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Regulation of the resistance and resilience of periparturient ewes to infection with gastrointestinal nematode parasites by dietary supplementation

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Abstract. Control of gastrointestinal nematode (GIN) parasites has traditionally been based on the premise of chemotherapeutic control with the resultant consequence being the development of anthelmintic resistance by GIN. An alternative premise to the management of GIN parasites is to improve the resistance and resilience of sheep to GIN infection by manipulating the nutritional environment at key periods of a sheep's life. One key period, is the periparturient phase in the reproductive cycle when ewes experiences a temporary loss, or diminution, of immunity to GIN parasites. This phase is associated with a considerable increased requirement for both metabolisable energy (ME) and metabolisable protein (MP). The increased requirement being greater for MP. The loss of immunity to GIN is associated with a diminished cell-mediated immune response in the gut mucosa the magnitude of which can be regulated by protein nutrition, or more specifically the supply of MP. Experimental studies which have increased MP supply, in housed and grazing periparturient ewes, have demonstrated significant improvements in resistance to GIN infection. Positive gut immune responses to an increased MP supply are believed to occur because the increased MP supply counters the combined pathological

consequences of GIN infection *per se* and the host's immune response, namely a net loss of amino acids. Susceptibility to GIN infection in the periparturient ewe may also be a function of a low priority for use of MP toward immune function but evidence from young animals suggests a disproportionate partitioning of amino acids to the gastrointestinal tract during GIN infection. It is proposed that the priorities for use of MP which predispose the ewe to GIN infection are altered following infection to favour a gut immune response. Despite being under the regulation of MP supply and genetic selection, the loss of immunity during the periparturient period cannot be fully restored by either approaches suggesting that other unidentified factors are involved in the periparturient loss of immunity. Resilience to GIN infection is responsive to both ME and MP supply. The practice of supplementing periparturient ewes to increase MP and ME supply, in order to enhance resistance and resilience to GIN infection, is gaining favour with graziers within some regions of Australia. Other benefits (e.g. increased reproductive rates) arise from such supplementation strategies which improve the cost effectiveness of this approach.

Keywords: Sheep-nematoda, metabolisable protein, periparturient, sheep, resistance, resilience, immunity.

Introduction

Infection of grazing sheep by gastrointestinal nematode (GIN) parasites is the cause of significant economic loss to the Australian sheep industry with the cost of production loss, mortality and control estimated in 1995 at $220M (AUD) (McLeod 1995). Control of GIN parasites in grazing sheep has been based on the premise of chemotherapeutic treatment aimed at removing existing infections and more recently on the short-term prevention of reinfection. The consequence of chemotherapeutic dependency has been the

development of anthelmintic resistance by nematode parasites; a situation which is now endemic (Love and Biddle 2000) to Australian sheep farms and worsening in severity (Besier and Love 2003).

There is an alternative premise to the management of GIN parasites, that is to ascribe the susceptibility (also described as low resistance) of grazing sheep to infection as the primary cause of the production loss. Management systems to control GIN parasites built upon this premise seek ways to increase host resistance and resilience to infection. This can be achieved by either (or both) of 2 management strategies namely manipulating the nutritional environment at key periods of a sheep's life (Kahn *et al.* 1999; 2001) or by selective breeding for increased host resistance (Woolaston *et al.* 1990). Enhancement of host resistance and resilience to GIN infection by manipulation of the nutritional environment will be the focus in this paper.

The terms resistance, susceptibility, immunity and resilience are used to describe the response of a host to infection. Definitions of these terms, similar to that provided by Gray (1995) are provided. Resistance to infection is the ability of an animal to reduce the number of GIN parasites that establish, reproduce and survive. Resistance to infection is generally mediated by enhanced immune response but in its broadest sense, resistance may not always be the result of immunological changes but, for example be the outcome of changes in grazing behaviour resulting in reduced larval intake. Where a resistant animal will prevent or greatly reduce an infection a susceptible animal will not. Resilience is defined as the extent to which an infected animal is able to maintain production but is not necessarily independent of resistance.

Susceptibility to GIN infection

Grazing sheep often remain susceptible to infection from GIN parasites for at least the first 12-18 months of life. Even when resistance is attained a number of factors influence its degree and persistency namely, the level (Windon *et al.* 1984) and continuity (Barger 1988) of infection, host physiology and level of nutrition. The key physiological period that disrupts host resistance is the periparturient period, defined as the period shortly prior to and after parturition, during which the ewe experiences a temporary loss, or diminution, of immunity to GIN parasites evidenced by a rise in faecal egg count (FEC) and described as the periparturient rise (PPR) in FEC (O'Sullivan and Donald 1970). Underlying the PPR are increased rates of establishment of incoming larvae, increased fecundity and decreased rejection of established GIN parasites (Barger 1993).

