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Modelling endogenous leucine flows at the jejunum and ileum in lambs exposed to the intestinal parasite *Trichostrongylus colubriformis*[*]

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ABSTRACT

A mathematical model is presented that compartmentalizes endogenous secretions into the gastro-intestinal tract, according to site of origin. This model was applied to data from three growing lambs (initial liveweight 25-30 kg) given a daily dose of 2500 *Trichostrongylus colubriformis* larvae for 12 weeks. At weeks 0, 6 and 12 of infection, endogenous leucine flows were determined during an 8 d intra-jugular infusion of [1-^{13}C]leucine, with samples taken from the jejunum, ileum and plasma. The infection had no effect on jejunal leucine flow (102.1 vs 105.5 mmol/d), but ileal leucine flow increased from 18.6 to 26.3 mmol/d (P=0.023). Endogenous leucine flow at the jejunum was unaffected by the infection (15.0 vs 18.9 mmol/d; P=0.116) but was doubled at the ileum (5.5 vs 10.4 mmol/d; P=0.025). Secretions into the small intestine contributed 58 (controls) to 65% (parasites) of ileal endogenous flow. The model also predicted that net portal drained viscera appearance was, at maximum, 79% of net appearance in the mesenteric vein.

KEY WORDS: endogenous secretions, mathematical models, digestive tract, sheep, parasites, stable isotopes

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INTRODUCTION

Endogenous protein secretions, plus associated losses, are an important feature of digestive tract metabolism in both ruminants (e.g., van Bruchem et al., 1997; Ouellet et al., 2002) and non-ruminants (e.g., de Lange et al., 1990; Hess et al., 1998). Various methodological and conceptual approaches have been used to quantify such secretions but the majority have considered the digestive tract as a single unit (e.g., de Lange et al., 1990), rather than a series of linked and interacting units (e.g., van Bruchem et al., 1997; Ouellet et al., 2002). Such a discrimination is particularly important in ruminants where the dominance of the rumen in endogenous transfers (e.g., Siddons et al., 1985; Ouellet et al., 2002) may obscure important responses in the lower intestines to various challenges.

Such challenges include lambs exposed to subclinical infection of the upper small intestine with the nematode *T. colubriformis,* resulting in increased nitrogen (N) flow in the ileal digesta, as well as reduced N retention (Poppi et al., 1986; Kimambo et al., 1988). Whether this is a consequence of reduced absorption of amino acids from the small intestine or increased flow of non-resorbed endogenous secretions, such as mucin, bile or cellular debris, remains unresolved. The current study addresses this question using a model approach that divides the gastro-intestinal (GI) tract into two compartments, pre- and post-jejunum. This model was also refined to predict the contribution of endogenous transfers to the differences in net leucine (amino acid) appearances across the mesenteric (MDV) and portal drained viscera (PDV) recently observed for a range of ruminant studies (Seal and Parker, 1996; MacRae et al., 1997; Berthiaume et al., 2001; Lobley et al., 2003). Part of these data have been reported in Abstract form (Yu et al., 1999).

MATERIAL AND METHODS

Animals and experimental procedure

Three lambs (Suffolk cross wethers, 25-30 kg liveweight), raised nematode-free from birth, were surgically prepared with cannulas in the rumen, jejunum and ileum at the age of 5 months (Poppi et al., 1986). The jejunal catheter was positioned caudal to the common duct from the bile and pancreas. Label in the digesta at the jejunum may therefore have arisen from fore-stomach inputs (including saliva), pancreas, bile and the upper small intestine. Additional inflows observed at the ileum will have arisen from small intestine epithelia (digestive enzymes, mucins) and desquamation losses. After a recovery period of two weeks, the animals were placed in metabolism crates and were fed a pelleted grass ration

(dry matter (DM) content 944 g/kg; N content 25.69 g/kg dry matter intake (DMI)) supplied as 24 equal portions at hourly intervals by means of automated feeders. Infection with *T. colubriformis* is often associated with reduced voluntary feed intake (Yu et al., 2000). To allow for this possibility the animals were fed two intakes for control measurements (600 vs 1000 g DM/d). This allowed assessment of the relationship between intake and endogenous flows were changes in intake to occur during the period of infection. In practice, during infection all animals consumed the 800 g DM/d offered.

