NUTRITIONAL IMPLICATIONS OF GASTROINTESTINAL AND LIVER METABOLISM IN RUMINANTS

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INTRODUCTION

The maintenance of an optimum nutrient balance in ruminant animals for growth, pregnancy and lactation is of key economic importance, requiring a wide range of adaptive responses to supply the necessary metabolites for different physiological states. The splanchnic bed, comprising the gastrointestinal tract and liver, plays a pivotal role in moderating the pattern of nutrients available for peripheral tissues. The intestinal tissues form an interface between the diet and the animal and have a direct influence on the flux of nutrients from the lumen into the bloodstream. The liver then forms the central metabolic junction, further moderating and distributing nutrients to peripheral tissues for maintenance or productive functions such as muscle deposition or milk synthesis. The pattern of nutrients appearing in the bloodstream does not necessarily reflect the quantity and form of those available for absorption from the gut lumen. Gastrointestinal tissues

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make use of metabolites produced by extensive metabolism of nutrients within the mucosa during the process of absorption in addition to those available in the arterial supply. This is evident from the significant difference between apparent absorption or disappearance of nutrients from the gut lumen and appearance of metabolites in the bloodstream (Bergman & Wolff, 1971; Tagari & Bergman, 1978).

EXPERIMENTAL TECHNIQUES

Techniques available for the investigation of nutrient absorption and possible interactions with other dietary components include many *in vitro* and *in vivo* procedures which have contributed to our understanding of nutrient availability. These procedures are also used to study specific metabolic processes within tissue types and across tissue beds.

ISOLATED TISSUE PREPARATIONS

The use of everted gut sacs made from intestinal segments was first developed by Wilson & Wiseman (1954) to investigate sugar transport (Crane & Wilson, 1958) and has since been applied to many other nutrients including amino acids (Phillips *et al.* 1976) and trace elements (Pearson *et al.* 1966; Seal & Heaton, 1983; Seal & Mathers, 1989). The relative insensitivity of the technique and the experimental difficulties associated with maintaining normal metabolic activity in the isolated tissue (Munck, 1972) have meant that this procedure has to a large extent been superseded by the use of isolated membrane vesicles developed from the initial methods of Kaback (1960). These methods have provided much of our present knowledge of amino acid uptake and transport, especially in the determination of specific rates of uptake and interactions and competition between different amino acids (Christensen, 1990). More recent approaches, which bridge the gap between artificial cells prepared from isolated membranes and intact cells *in vivo*, have centred on the use of tissue cultures of intestinal epithelial cell lines grown in monolayers (for review, see Hidalgo *et al.* 1989). In addition, isolated ruminal epithelial cells and papillae have been used to investigate developmental and diet induced changes in ruminal tissues (Harmon *et al.* 1991*a*; Baldwin & Jesse, 1992, 1993). Identification and localization of individual transport systems now involve the use of molecular biology techniques and have been applied to whole animal investigations. For example, the sodium–glucose cotransporter has been sequenced and characterized at the molecular level (Hediger *et al.* 1987*a*, *b*) and polyclonal antibodies raised to a synthetic polypeptide corresponding to a section of the sequence have been used to investigate the development and dietary regulation of glucose transport systems in neonatal lambs (Shirazi-Beechey *et al.* 1991*a*, *b*). Further development of these techniques will undoubtedly expand our knowledge of nutrient transporters.

Much of our understanding of liver nutrient metabolism and biochemistry is founded on *in vitro* studies using liver slices (Krebs & Henseleit, 1932) and homogenates (Ratner, 1947). As with intestinal cells, liver cells can be isolated, incubated and maintained as long as four days (Pogson *et al.* 1984), but prolonged monolayer culture has only recently been used to study metabolism of ruminant hepatocytes; their metabolic viability is often short-lived when maintained in culture (Faulkner & Pollock, 1990) and much of the *in vitro* work on ruminant hepatocyte metabolism has been limited to short-term incubations (Aiello *et al.* 1989). *In vitro* studies have provided and will continue to provide invaluable insights into specifics of liver biochemistry and metabolism. However, limitations of *in vitro* procedures must be considered when applying data obtained *in vivo*. The heterogeneity of

cells obtained is considerable, both in terms of cell type and location relative to blood supply. In addition, the lack of blood flow for delivery of substrate and removal of waste, as well as the limited metabolite exchange between cells, affects the viability and sensitivity of incubated cells. Supraphysiological concentrations of substrates are often required to maintain cell viability and elicit a metabolic response, and metabolic responses to substrate additions *in vitro* can differ markedly from responses observed *in vivo* (Reynolds *et al.* 1992*c*).