Immunocompetence is not lost against all the major genera of GIN parasites. The periparturient ewe exhibits an increased susceptibility to infection with *Trichostrongylus colubriformis* (O'Sullivan and Donald 1973; Gibbs and Barger 1986) and *Teladorsagia circumcincta* (Brunsden 1970; Gibbs and Barger 1986; Jackson *et al.* 1988). In contrast, there appears to be only partial or no loss of immunity to *Haemonchus contortus* (O'Sullivan and Donald 1973; Gibbs and Barger 1986) or *Trichostrongylus vitrinus* (Jackson *et al.* 1988).

The loss of immunity characterised by the PPR is associated with a diminished cell mediated immune response in the gut mucosa. This response results in a reduction in (i) mast cell hyperplasia; (ii) generation of globule leucocytes; and (iii) eosinophil response (O'Sullivan and Donald 1973). It is possible that the reduced numbers of these effector cells during the periparturient period is a function of periparturient effects on the differentiation of immature precursor cells to effector cells (e.g. mast cells, globule leucocytes and eosinophils) as evidenced in lactating rats infected with *Nippostrongylus brasiliensis* (Dineen and Kelly 1972).

Predisposing factors for susceptibility of the periparturient ewe to GIN infection

The factors which predispose the reproductive ewe to the PPR have been the subject of much investigation and are generally considered to be mediated by hormonal or nutritional changes associated with pregnancy and lactation. A rise in plasma prolactin concentration following parturition had been suggested as being the primary cause for the PPR (Dunsmore 1965) but subsequent studies (Coop *et al.* 1990; Jeffcoate *et al.* 1990) have cast significant doubt on the importance of prolactin in the PPR.

The nutritional changes that predispose the ewe to the PPR are proposed to be a function of 3 factors namely, (i) the large increased requirement for both metabolisable energy (ME) and metabolisable protein (MP) due to the demands of the conceptus and for lactation; (ii) an imbalance between nutrient requirement and supply; and (iii) a low partial priority of the gut immune system for MP relative to usage for maintenance of body protein, pregnancy and lactation.

The increased requirement for ME and MP during pregnancy and lactation are considerable (Fig. 1). For example, a 50 kg single-bearing Merino ewe maintaining maternal liveweight and consuming a forage diet of 11.5 MJ ME/kg DM and 170 g CP/ kg DM typically requires 9.5 MJ ME/day at mating, 14.0 MJ ME/day 2 weeks before parturition and 23.0 MJ ME/day 3 weeks post partum when milk production will approach 1.7 kg/day. Over the same period, MP requirements are calculated to increase from 60 g/day at mating to 90 g/day 2 weeks before parturition and reach 190 g/day 3 weeks post partum (Freer *et al.* 1997). The requirement for MP relative to ME increases slightly during pregnancy and reaches its maximum value of about 8.5 g/MJ ME at peak lactation. Requirements for both ME and MP are further increased in the twin-bearing ewe such that MP:ME requirement approaches 9.0 g/ MJ ME.

INSERT FIGURE 1

Of equal importance to the PPR is the MP pressure which has been defined as the balance between MP requirement and MP supply (Kahn et al. 2003a). The MP pressure can be increased as a result of increased requirement – as is the situation during lactation – and as a result of reduced supply. In many commercial grazing situations, both mechanisms may be operative and contributing to the PPR. High MP pressure refers to situations where requirements exceed supply and low MP pressure where supply meets or exceeds requirements.

The third nutritional factor that has been proposed to predispose the reproductive ewe to the PPR is the low priority of the gut immune system for use of MP (Coop and Kyriazakis 1999). As a consequence of the low priority, maintenance of the gut immune system may be compromised during the periparturient period when MP requirements often exceed supply; this will discussed in detail later in this paper.

In summary, the periparturient ewe experiences an increased requirement for MP which predisposes it to an increased MP pressure. Contemporaneously, grazing periparturient ewes on commercial properties are often not provided with sufficient herbage of a quality which can meet the extra MP requirements resulting in a further increase in MP pressure. In addition, the gut immune system of the periparturient ewe is proposed to have a low partial priority for use of MP. Under these conditions, susceptibility of the periparturient ewe to GIN infection increases. When infected with GIN the pathological effects of resident GIN parasites and the actions of the gut immune system further increase MP requirements.