The experiment was run as four separate measurement periods. For four weeks, the animals each received 600 g of ration per day. Measurements were taken during the last 8 days of this feeding regime (period 1). For the following four weeks, the animals were fed 1000 g of ration per day, with measurements being taken during the last 8 days (period 2). Thereafter, the sheep each received 800 g of ration per day, plus a daily oral dose of 2500 *Tricostrongylus colubriformis* 3rd stage larvae for 12 weeks, with measurements being taken during weeks 6 (period 3) and 12 (period 4) of dosing. This procedure had been used on a number of occasions previously in this laboratory (MacRae et al., 1982; Poppi et al., 1985, 1986; Hoskin et al., 2002) and had consistently induced a primary infection (weeks 5-7 of dosing) followed by the development of an immune response (by weeks 11-13 of dosing). One characteristic response of such infections has been the increased flow of nitrogen leaving the ileum of infected animals (see Poppi et al., 1986; Kimambo et al., 1988). Prior to each measurement period, a temporary polyvinylchloride catheter was inserted into each external jugular vein, one for infusion of [1-^{13}C]leucine and the other for blood sampling. During each measurement period the animals received a continuous jugular infusion of [1-^{13}C]leucine (99 atom %, 6 mmol/d, Masstrace, Woburn, MA) for 8 days. Digesta markers (^{103}Ru phenanthroline and ^{51}Cr EDTA) were prepared as described by MacRae et al. (1979) and infused through the rumen cannula at rates of 1 and 3 μCi/h, respectively, for 4 days prior to and throughout the collections of jejunal and ileal digesta. On each of d 5–8 of the measurement periods four blood samples (10 ml) were taken at 3-hour intervals. Digesta (4 × 3 h samples each of 50 ml) was collected from the ileum on d 5 and 7 and from the jejunum on d 6 and 8.

Chemical analysis

Details of the procedure for preparation and measurement of [1-^{13}C]leucine enrichment on the blood samples have been described previously by Yu et al. (2000). Digesta sampling, preparation and assay for ^{51}Cr and ^{103}Ru were as described by Poppi et al. (1986), with flow rates calculated using the dual phase marker procedures of Faichney (1975).

Model calculations

Continuous infusion with [1-^{13}C]leucine for several days results in labelling of proteins throughout the body. Based on first order kinetics, for rapid turnover tissues (i.e. containing proteins with an average half-life < 2 d), the proteins should attain similar enrichments to the appropriate precursor pool (assumed to be plasma free leucine) within 5-8 days (i.e. 4 half-lives). Such rapid turnover occurs for most ovine tissues drained by the MDV and PDV (Lobley et al., 1994). Thus, the contribution of endogenous leucine to total leucine in the digesta can be obtained from the isotope dilution and the respective flows derived from an appropriate model.

Endogenous flow

Let F_y denote total leucine flow at site y of the GI tract, where y refers to either jejunum or ileum. Let x refer to a gastro-intestinal site preceding y, with x being either 'mouth' or jejunum. The digesta flow at y can be separated into leucine present in undigested digesta originating from site x ($F_{undig\ x}$), and endogenous flow (EF) derived from endogenous leucine secretions into the GI tract between sites x and y:

$$F_y = F_{undig\ x} + EF$$

For the enriched [1-^{13}C]leucine:

$$E_y \times F_y = E_x \times F_{undig\ x} + E_{end} \times EF$$

where E_y and E_x are the leucine enrichments (molar percent excess) of the digesta at sites y and x, respectively, and E_{end} is the leucine enrichment of the precursor pool (assumed to be plasma). Solving these two equations for EF gives:

$$EF = \frac{E_y - E_x}{E_{end} - E_x} \times F_y \qquad (1)$$

The endogenous flow at the jejunum, $EF_{jejunum}$, is obtained from setting x and y equal to mouth and jejunum, respectively. The endogenous flow at the ileum, EF_{ileum}, is obtained from setting x to be mouth and y to be ileum. The jejunal endogenous flow is not strictly a loss to the animal, as part may be recovered in the small intestine. The endogenous flow at the ileum, however, forms a net loss to the animal as absorption beyond the ileum is considered negligible.