WHOLE ANIMAL EXPERIMENTS

Approaches for the study of liver metabolism *in vivo* include hepatectomy or portacaval shunts to remove the contributions of liver metabolism (Shoemaker, 1964). In addition, the isolated perfused liver has proved a useful approach for studying metabolism of the intact liver using strict control of substrate delivery. First used in 1875, the technique is effectively a 'bridge between *in vitro* and *in vivo* studies' (Shoemaker, 1964). By comparing responses to antegrade and retrograde infusion of substrates, the isolated perfused liver has recently been used to determine the degree to which zonal distribution of hepatocytes along the liver acinus affects the metabolism of specific compounds (Häussinger, 1983).

In vivo techniques such as ligated intestinal loops and intestinal perfusion procedures have been extensively applied with rats to investigate intestinal uptake, but their application in large animals is costly and impractical. Early studies of rumen volatile fatty acid absorption and metabolism did, however, use anaesthetized sheep in this way (Pennington, 1952). Current understanding of the flow of nutrients along the gastrointestinal tract of large animals has been achieved through the extensive use of permanent or semi-permanent intestinal cannulae (Brown *et al.* 1968), which together with the use of non-absorbable marker substances (Owens & Hanson, 1992) allow the processes of digestion to be studied in different regions of the intestine. This approach, however, is limited by the nature of the preparations to measuring the rate of disappearance of substances from the digesta, and takes no account of the fate of these nutrients once they leave the gut lumen. The situation is further complicated by recycling of nutrients and secretory products back into the lumen, together with intestinal cells sloughed during villus growth and development.

The use of multicatheterization procedures has made the largest contribution to our knowledge of this area of ruminant gastrointestinal and liver metabolism. Originally developed for use in the study of liver metabolism in dogs (Shoemaker *et al.* 1959), the technique has been applied to sheep (Katz & Bergman, 1969*a*, *b*) and cattle (Symonds & Baird, 1973; Huntington *et al.* 1989) to measure net absorption and metabolism of nutrients across the splanchnic bed. When used in combination with other techniques such as liver biopsy (Shoemaker, 1964), digestion trials and calorimetry (Reynolds *et al.* 1991*b*), measurements of digesta flow and nutrient disappearance from the gut lumen (Tagari & Bergman, 1978) or infusion of nutrients into the rumen (Huntington *et al.* 1983; Seal & Parker, 1991*a*, 1993*a*, *b*), abomasum (Guerino *et al.* 1991) or intravenously (Baird *et al.* 1980; Balcells *et al.* 1992) the technique can yield invaluable data describing the role of the splanchnic bed in the delivery of nutrients to peripheral tissues. The combination of multicatheterization techniques and isotopic measurements of nutrient turnover also enables the measurement of unidirectional metabolism by portal drained viscera (PDV) and liver (Bergman, 1975).

MEASUREMENT OF BLOOD FLOW

Application of the Fick principle (Zierler, 1961) to measurements of venous–arterial concentration differences of nutrients and blood flow in the venous drainage is used to calculate net rates of metabolism across tissues. Intravascular infusions of radiolabelled substrates and measurement of changes in metabolite specific activity across tissues are used to differentiate between these net flux rates and actual utilization rates within tissues (Bergman *et al.* 1970). The key determinant for both these processes is the accurate measurement of blood flow. Several techniques have been used including indicator dilution or liver clearance using sulphobromophthalein (Bradley *et al.* 1945), labelled erythrocytes (Schambye, 1955; Conrad *et al.* 1958), indocyanate green (Shoemaker, 1964; Wangsness & McGilliard, 1972), *para*-amino hippuric acid (PAH) (Roe *et al.* 1966), thermal dilution methods (White *et al.* 1967), and electromagnetic or Doppler electronic flow probes (Carr & Jacobson, 1968; Prewitt *et al.* 1975; Durand *et al.* 1988; Huntington *et al.* 1990). There have been recent improvements in the use of the Doppler principle for measurement of total volume flow in blood vessels, but anatomical constraints at the junction of the anterior mesenteric, gastrosplenic and gastroduodenal veins limit the usefulness of this technique in most cattle (Huntington *et al.* 1990). In sheep, which are more likely to have a common portal vein, the probes have been used successfully for measurements of portal vein blood flow (E. N. Bergman, personal communication), although the measurement of hepatic artery or total liver blood flow is also required for measurement of liver flux. Liver clearance techniques must be used in combination with other techniques for measuring portal vein flow in order to calculate liver flux (Shoemaker, 1964), although many researchers assume portal flow contributes a fixed proportion of liver flow and do not obtain direct measurements. To date the majority of studies in ruminants has used PAH dilution as the preferred method for measuring blood flow in long term studies. As PAH is acetylated in the liver, analytical procedures developed for sheep include deacetylation (Katz & Bergman, 1969*b*). In cattle, deacetylation affects total concentration of PAH measured using automated procedures, but not venous–arterial concentration differences, and therefore does not affect blood flow determinations (Huntington, 1982).