Consequences of GIN infection on protein metabolism

The importance of protein nutrition in the aetiology of the PPR is further increased by the response of the host to GIN infection and the direct pathological effects of resident GIN parasites, particularly blood loss induced by *Haemonchus contortus*. Infections with abomasal and intestinal GIN result in an increased loss of endogenous protein into the gut in the form of blood, plasma, mucin and sloughed cells (Kimambo *et al.* 1988; Rowe *et al.* 1988). Aside from the blood feeding activities of *H. contortus* (which may result in blood loss equivalent to 20 g crude protein/day (Rowe et al. 1988)), losses of other endogenous proteins are largely the result of the host immune response to infection. Rejection of both incoming infective larvae and established adults is associated with increased permeability and mucus secretion in the gut as a result of the release of mast cell derived mediators such as histamine, proteases, serotonin and leukotrienes (Balic *et al.* 2000). Losses of protein into the gut, as a result of GIN infection, can be substantial and have been estimated to be in the range 20-125 g crude protein/day with infections of *Trichostrongylus colubriformis* (Poppi *et al.* 1986; Kimambo *et al.* 1988).

Fortunately, for the nutrient economy of the grazing sheep, protein digestion and absorption is largely unaffected by GIN infection (Bown *et al.* 1984) and 75-100% of endogenous protein loss is reabsorbed prior to the ileum (Poppi *et al.* 1986; Rowe *et al.* 1988). There are, however, major metabolic inefficiencies as a result of this increased recycling of endogenous protein which result in a net loss of amino acids due to incomplete reabsorption and breakdown and catabolism of essential and nonessential amino acids with subsequent loss of amino groups as urinary urea. The net effect of these changes is an increase in the MP requirement of the animal.

In addition to a net loss of amino acids, GIN infection also results in changes to amino acid use and availability to various tissues (Yu *et al.* 2000; Bermingham *et al.* 2000). Using tracer kinetic studies, Yu *et al.* (2000) demonstrated that when young sheep

were infected with *T. colubriformis*, sequestration of amino acids by the gastrointestinal tract increased by about 25% with two-thirds of this increase occurring across the small intestine. As a direct result of increased amino acid sequestration, oxidative losses of amino acids across the gastrointestinal tract increased by about 30% providing a net amino acid loss, due to oxidative losses, equivalent to 6 g crude protein/day. Surprisingly, infection was observed to have no effect on whole-body protein synthesis because the availability of amino acids to skeletal muscle appeared to be reduced to a similar extent that usage by the gastrointestinal tract was increased.

The gastrointestinal tract is a metabolically active tissue which accounts for about 5% of total body protein in ruminants but about 30% of whole-body protein synthesis (Lobley 1994), with many of these proteins eventually being secreted into the gut lumen. Based on the findings of Yu *et al.* (2000) it can be calculated that GIN infection may increase mean protein synthesis in the gastrointestinal tract to 40% or more of whole-body protein synthesis. Increased usage of amino acids by the gastrointestinal tract during GIN infection, at times of constant whole-body protein synthesis, supports earlier observations (Symons and Jones 1985) that infection with *T. colubriformis* reduces the rate of protein synthesis in wool follicles and skeletal muscle.

The combined effects of GIN parasitism and the host response act in concert to increase endogenous protein loss - through incomplete reabsorption of secreted proteins and by increased protein oxidation in the gastrointestinal tract - and reduce availability of both recently-absorbed and circulating amino acids to commercially productive tissues such as skeletal muscle and wool follicles. These effects are consistent with the production losses experienced by sheep with GIN infections and the beneficial effects for host resistance and resilience that have been observed when sheep are supplemented to increase MP supply (discussed later in this paper).

Nutrient partitioning in the periparturient ewe

Partitioning of protein among various body tissues (e.g. skeletal muscle, internal organs, wool, mammary gland) is affected by factors such as hormones, nutrition and age (Nieto and Lobley 1999; Oddy 1999) and is also altered as a consequence of genetic selection for traits such as body weight (Thompson *et al.* 1985) and wool growth (Kahn 1996). The way that amino acids and peptides are partitioned in the periparturient ewe and how that may be influenced by GIN infection is central to understanding the basis of the nutritional regulation of the PPR.