EF_{ileum} represents the net endogenous loss across the whole digestive tract and can be separated into endogenous flow derived from pre-jejunal ($EF_{ileum,prejej}$) and post-jejunal secretions ($EF_{ileum,postjej}$). Setting x = jejunum and y = ileum in equation (1) yields $EF_{ileum,postjej}$ and then $EF_{ileum,prejej}$ is given by $EF_{ileum} - EF_{ileum,postjej}$. See also Figure 1.

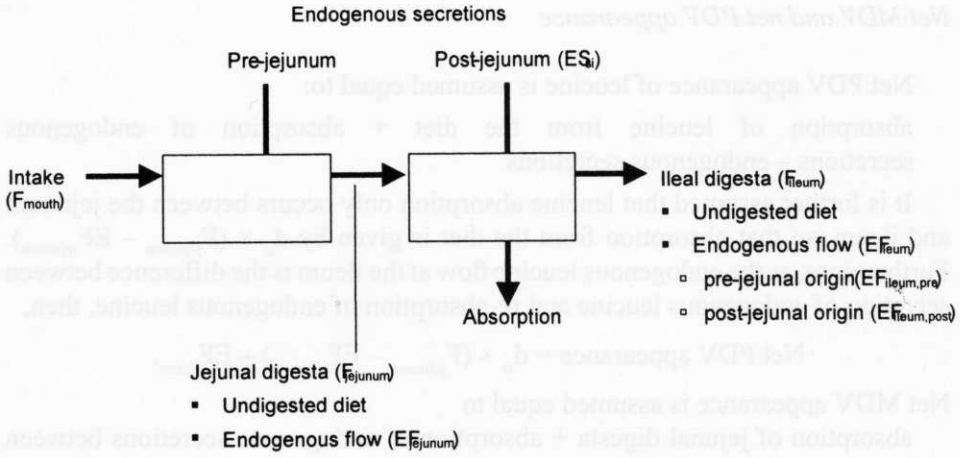

Figure 1. Schematic representation of model used for calculation of endogenous flows at jejunum and ileum (p. 592-594). Model variables are given between parentheses

Digestibility

Apparent digestibility of the whole tract, d_{app}, is given by

$$d_{app} = 1 - \frac{F_{ileum}}{F_{mouth}}$$

Real digestibility of the whole tract, d, is given by

$$d = 1 - \frac{F_{ileum} - EF_{ileum}}{F_{mouth}}$$

Apparent and real digestibilities between jejunum and ileum ($d_{app,si}$ and d_{si}, respectively) are given by

$$d_{app,si} = 1 - \frac{F_{ileum}}{F_{jejunum}}$$

$$d_{si} = 1 - \frac{F_{ileum} - EF_{ileum,postjej}}{F_{jejunum}}$$

Endogenous secretions into the small intestine (ES_{si}) are obtained from

$$ES_{si} = \frac{EF_{ileum,postjej}}{1 - d_{si}}$$

Net MDV and net PDV appearance

Net PDV appearance of leucine is assumed equal to:

absorption of leucine from the diet + absorption of endogenous secretions – endogenous secretions.

It is further assumed that leucine absorption only occurs between the jejunum and ileum, so that absorption from the diet is given by $d_{si} \times (F_{jejunum} - EF_{jejunum})$. Furthermore, as the endogenous leucine flow at the ileum is the difference between secretion of endogenous leucine and re-absorption of endogenous leucine, then,

$$\text{Net PDV appearance} = d_{si} \times (F_{jejunum} - EF_{jejunum}) - EF_{ileum},$$

Net MDV appearance is assumed equal to

absorption of jejunal digesta + absorption of endogenous secretions between jejunum and ileum – endogenous secretions between jejunum and ileum.

Then,

$$\text{Net MDV appearance} = d_{si} \times F_{jejunum} - EF_{ileum,postjej}$$

The difference between net MDV appearance and net PDV appearance is the endogenous flow at the jejunum ($EF_{jejunum}$). These derived MDV and PDV appearances do not include estimates for leucine oxidation (Lobley et al., 1996; Yu et al., 2000).

Statistical analyses

Measurement of endogenous flows through labelling of whole body protein requires long term infusion of stable isotope (8 d per period repeated for 4 periods). Due to the high cost of isotope infusion the present study was limited to only 3 animals. One of the lambs started the experiment delayed by one period. As a consequence, measurements for period 4 (week 12) were not obtained for this animal, which meant that the data did not provide sufficient information to compare weeks 6 and 12 of infection. This was confirmed by ANOVA using contrasts to compare weeks 6 and 12, which yielded no significant differences. Therefore, periods 1 and 2 were combined to form a control group and periods 3 and 4 were combined to form the parasite group in order to increase the degrees of freedom.