RUMINANT SPLANCHNIC VASCULATURE

Anatomical differences between bovine and ovine splanchnic vasculature are highlighted in Fig. 1. The collateral branch of the mesenteric vein (h) in the bovine is not found in the sheep and forms a looped structure in the mesenteric drainage of this species, through which venous blood may flow in either direction before mixing at the anterior mesenteric vein (g). In cattle, the junction of anterior mesenteric and gastrosplenic veins occurs over a relatively shorter distance than that in the sheep, where the separation of these vessels is generally more distinct, with the gastrosplenic vein joining at a less acute angle to the mesenteric vein. This provides a common portal vein prior to the porta hepatis which is often not present in cattle. Consideration of these differences is important in the location of catheters for measuring absorption across the mesenteric drained viscera (MDV) and PDV in these species. Tissues of the PDV include the entire digestive tract and associated organs comprising the pancreas, spleen and mesenteric fat. Catheters inserted into specific blood vessels can therefore be used to identify metabolism across specific tissue beds. The gastrosplenic vein drains the rumen, reticulum, omasum, cranial abomasum, spleen and pancreas; the anterior mesenteric vein the small intestine, caecum, large intestine, mesenteric fat and pancreas; and the gastroduodenal vein the caudal abomasum, cranial duodenum and pancreas. Measurements of venous–arterial concentration differences from

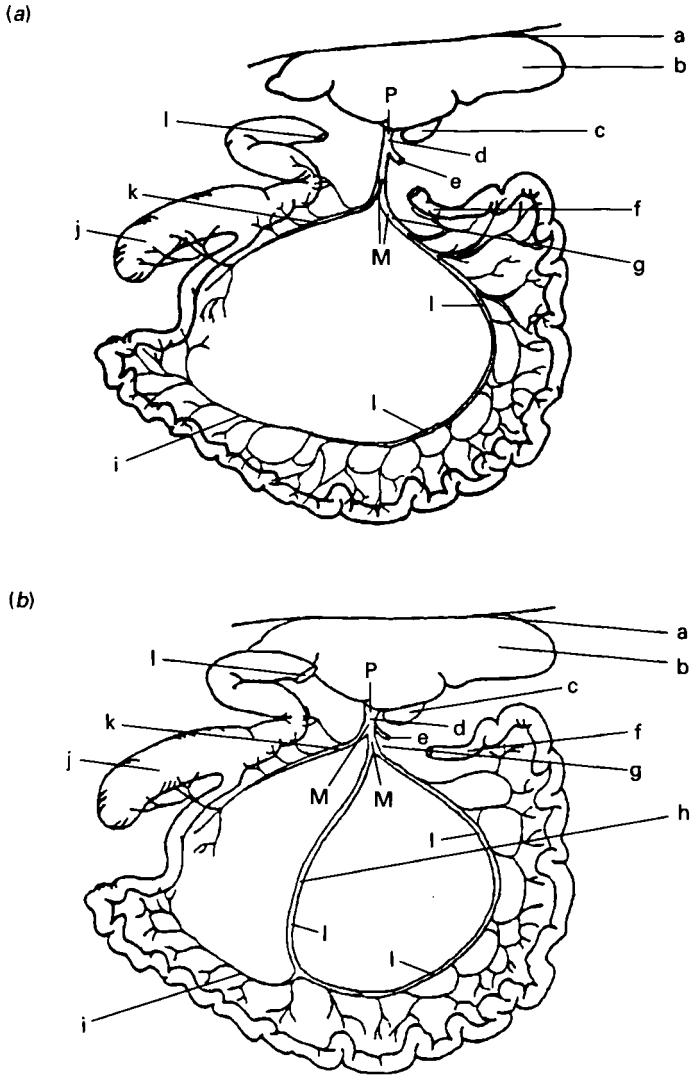

Fig. 1. Schematic view of ovine (*a*) and bovine (*b*) splanchnic vasculature showing anatomical differences between the two species (adapted from Huntington *et al.* 1989). a, Diaphragm; b, liver; c, gall bladder; d, portal vein; e, gastrosplenic vein; f, jejunum; g, anterior mesenteric vein; h, collateral branch of mesenteric vein; i, distal branch of mesenteric vein; j, caecum; k, ileocaecal vein; l, large intestine; l, sites of infusion catheters; M, sites of mesenteric sampling catheters; P, site of portal sampling catheter.

these vessels have been used to differentiate stomach and post-stomach absorption of nutrients (Reynolds & Huntington, 1988*a*, *b*; Seal *et al.* 1992).