With respect to the periparturient ewe, it appears that maintenance of immunity to GIN infection is not given a high priority. If this was not so, then, unless MP supply was grossly inadequate, MP may be preferentially partitioned to the gastrointestinal tract to support the gut immune system and diminish or even ablate the PPR. Recognising that this situation appears not to exist, Coop and Kyriazakis (1999) proposed that in the reproductive ewe, the MP requirements for immunocompetence have a lower partial priority than either the requirements of pregnancy, lactation or maintenance of body protein. In a practical context, this framework would predict that when MP supply was limiting, protein metabolism would be such that the insult to immunity to GIN would be considerably greater than effects on pregnancy (e.g. birth weights), lactation (e.g. milk yields) and body protein (e.g. repair and replacement of tissue).

The high partial priority for use of MP for maintenance of body protein implies that body protein will have only a very limited role in supplying a source of recycled amino acids for the gastrointestinal tract during GIN infection. The validity of this proposal has recently been questioned by Houdijk *et al.* (2001a) who demonstrated that the PPR was reduced in magnitude in lactating ewes that had a greater body protein mass at parturition.

These authors concluded that the positive effect of body protein mass on reducing the PPR may have been a consequence of the release of labile amino acids from tissue which would ultimately be available for use by the gut immune system during GIN infections. The importance of a source of labile amino acids from which the gut immune system may benefit during GIN infections is consistent with the observation (Yu *et al.* 2000) that over 80% of amino acid metabolism in the gastrointestinal tract is derived from arterial sources. On the basis of earlier results, Houdijk *et al.* (2001b) have suggested that the ordering of priorities for use of MP should be modified to allow for essential (high priority) and labile (low priority) components of body protein.

While there is evidence that an order of priorities for use of MP among various tissues exists, it is important to consider that these priorities are far from absolute. For example, Kahn *et al.* (2003a) demonstrated beneficial effects, from supplementation to increase MP supply, on reducing calculated maternal weight loss (presumably body protein) and FEC but no benefits for the proposed higher priority function of birth weight.

There may be at least two stages to the PPR which require separate consideration of possible nutrient partitioning priorities. The first stage may be concerned with factors that predispose the periparturient ewe to the loss or diminution of immunity to GIN and the second stage may involve priorities of nutrient use during the response to GIN infection. Predisposition to GIN infection in the first stage is argued by Coop and Kyriazakis (1999) to be a function of a low partial priority for use of MP by the gut immune system at a time when the requirements of the conceptus and/or the mammary gland are increasing. During the second stage, the partial priority of the gastrointestinal tract for amino acids involved in the gut immune response to GIN infection may increase to a point where it has priority over many other body tissues. This is the situation in young sheep acquiring immunity to

infection from *T. colubriformis* (Yu *et al.* 2000). Whether this situation holds in the infected periparturient ewe is uncertain.

The 2-stage framework can account for both the increased susceptibility to GIN infection and subsequent attainment of resistance. Importantly, the 2 stage framework does not provide a unique solution to the PPR phenomenon nor does it make redundant the importance of MP pressure. It has been demonstrated (O'Sullivan and Donald 1970) that factors which reduce MP pressure, such as decreased requirements for lactation associated with weaning, can terminate the PPR. Changes to both MP pressure and partitioning of MP may operate together to determine the magnitude of the PPR but this proposal remains to be verified.

Nutritional regulation of resistance to GIN infection

O' Sullivan and Donald (1970) provided evidence for the nutritional regulation of the PPR in an experiment which demonstrated the effect of weaning on FEC and worm counts. These authors observed a typical PPR, characterised by rising FEC, associated with lactation but weaning of lambs at about 7 weeks of age effectively interrupted the PPR. Over the 6 weeks that followed weaning, FEC of unweaned ewes continued to increase but declined in weaned ewes to a level similar to non-reproductive ewes. Worm burdens of ewes were determined 13 weeks after lambing at which time earlier-weaned ewes had significantly fewer established worms than lactating ewes. That weaning, which would have rapidly reduced MP and ME requirements for lactation, resulted in a substantial and almost immediate decline in FEC (relative to unweaned ewes) suggests strongly a causal, rather than associative, link between nutrient requirements and the PPR.

More direct evidence for the role of protein nutrition in regulating resistance to GIN infection is evidenced from nutritional studies which have increased MP supply to

periparturient ewes (Donaldson *et al.* 1998) and young animals (Bown *et al.* 1991, van Houtert *et al.* 1995). For example, Donaldson *et al.* (1998) infected Coopworth ewes with *T. colubriformis* and *T. circumcincta* for 7 weeks before parturition in a factorial experiment that continued until 3 weeks post partum and included 2 levels of ME and 2 levels of MP. Increased MP supply reduced FEC from 3 weeks prior to parturition, ME supply had little influence on FEC and there was no interaction. Worm burdens supported the FEC results and were reduced by 87% (12,020 to 1,540) in ewes which had a greater MP intake but were unaffected by ME intake (Fig. 2).