All data were analysed by ANOVA in Genstat 5 release 4.2 (Lawes Educational Trust, Rothamsted, Herts, UK), with animals treated as blocks and the absence or presence of parasite as treatment. As digesta flows have been shown to increase linearly with intake (see MacRae and Ulyatt, 1974), differences in intake (600 and 1000 g DM/d for control periods and 800 g DM/d during infection) were accounted for by including observed intake as a covariate. Mean values for absence and presence of parasites are based on n=6 and n=5 (due to one missing value for period 4), respectively.

RESULTS

Leucine enrichments in the plasma showed a small increase of 4.3%/d (P=0.001, data not shown) between d 5 to 8. The leucine enrichments in jejunal and ileal digesta also showed numerical increases of 5.7 (P=0.271) and 3.7%/d (P=0.417), respectively, over the same period. These increases in enrichment presumably involve recycling of labelled leucine from protein breakdown. As these changes were small numerically and within the range also reported for short-term (< 10 h) recycling (Connell et al., 1997) it was assumed that steady state conditions were achieved.

Inclusion of intake as a covariate was significant (P<0.05) for DM, N and leucine flows at the jejunum, DM and N flows at the ileum, net MDV and PDV appearances of leucine, plus endogenous leucine flow at the jejunum. For ileal leucine flow a trend was observed (P=0.099).

Digesta flows

Average intakes of DM, N and leucine were similar under control and parasite challenged conditions, as were DM flows at the jejunum and ileum. N flows were higher in parasitised animals at both the jejunum (19%; P=0.064, Table 1) and ileum (27%; P=0.007). Leucine flow at the ileum was also increased (41%; P=0.023, Table 2).

DM flow at the jejunum was 142 g/d less than DM intake (P<0.001, Table 1). N flow at the jejunum, however, exceeded N intake by 12 g N/d (P<0.01), whereas leucine jejunal flow exceeded intake by 36 mmol/d (P<0.003, Table 2).

TABLE 1

DM flows (g/d) and N flows (g/d)[1]

	Control	Parasite	SED	P
DM flows				
intake[2]	752	732	19.6	0.507
jejunum	596	604	43.7	0.573
ileum	313	317	25.0	0.646
N flows				
intake[2]	26.1	25.0	0.6	0.190
jejunum	34.6	41.1	3.4	0.064
ileum	9.7	12.3	0.8	0.007

[1] means for control and parasite based on n=6 respectively n=5. Standard error of difference (SED; 6 degrees of freedom) and P-values from ANOVA with blocking for animal and presence or absence of parasite as treatment effect and intake included as covariate

[2] SED (5 degrees of freedom) and P-values from ANOVA with blocking for animal and period as treatment effect. Effect of parasite was tested using contrasts

TABLE 2

Leucine flows at jejunum and ileum (mmol/d). Endogenous leucine flows are model-derived. Model variables are given between parentheses (see p. 592-594 for details)[1]

	Control	Parasite	SED	P
Intake (F_{mouth})[2]	68.5	66.7	1.8	0.507
Total flow jejunum ($F_{jejunum}$)	102.1	105.5	10.1	0.634
Endogenous flow jejunum ($EF_{jejunum}$)	15.0	18.9	2.3	0.116
% of jejunal flow	14.8	17.8	2.2	0.215
Total flow ileum (F_{ileum})	18.6	26.3	2.6	0.023
Endogenous flow ileum (EF_{ileum})	5.5	10.4	1.6	0.025
% of ileal flow	29.3	38.7	3.9	0.065
from secretions pre-jejunum ($EF_{ileum,prejej}$)	2.3	3.6	0.6	0.051
from secretions into small intestine ($EF_{ileum,postjej}$)	3.2	6.8	1.4	0.048

[1] means for control and parasite based on n=6, respectively n=5. Standard error of difference (SED; 6 degrees of freedom) and P-values from ANOVA with blocking for animal and presence or absence of parasite as treatment effect and leucine intake included as covariate

[2] SED (5 degrees of freedom) and P-values from ANOVA with blocking for animal and period as treatment effect. Effect of parasite was tested using contrasts