Generally there are three to five major and any number of smaller hepatic veins which empty into the bovine vena cava (Fig. 2). These major veins drain the left lateral lobe (one or two veins), central liver (one or two veins draining the quadrate and right lobes) and the caudate process. Using a paracostal or 12th rib resection for surgical approach, the central vein, usually lying adjacent to the gall bladder, is the most accessible and drains the largest portion of the liver (Huntington *et al.* 1989). However, most workers with sheep have used a branch of the left lateral vein for catheterization (Katz & Bergman, 1969*a*). Assuming

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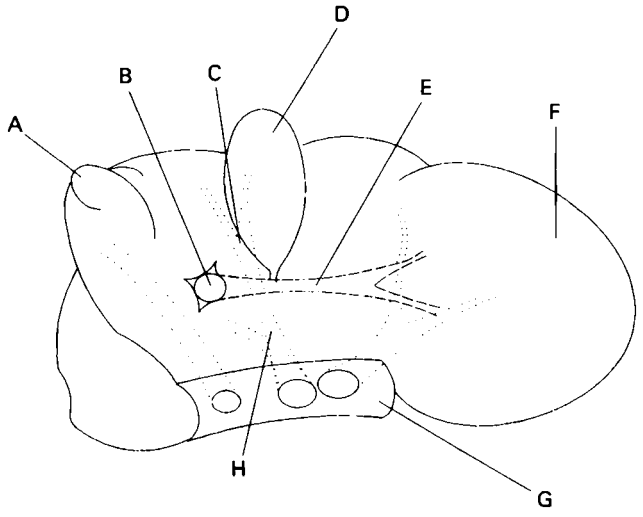

Fig. 2. Schematic view of major hepatic blood vessels of the bovine liver viewed from the visceral surface. A, caudate process; B, porta hepatis; C, insertion point for hepatic vein catheter; D, gall bladder; E, tip location of portal catheter; F, left lateral lobe; G, vena cava; H, tip location for hepatic vein catheter.

complete mixing of portal vein blood prior to the porta hepatis, the vein used should not affect data obtained.

Regional differences in the distribution of portal vein blood to the liver have been demonstrated in sheep (Hancock & Milligan, 1985), but are diminished by rumen development in lambs (Heath & Perkins, 1985). Laminar flow in the portal vein and regional differences in blood supply to the liver may be of greater concern in cattle which have little, if any, common portal vein prior to the porta hepatis. Indeed, cattle whose portal veins do not enter the liver at a perpendicular angle to the surface of the liver should not be used for splanchnic catheterization studies, because the turbulence which mixes portal blood at the porta hepatis may be reduced (Reynolds *et al.* 1988*a*), and portal vein catheter tips should always be introduced well past the porta hepatis and into the left lateral lobe to take advantage of mixing of portal blood at the porta hepatis (Reynolds *et al.* 1988*a*; Huntington *et al.* 1989). While there is inherent variation in blood flow over time, errors associated with measurement of blood flow are greatly reduced when careful attention is given to placement and immobilization of sampling and PAH infusion catheters (Huntington *et al.* 1989).

For compounds whose net metabolism by PDV and liver is low relative to their high rates of blood flow, venous–arterial concentration differences are low and difficult to measure. For example, venous–arterial concentration differences across the PDV are quite large for ammonia but extremely small for many individual amino acids. Therefore it is essential that the analytical techniques used are as sensitive and precise as possible, and that within individual studies analytical procedures are strictly adhered to. Variation in patterns of net metabolism over time and sampling protocols must also be carefully considered in applying these techniques for specific experiments. Many researchers feed daily rations in equal meals delivered at frequent intervals to reduce postprandial responses and then sample over shorter time periods, particularly in experiments involving the infusion of labelled substrates for which 'steady state' conditions are required. However, frequent feeding disrupts normal diurnal behaviour patterns, and level of intake and diet digestibility also

affect postprandial responses. For example, in steers fed every 2 h a highly digestible, high protein diet at low intakes, postprandial increases in blood flow and ammonia absorption were still dramatic (Maltby, 1993). Higher intakes reduce postprandial responses, but in growing animals assessment of the efficiency of utilization of nutrients requires measurements at varying increments of intake. Researchers must assess sample size, blood volume taken and processing and analytical constraints against sampling frequency, duration and period. Generally, longer sampling periods and slow, frequent sampling reduce error, especially in animals fed once or twice daily (as would occur in production circumstances) or for the study of compounds whose metabolism is subject to inherent variation such as insulin and glucagon (Reynolds *et al.* 1989). Where characterization of changes in metabolism over short time periods is not needed, integrated sample withdrawal provides the most accurate quantitative estimate of total metabolism (Harris *et al.* 1992).