INSERT FIGURE 2

The importance of MP supply to the resistance of grazing periparturient ewes to GIN infection has also been confirmed (Kahn *et al.* 1999; Kahn et al. 2003a). One hundred and twenty Merino ewes, subjected to artificial and mixed field infections while grazing at pasture, were subjected to 1 of 3 supplement groups designed to provide, 0 or 250 g/day cottonseed meal (CSM; 92% DM; 920 g OM/kg DM; 8 g phosphorus (P)/ kg DM; 396 g CP/kg DM; *circa* 50% rumen undegradable dietary protein) pellets for 5 weeks before or 6 weeks after the start of parturition (Kahn et al. 2003a). Supplementation with CSM was expected (Freer *et al.* 1997) to increase supply of MP by approximately 45 g/day, sulphur amino acids by 1.5 g/day, phosphorus by 1.8 g/day and ME by 2.6 MJ/day. Prepartum supplementation reduced FEC but post partum supplementation was ineffective (Figure 3). Averaged over the 21-week experimental period, the 5-week period of prepartum supplementation reduced FEC by 43% (204 epg) relative to the unsupplemented control.

INSERT FIGURE 3

The beneficial effects of CSM supplementation on the resistance of grazing periparturient Merino ewes to GIN infection has been subsequently confirmed (Kahn *et al.*

2003b) in a similar experiment but significant benefits to FEC were only recorded during the post partum period. Variation in the temporal importance of supplementation were explained by the authors as a function of MP pressure. In both experiments (Kahn *et al.* 2003ab), significant benefits to resistance from supplementation were only recorded during periods of high MP pressure as indicated from estimated maternal weight loss.

While maternal weight loss may be a practical indicator of the likely magnitude of the PPR and subsequent immunoresponsiveness to increased MP supply it does not provide an indication as to the specific importance of body protein mass in the maintenance of immunity to GIN infection. Houdijk *et al.* (2001a) proposed that body protein mass (but not body fat) may have an important function in reducing the PPR by providing amino acids, during times of MP insufficiency, to support the response of the gastrointestinal tract to GIN infection. These authors fed twin-bearing ewes, infected with *T. circumcincta*, such that by 3 weeks prepartum they would either have maintained body protein and fat, maintained body protein and lost body fat or lost body protein and fat. At this stage, ewes were offered isoenergetic foods that allowed for either a low (*circa.* 210 g MP/day) or high (*circa.* 350 g MP/day) MP supply during late pregnancy and lactation.

Ewes fed to lose body protein and fat developed higher FEC (Fig. 4) during lactation but ewes fed to lose only body fat did not, indicating the importance of body protein mass in determining the magnitude of the PPR. These ewes also mobilised less body protein during lactation which led Houdijk *et al.* (2001b) to propose that the importance of body protein mass in regulating the PPR is as a source of labile amino acids able to be sequestered by the gastrointestinal tract (Yu *et al.* 2000) and used in the gut immune response. This proposition is supported by the observation that MP supply was considerably more effective in reducing FEC in those ewes which lost body protein and fat during pregnancy: although lower FEC was recorded for a period just in excess of 3 weeks.

Loss of body fat alone did not increase FEC indicating that body fat mass is not associated with the PPR.

INSERT FIGURE 4

Taken together, these experiments (discussed previously) support the premise that MP supply, both from dietary and microbial sources (exogenous) and body protein (endogenous), is inimically linked to the PPR. In addition, there is evidence that the relationship between MP intake and host resistance to *T. circumcincta* infection in periparturient ewes is almost linear (negative slope) over the range 175 – 350 g MP/day (Donaldson *et al.* 2001). Within this range of MP intake, it can be calculated, from the data provided by Donaldson *et al.* (2001), that *T. circumcincta* worm burdens would be reduced by approximately 5800 for every 100 g/day increase in MP intake.

Persistency of the periparturient rise in FEC

Despite being under the regulation of exogenous and endogenous MP supply and genetic factors, there is evidence (Woolaston 1992; Donaldson *et al.* 1998; Donaldson *et al.* 2001; Houdijk *et al.* 2001a; Kahn et al. 2003a) that MP supply *per se* cannot ablate fully the PPR. For example, Woolaston (1992) observed that Merino ewes, from a line which had been selected solely on the basis of low FEC after weaning for the previous 17 years, still exhibited a PPR, although much reduced relative to unselected ewes. After 23 years of selection, Kahn *et al.* (2003a) reported the existence of a PPR in ewes from the same genetically resistant line which also received supplementation with cottonseed meal pellets to increase MP supply.