Endogenous flows and digestibilities

Endogenous leucine flow at the jejunum was not affected by the parasite infection (P=0.116), and averaged 16% of total jejunal leucine flow. Endogenous flow at the ileum was lower than for jejunum (37-55%; P<0.001) but was almost doubled for the parasitised animals (+ 5 mmol/d; P=0.025, Table 2). In consequence, the endogenous leucine flow as a proportion of total ileal leucine flow tended to be higher for the infected animals than for the controls (39 vs 29%; P=0.065). Separation of the ileal endogenous flow according to origin (pre- or post-jejunum) showed that the contribution of secretions into the small intestine to ileal endogenous flow was more than doubled for the infected animals (+ 3.6 mmol/d; P=0.048, Table 2) with also increases from those of pre-jejunal origin (+ 1.3 mmol/d; P=0.051).

Apparent digestibilities of leucine for the whole tract (P=0.027) and for the small intestine (P=0.076) were lower for the parasitised animals (Table 3) but real digestibilities were similar (mean 81%). Predicted net PDV appearance was 21% less than net MDV appearance (Table 3; P<0.001), but neither value was affected by the parasite challenge.

TABLE 3

Leucine digestibilities (%), endogenous leucine secretions into the small intestine (mmol/d), and net MDV and PDV leucine appearances (mmol/d). All quantities are model-derived. Model variables are given between parentheses (see p. 592-594 for details)[1]

	Control	Parasite	SED	P
Apparent digestibility small intestine ($d_{app,si}$, %)	81.2	74.9	2.9	0.076
Real digestibility small intestine (d_{si}, %)	84.4	81.4	2.0	0.176
Endogenous secretions into small intestine (ES_{si})	21.6	37.1	7.8	0.120
Apparent digestibility whole tract (d_{app}, %)	72.6	60.5	4.0	0.027
Real digestibility whole tract (d, %)	80.6	76.1	2.4	0.116
Net MDV appearance	83.5	79.2	9.2	0.767
Net PDV appearance	68.5	60.3	8.6	0.441
% of net MDV appearance	81.7	75.9	3.5	0.142

[1] means for control and parasite based on n=6 respectively n=5. Standard error of difference (SED; 6 degrees of freedom) and P-values from ANOVA with blocking for animal and presence or absence of parasite as treatment effect and leucine intake included as covariate

DISCUSSION

Endogenous model considerations

The model developed has general applicability and although presented for a two-compartment system, additional units can be easily added if appropriate sampling sites are available. Likewise, the model can be extended to allow the precursor pool to differ for each of the compartments, in order to reflect the nature of endogenous material secreted into various parts of the tract (see for example Ouellet et al., 2002). Such models of the GI tract allow for the endogenous loss at the terminal compartment (e.g., ileum or faeces) to be partitioned between the various sites of origin. Furthermore, the response to a challenge can be quantified for each of the individual compartments. In this particular instance, because of the positioning of a cannula at the jejunum, the model could be extended to predict the impact of site specific secretion and reabsorption on net MDV and PDV appearances.

The derived endogenous flows are sensitive to the precursor pool chosen. In the present case, systemic plasma free leucine was selected and this follows the traditional choice, based on ease of access, for many ^{15}N and ^{13}C approaches (e.g., de Lange et al., 1990; Leterme et al., 1996; van Bruchem et al., 1997; Hess et al., 2000). Ideally, more direct precursor sources, such as pancreatic secretions, epithelial cells (Ouellet et al., 2002) or specific secreted proteins (e.g., mucins;

Leterme et al., 1998) would be preferred. The precursors may have different enrichments from plasma with proportional effects on the estimated endogenous flows and losses. For example, if endogenous protein enrichment were only 38% of that of plasma (based on mucin in pigs; Leterme et al., 1998) this would increase the absolute endogenous flows at the jejunum and ileum by a factor of 2.6 for both control and infected animals. Nonetheless, provided the relationship between precursor pool and plasma is unaffected by treatment the direction of response will be unaltered. In practice, the various endogenous protein inflows will have different enrichments, encompassing a range of 38-100% of that of plasma (Hess et al., 1998; Leterme et al., 1998; Ouellet et al., 2002) and more complex models, such as those described for the rumen (Zuur et al., 2001; Ouellet et al., 2002) will need to be developed to aid future advances. These models, based on the principles described in the current paper and elsewhere (Zuur et al., 2001) can also be applied to multi-labelling approaches (e.g., Hess et al., 1998; Leterme et al., 1998). This avoids the complications that some secreted protein may contain disproportionate amounts of some amino acids, as is the case with mucins that are rich in both threonine and valine (Mukkur et al., 1985; Lien et al., 1997) and may be under-represented by leucine labelling.

