritional status and adjust the quality and quantity of their diet to meet changes in demands. An early report suggested that goats became more selective in their diet during the course of infection with coccidia (Aumont et al., 1984). Infected goats given access to hay became more selective in their diet from a single feed, so that during the course of the infection the following changes were observed: a fall in the content of organic matter and of dry matter plus a decrease in crude fibre and an increase in nitrogen content in the dry matter ingested. These variations were particularly pronounced in those infected animals which excreted the highest number of ooyysts. It has been established recently that monogastric animals given access to 2 foods as a choice which differed in their protein composition are able to select a diet of higher protein content and meet their protein requirements during the early phase of growth (Kyriazakis & Emmans, 1991; Shariatmadari & Forbes, 1993). More recently, it has been shown that sheep are able to select a ration which meets the requirements for rapid growth and avoids excess intake of protein when offered a choice between 2 diets with different protein to energy ratios (Hou et al., 1991; Kyriazakis & Oldham, 1993). These observations raise the question as to whether young growing sheep infected with gastrointestinal nematodes are able to modify their diet selection in order to alleviate the increase in protein requirements which results from infection. A pilot experiment (Kyriazakis et al., 1994) suggested that sheep trickle-infected with *T. colubriformis* were able to adjust their diet selection by increasing the proportion of a high protein ration consumed but the trial was of insufficient duration to assess the long-term effects, in particular, during the development of immunity. Between weeks 4–8 of infection the infected animals consumed approximately 30% more of the high protein ration compared to uninfected controls.

Recently, a longer term trial has been conducted (Kyriazakis et al., 1996) in which lambs were infected daily with 2500 L3 *T. colubriformis* for up to 27 weeks and offered a free choice between 2 feeds (86 g CP/kg or 206 g CP/kg fresh weight) each with the same ME...
concentration (10.4 MJ/kg FW) and non-limiting in minerals and vitamins. Parasitism reduced the average daily feed intake from week 5 to week 12 and over the 27 week period it was 0.92 of the controls. The proportion of the high protein diet selected by the infected lambs started to increase around week 5 and remained elevated above that of the uninfected controls up to week 20 of infection (mean high protein diet selected by infected animals over weeks 5–18 was 749 g/kg total feed intake compared to a mean of 646 g/kg total feed intake for the uninfected controls). Some of the difference in diet selection between the infected and control sheep could be due to differences in growth rates of the lambs as the infected lambs grew at a slower rate within a comparable time interval and hence would be expected to have a higher protein requirement in relation to energy than the controls. However, if one compares the diet selection between a standardised weight range the proportion of the high protein diet selected was still higher in the parasitised lambs, 787 vs 699 g/kg total feed intake in the controls.

Recent trials in which lambs were infected daily with 4000 *T. circumcincta* L₁ for 18 weeks and offered a free choice between a low (86 g CP/kg FW) and a high protein (188 g CP/kg FW) ration have confirmed these findings (Kyrizakis & Coop, unpublished data). A reduction in voluntary food intake commenced from week 2 of infection and continued up to weeks 5–6 after which it gradually returned to control levels. The proportion of the high protein feed selected by the parasitised sheep increased from week 4 and remained elevated up to week 8 of the infection. The changes in diet selection occurred earlier and were of shorter duration in the *T. circumcincta*-infected lambs compared to those given *T. colubriformis* infection. The timing of the increase in selection of the higher protein feed in both the abomasal and intestinal nematode infection experiments coincided with the period when it has been shown that plasma protein leakage occurs and an increase in protein requirements would be expected. The mechanisms involved in diet selection are currently unknown but their elucidation may enable manipulation to the advantage of the host. In the light of these experimental findings it would be useful to investigate whether parasitised sheep can modify their diet selection when grazing pastures of differing nutrient composition such as grass/clover swards.