The experimental evidence suggests that factors other than MP supply and genetic selection play a role in the PPR. I propose that the PPR *per se* is initiated by hitherto unidentified factors but that its magnitude is strongly regulated by MP supply and genetic

selection. Clarification of these unidentified factors is a matter of speculation but it seems probable that immune modulating agents such as hormones, other than prolactin (see above), or neuropeptides may play a role (Berczi and Nagy 1998).

Nutritional regulation of resilience to GIN infection

The major effect of GIN infection on nutrient supply is via a reduction in feed intake, particularly during lactation (Leyva *et al.* 1982), with specific effects resulting in a net loss of amino acids. Reduced feed intake also impacts on energy metabolism through a reduction in the gross efficiency of use of ME for production. The reduction arising from a greater fraction of total ME intake being used for maintenance and presumably by increased ME use by the gut associated with increased protein synthesis. There is therefore a solid basis to presume that ME and MP intake would be effective in regulating resilience to GIN infection.

In the experiment by Donaldson *et al.* (1998) as previously described, Coopworth ewes infected with *T. circumcincta* and *T. colubriformis* were offered foods to provide for 2 levels of ME and MP (Table 1). Over the 9 weeks prior to parturition, weight gain (including conceptus) was increased in single-bearing ewes by 50% (85 g/day) and in twin-bearing ewes by 45% (108 g/day) when offered foods that allowed for a higher ME intake. Weight gain also responded to an increased MP intake but to a much smaller degree.

INSERT TABLE 1

The increased resilience of periparturient ewes brought about by an increased ME intake is in contrast to that reported by Bown *et al.* (1991) for young sheep. On the basis of abomasal infusions of either casein or glucose, to young Dorset Down x Coopworth sheep infected with *T. colubriformis*, Bown *et al.* (1991) demonstrated that casein infusion increased body weight gain and N retention in the carcass of infected sheep to levels not

dissimilar to uninfected control sheep. Infusion with glucose also increased N retention but values were still 40% lower than control animals.

In contrast to the findings of Bown *et al.* (1991), Kahn *et al.* (2000) fed young Merino sheep, infected with *T. colubriformis*, diets formulated to provide for 2 levels of digestible energy (DE) and MP intake and reported that weight gain was responsive to both DE and MP intake. Increasing DE intake by 20%, from 0.28 MJ/ kg bodyweight to 0.34 MJ/kg bodyweight, resulted in a 133% increase in carcass gain, over a 10-week period. Increasing MP intake by 60% from 1.7 g MP/kg bodyweight to 2.7 g MP/kg bodyweight, resulted in a 93% increase in carcass gain. In the experiment reported by Kahn *et al.* (2000) DE intake reduced worm burdens and it is possible that this may account for the larger effects on resilience than induced by abomasal infusions of glucose.

To the best of my knowledge, there are no other reports in the literature which describes the relative benefits of ME and MP intake on the resilience of periparturient ewes to GIN infection. In the absence of other reports, I conclude that both ME and MP intake are able to regulate the resilience of periparturient ewes to GIN infection.

Conclusions

Manipulating the nutritional environment at key periods of a sheep's life to improve the resistance and resilience of sheep to GIN infection is proposed as an alternative to chemotherapy in the management of GIN parasites. One key period, is the periparturient phase in the reproductive cycle when ewes experience a temporary loss, or diminution, of immunity to GIN parasites. Increasing the supply of MP to periparturient ewes has been demonstrated to increase resistance to GIN infection under both housed and grazing conditions and MP from both exogenous and endogenous sources is important. In contrast, resilience to GIN infection appears to be sensitive to both ME and MP intake.

Increased resistance to infection appears to result from a positive association between increased MP supply and gut immune responses.

There is indirect evidence that partitioning of MP towards the gastrointestinal tract has a low partial priority relative to other body tissues in the (as yet resistant) periparturient ewe and that this low partial priority is one factor which predisposes periparturient ewes to a loss of immunocompetence and expression of the PPR. Priorities for partitioning of MP among body tissues may change during GIN infection to favour the reacquisition of immunity. Despite being under the regulation of MP supply, the loss of immunity during the periparturient period cannot be fully restored by nutrition. Maternal weight loss and more precisely body protein mass may be good indicators of the likely immunoresponsiveness of periparturient ewes to increased MP supply. The practice of supplementing periparturient ewes to increase MP and ME supply, in order to enhance resistance and resilience to GIN infection, is gaining favour with graziers within some regions of Australia. Other benefits (e.g. increased reproductive rates) arise from such supplementation strategies which improve the cost effectiveness of this approach.