Digesta flows and responses to parasite infection

Net gains of N flows between mouth and duodenum are typical for conserved diets (Beever et al., 1971; MacRae and Ulyatt, 1974; Siddons et al., 1985) and this appears to persist to the jejunum for both N (48%) and leucine (54%) flows during the current study. This may be due to additions of either endogenous secretions and/or leucine synthesis *de novo* by microbes using N from dietary sources or urea. In both sheep and cows dietary ammonia and endogenous urea inputs can increase microbial protein-N flows by 12-27% (Siddons et al., 1985; Zuur et al., 2001). In practice, however, only half of the observed net leucine gain could be explained by endogenous secretions (see later).

Although the roundworm *T. colubriformis* infests the upper section of the small intestine, there were no significant changes in either total or endogenous leucine flows to the jejunum. In contrast, total N flow at the jejunum was increased (19%) by the presence of parasites and this persisted to the ileum where the increased N was similar to that observed previously (2.6 N/d vs 2.5-4.0 gN/d, Poppi et al., 1986; Kimambo et al., 1988). Why then was there no extra jejunal leucine flow, particularly as an increase was observed at the ileum? Possibly this reflects that upper small intestine secretions induced by parasites are relatively low in leucine. Alternatively, such secretions maybe masked by the large endogenous losses that occur prior to the jejunum (here equivalent to 5.4 g N/kg DMI). Against this background, detection of changes in jejunal endogenous flow of only 3 (of total

flow) or 20% (of endogenous flow) would be difficult with the limited number of animals and associated variance.

In contrast, parasitism increased both the absolute endogenous flow of leucine at the ileum (by 100%, + 5 mmol/d) and the proportion relative to jejunal endogenous flow (55 vs 37% for control conditions). As real digestibility was not different between the control and infected sheep, this must be due mainly to the 72% increase in post-jejunal secretions induced by the presence of parasites. The reason for increased post-jejunal secretions is unknown but parasites do excrete a variety of products to assist their hold-fast capacity within the small intestine (Lee, 1996) and also to counteract the immune response of the host (Knox, 1994). These secretions, and the presence of increased numbers of inflammatory cells within the epithelial population, can also induce hypersensitivity reactions within the mucosa leading to increased permeability of the tract and elevated inflows of plasma proteins into the lumen (Poppi et al., 1986).

Nonetheless, the post-jejunal secretions were relatively low (21 and 35% of jejunal flow for control vs infected) and their incomplete re-absorption was not enough to account for all the net endogenous loss at the ileum. Instead, approximately 25% of the increased loss (equivalent to 1.3 mmol/d) arose from pre-jejunal endogenous inputs, indicative of either increased flow at the jejunum or lower digestibility of the secreted material. Together, these elevated endogenous secretions account for more than 60% of the increased leucine flow (and hence loss) at the ileum and will contribute to the lower net availability of amino acids and reduced protein gain observed with such infections (Poppi et al., 1986; Yu et al., 2000).

Net MDV and net PDV appearance

The position of the cannulas allowed the ileal endogenous flow to be separated into contributions from pre- and post-jejunal sources. The more common duodenal-ileal sampling (e.g., Siddons et al., 1985; Ouellet et al., 2002) results in amalgamation of pancreatic (plus bile) secretions with flows from small intestine sources. Use of the jejunal cannula leads to inclusion of pancreatic duct flows with fore-stomach secretions and thus inputs from the small intestinal epithelia can be quantified. Because endogenous secretions into the jejunal-ileal section of the GI-tract are mainly MDV-derived (e.g., cell wall desquamation and secretion of digestive enzymes), this allowed for the model to be extended to predict both the net appearance of leucine across the MDV and PDV and the contribution that partially reabsorbed endogenous secretions make to the MDV net appearance.