**OTHER FACTORS IN FEED INFLUENCING PARASITE INFECTIONS**

This overview has focused primarily on protein supplementation as recent research has been directed towards this area. However, there is considerable evidence to show that both macro-minerals and trace elements can influence the host–parasite relationship. The majority of studies have investigated effects of gastrointestinal parasitism on phosphorus (P) metabolism; early work showed that intestinal nematode infections can impair the apparent absorption of P from the intestine, reduce retention of P (Wilson & Field, 1983; Poppi et al., 1985; Bown et al., 1989) and result in reduced mineralisation of the skeleton (Sykes et al., 1975; 1979). These parameters were unaffected by infection with an abomasal nematode *T. circumcincta* (Wilson & Field, 1983). Few studies have investigated phosphorus supplementation of nematode infections as it may be difficult to increase the availability of P to the tissues due to the impaired absorption. However, Coop & Field (1983) were able to show that an increase in the P content of the diet (from 1.88 to 2.75 g P/kg DM) increased the weight gain of lambs receiving 2500 Trichostrongylus vitrinus L₃/day. The faecal egg counts and total *T. vitrinus* burdens were higher (10,950 worms) in lambs receiving the low P diet compared to those on the high P ration (1240 worms), suggesting that P levels may impair the development of resistance to continuous infection.

Although trace element deficiency and nematode infections occur concurrently in many grazing situations the precise inter-relationships have received little attention. Bang et al. (1990a) showed that infection of sheep with *T. circumcincta* affected copper (Cu) metabolism primarily through the elevation of the pH of the abomasum. The data suggest that reduced abomasal acidity decreases the solubility of administered copper oxide wire particles (COWP) and hence lowers the uptake of Cu by the liver. Further studies (Bang et al., 1990b) showed that administration of COWP, which release soluble Cu in the abomasum, 5 days prior to infection with gastrointestinal nematodes reduced the establishment of *H. contortus* and *T. circumcincta* in treated lambs by 96 and 56% respectively. There was no significant effect of COWP treatment on the establishment of an intestinal parasite, *T. colubriformis*. The level of COWP administered was higher than the normally recommended level in order to ensure that abomasal soluble Cu concentrations were sustained. These findings need to be taken into account when assessing and treating Cu-deficiency in the field. Two recent trials have reported the effect of molybdenum (Mo) supplementation in sheep either trickle-infected with *T. vitrinus* or with *H. contortus* (Suttle et al., 1992a, 1992b). The addition of Mo to the diet reduced the worm populations by 23 and 78% respectively and higher numbers of intraepithelial mast cells occurred.
in the supplemented *Haemonchus*-infected lambs. Although Mo is a copper (Cu) antagonist the effects of Mo could not be attributed simply to Mo-induced Cu depletion. Indirect evidence suggested that Mo may enhance the immune response in addition to having a direct effect on the parasite. Selenium deficiency does not appear to affect resistance to nematode infection (McDonald *et al.*, 1989) whereas it has been reported that cobalt deficiency can induce higher faecal egg counts and increased pepsigenous levels in lambs experimentally infected with *T. circumcincta* (Ferguson *et al.*, 1989). Clearly, the role of these and other trace elements in the complex parasite/nutrition interaction merit further study.

**FUTURE WORK**

Although many aspects of the interaction between nutrition and helminth parasites have been established many features remain to be examined. These include the influence of nutrition on established infections, nutritional influences on immune responses to parasites and nutritional interactions with genetic resistance. There is clearly scope for examining the effects of supplementation in greater detail and improvements in supplementation through protected protein technology. The recent availability of protected amino acids will enable specific effects to be studied. Feed interaction and feed selection in parasitised ruminants require further investigation. There is also a need to examine metabolic responses to parasites at the tissue level and particularly with regard to changes in protein metabolism. Recently developed techniques (MacRae *et al.*, 1995) employing tracers to measure the arterial and lumenal sequestration of amino acids for protein synthesis of gastrointestinal tract tissues should extend the present understanding of the metabolic responses of the intestine to gastrointestinal parasitism. The exploitation of genetic resistance holds enormous potential as a sustainable method of parasite control. Preliminary evidence suggests that nutrition can markedly influence the expression of genotype. In order to successfully exploit these genetic traits the nutritional requirements of different breeds exposed to parasite challenge need to be evaluated. The intricate relationship between parasites and metabolism of the ruminant host and the influence of nutrition on this relationship, deserves greater study, not only because of the intrinsic importance of parasites as one of the major constraints to ruminant survival and productivity but also because of the fundamental knowledge these studies can provide on the interaction between ruminant metabolism, production and disease.

**REFERENCES**