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Table 1: Weight gain (including conceptus) of Coopworth ewes over the last 9 weeks of pregnancy when infected with *T. circumcincta* and *T. colubriformis* and offered foods to provide for 2 levels of metabolisable energy (ME) and metabolisable protein (MP) intake. Adapted from Donaldson *et al.* (1998).

No lambs born	ME intake (MJ/day)	MP intake (g/day)	Weight gain (kg)	Weight gain (g/day)
Single	9.8		10.6	167
Single	12.6		15.6	252
Twin	12.1		15.0	237
Twin	15.0		21.8	345
Single		86	12.4	197
Single		102	14.0	222
Twin		102	16.8	267
Twin		129	19.9	316

Figure 1. Calculated requirements for metabolisable protein (g/day; solid line) and metabolisable energy (MJ/day; broken line) of a 50 kg single-bearing Merino ewe when consuming a forage diet of 11.5 MJ ME/kg DM and 170 g crude protein/ kg DM. Calculated from Freer *et al.* (1997).

Figure 2. Worm burdens of Coopworth ewes determined 3 weeks post partum following a 10 week period of being fed diets that provided for a low (E1) and high (E2) metabolisable energy intake and a low (P1) and high (P2) metabolisable protein intake. Adapted from Donaldson *et al.* (1998).

Figure 3. Faecal egg counts of Merino ewes grazing at pasture which were either unsupplemented (circle) or supplemented with 250 g/day cottonseed meal pellets for the 5 weeks prior to (square) or 6 weeks after (triangle) the start of a 4 week lambing period. Adapted from Kahn *et al.* (2003a).

Figure 4. Faecal egg counts of Border Leicester x Scottish Blackface ewes infected with *T. circumcincta*, with low (solid lines) and high (dashed lines) body protein mass at parturition and fed foods that allowed for either a low (circles) or high (squares) metabolisable protein intake. Adapted from Houdijk *et al.* (2001a).

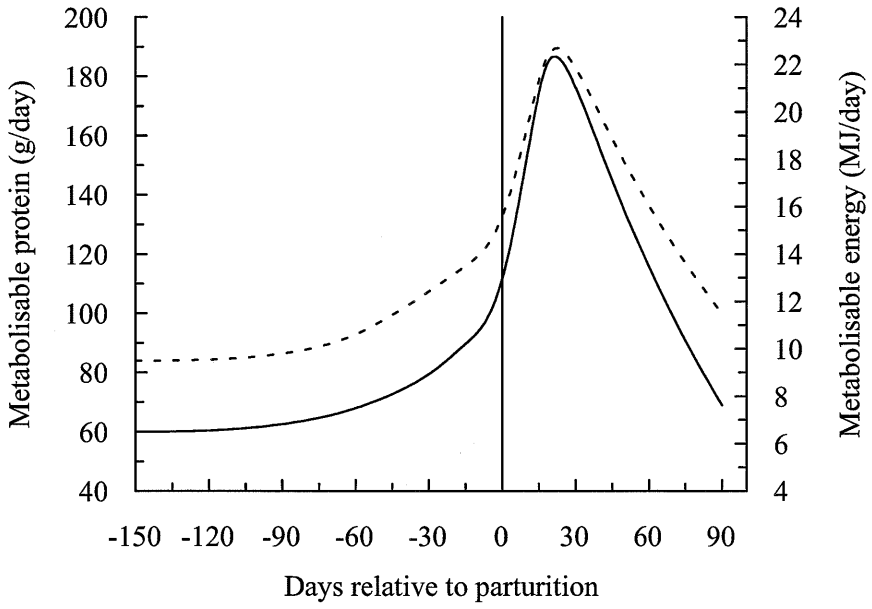

Figure 1.