The predicted net PDV appearance was slightly greater to that measured directly by arterio-venous procedure in similar parasitised lambs (64.4 vs 55.3 mmol/d; Yu et al., 2000). This probably reflects that no oxidation of leucine by

digestive tract tissues (Lobley et al., 1996; Yu et al., 2000) was included within the model, this can reduce net leucine appearance by 20% (Lobley et al., 2003). Recent studies, for which net appearances were measured directly but had no measurement of endogenous flows, have shown that net PDV appearance of leucine is 31-44% less than across the MDV (Seal and Parker, 1996; MacRae et al., 1997; Berthiaume et al., 2001; Lobley et al., 2003). Part of this difference may involve recycling of endogenous protein derived from non-MDV compartments of the PDV (e.g., forestomach secretions, pancreas; Siddons et al., 1985; Zuur et al., 2001) that are then digested within the small intestine and absorbed into the mesenteric vein. The model predicted a maximum PDV:MDV net leucine appearance of 0.78, accounting for at least half of the differences observed in the other studies. The PDV:MDV ratio will become lower if account is taken that more leucine is oxidized by the PDV than MDV tissues in both normal (Lobley et al., 2003) and parasitised (Yu et al., 2000) animals. The predicted ratio will also decrease if a lower enrichment than that of systemic plasma free leucine is used. It was noted that the leucine flow at the jejunum exceeded leucine intake plus endogenous leucine and, if this were due to underestimation of endogenous flows caused by overestimation of precursor enrichment, then the model could be adapted based on balancing this difference. This led to a predicted precursor enrichment half that of systemic free leucine, within the range noted for porcine studies (Hess et al., 1998). The predictions from the model then increased the percentage contribution of endogenous secretions from 16 to 34% for jejunal digesta and to 64 (controls) and 80% (infected) for ileal digesta. This did not alter estimated net MDV appearance but the PDV:MDV ratio decreased to 61 and 53% for controls and parasitised animals, respectively, close to control values reported by direct measurements (Seal and Parker, 1996; MacRae et al., 1997; Berthiaume et al., 2001; Lobley et al., 2003).

CONCLUSIONS

The model developed allows compartmentalisation of the endogenous secretions into the digestive tract. When applied to data from sheep infected with roundworms in the upper small intestine the model predicted that more than 60% of the increased leucine flow at the ileum was of endogenous origin, divided approximately 1:3 between pre- and post-jejunal secretions. This did not occur through changes in small intestine digestibility but through a substantial increase (70%) in post-jejunal endogenous secretions. Thus, even though the parasites infest the upper small intestine they exert substantial effects on the lower small intestine. These may have been a combination of increased mucosal secretions and desquamation plus plasma losses through increased small intestine permeability.

The model was also able to show that much of the reported differences in net leucine (amino acid) appearance in the mesenteric and portal veins could be accounted for by differences between the site of synthesis of secreted material and the site of absorption.

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STRESZCZENIE

Model przepływu endogennej leucyny przez jelito czcze i biodrowe u jagniąt zakażonych jelitowym pasożytem *Trichostrongylus colubriformis*

Przedstawiono matematyczny model, w którym rozdzielono endogenną sekrecję w różnych odcinkach przewodu pokarmowego. Model ten zastosowano przyjmując dane od trzech rosnących jagniąt (początkowa m.c. 25-30 kg) otrzymujących dzienną dawkę 2500 larw *Trichostrongylus colubriformis*, przez 12 tygodni. W tygodniu 0, 6 i 12 infekcji oznaczano przepływ endogennej leucyny w ciągu 8-dobowej infuzji [1-^{13}C] leucyny do żyły jarzmowej, pobierając próby z jelita czczego, biodrowego i osocza krwi. Infekowanie nie miało wpływu na przepływ leucyny przez jelito czcze (102,1 vs 105,5 mmol/d), ale przepływ leucyny przez jelito biodrowe zwiększał się z 18,6 do 26,3 mmol/d (P=0,023). Przepływ endogennej leucyny przez jelito czcze nie był zależny od zakażenia (15,0 vs 18,9 mmol/d; P=0,116), natomiast zwiększał się w jelicie biodrowym (5,5 vs 10,4 mmol/d; P=0,025). Sekrecja do jelita cienkiego wynosiła 58 (kontrola) do 65% (zakażone jagnięta) endogennego przepływu w jelicie biodrowym. Na podstawie modelu można także przewidzieć, że przepływ netto przez żyłę wrotną osiągał 79% przepływu netto przez żyłę krezkową.