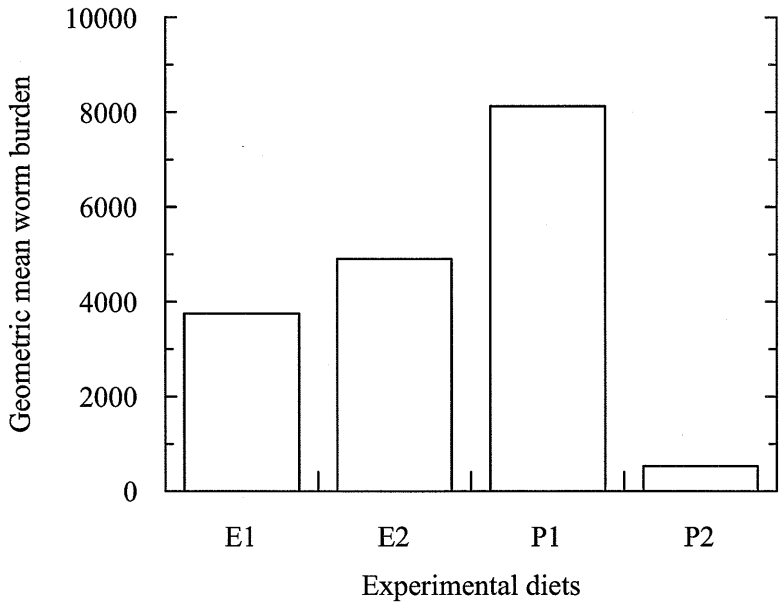

Figure 2.

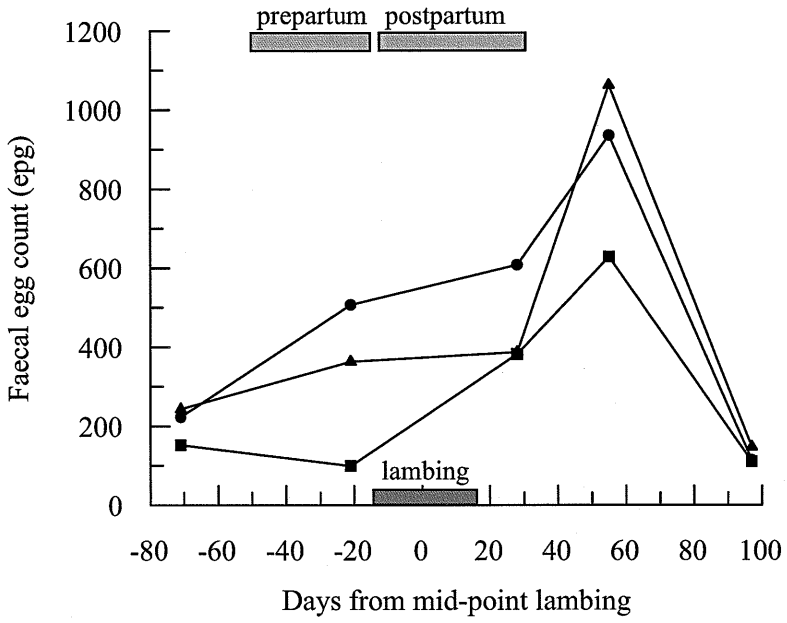

Figure 3.

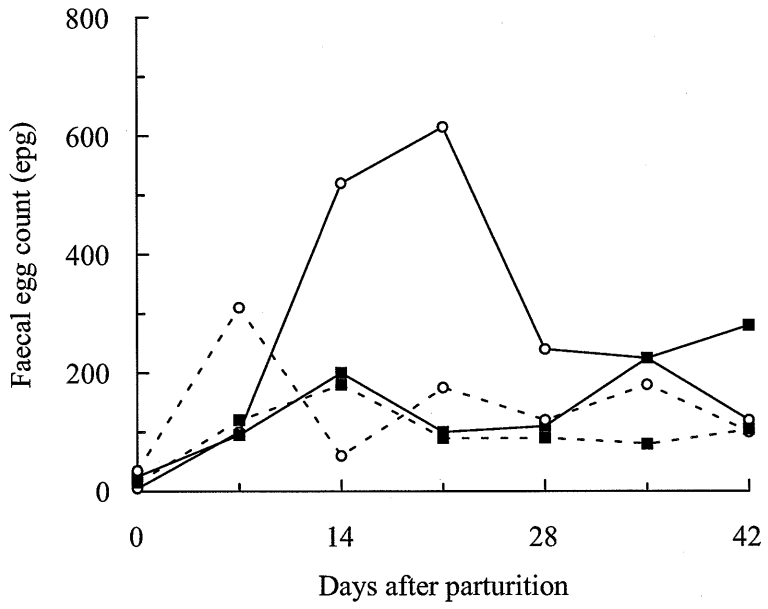

Figure 4.

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