ENERGY

Techniques for estimating tissue oxygen consumption include *in vitro* incubation of isolated cells or tissue biopsies obtained during experiments by endoscopy and at slaughter in addition to direct measurements of oxygen removal across tissue beds *in vivo* using animals with indwelling catheters. *In vitro* techniques are also used to investigate the partitioning of energy expenditure by particular biochemical processes such as Na^+, K^+-ATPase dependent respiration and protein synthesis through the use of specific metabolic inhibitors (McBride & Kelly, 1990). These experiments underline the energy requirements of the gastrointestinal tract and liver, which constitute about 10–13% of total body mass but account for 38–50% of whole body oxygen consumption (Table 1). Of this total energy expenditure between 28 and 61% is associated with the maintenance of Na^+, K^+-ATPase (EC 3.6.1.3) activity in the gastrointestinal mucosa, 20–23% with protein synthesis and 4% with protein degradation (McBride & Kelly, 1990). Oxygen consumption increases following meal consumption (Christopherson & Brockman, 1989; Kelly *et al.* 1989) and changes with level of feed intake (Webster *et al.* 1975; McBride & Milligan, 1985; Burrin *et al.* 1989). The heat increment of feeding has been attributed to several factors including those directly associated with eating, changes in microbial fermentation in the gut, increased metabolic activity in non-intestinal tissues and changes in the metabolic activity of the PDV, the latter being quantitatively the most important in animals fed above maintenance (Webster, 1980).

The relationship between metabolizable energy (ME) intake and PDV heat production, calculated from PDV oxygen consumption using the factor of McLean (1972), is shown in Fig. 3. It is interesting that although there is close correlation between experiments across a wide range of diets, those animals fed diets based on ensiled forages with a higher non-digestible fibrous component tend to produce more PDV heat per unit ME intake than animals fed diets based on concentrates or dried forage. This may be equated to the increased work of digestion related to the physical and chemical nature of the diet, gut fill and changes in the components of ME absorbed (Webster, 1980; Johnson *et al.* 1990). The expenditure of energy in the physical digestion of feedstuffs is apparent from animals maintained by intragastric infusions (Fig. 3), which had lower rates of PDV oxygen consumption compared with those fed lucerne (Gross *et al.* 1990*a*). The small intestines of these animals were empty of digesta and showed considerable tissue atrophy. Similarly, in animals fasted for 65 h in which the digesta content of the gastrointestinal tract would be temporarily reduced, PDV heat energy was decreased by 43% to 0·09 MJ/d per $kg^{0.75}$ compared with concentrate fed controls (Huntington *et al.* 1990). This latter figure is

Table 1. *Contribution of gastrointestinal tract and liver to whole body oxygen consumption*

Tissue	Animal	% of whole body O_2 consumption	Reference
		Determinations *in vitro*	
Rumen	Steers	16·9–19·3	Kelly *et al.* (1989)
Duodenum	Cows		
	Dry	34·9	McBride & Milligan (1984)
	Lactating	53·8–55·0	
	Sheep		
	Fasted	28·6	McBride & Milligan (1985)
	Fed	48·1–61·3	
Jejunum	Steers	26·1 26·2	McBride *et al.* (1989)
		Determinations *in vivo*	
PDV*	Heifers	22·6–27·5	Reynolds *et al.* (1991*b*)
PDV	Cows		
	Lactating	17·5	Huntington & Tyrrell (1985)
PDV	Cows		
	Lactating	20·0	Reynolds *et al.* (1986)
PDV	Steers	25·0	Huntington *et al.* (1989)
PDV	Steers	19·8–24·0	Huntington *et al.* (1990)
PDV	Steers		
	Fed	19·9–25·4	Eisemann & Nienaber (1990)
	Fasted	17·8–19·9	
PDV	Steers	18·9–23·2	Reynolds *et al.* (1992*a*)
PDV	Sheep	19·0–28·0	Burrin *et al.* (1989)
Liver	Heifers	18·5 ·26·3	Reynolds *et al.* (1991*b*)
Liver	Steers	17·5–30·9	Huntington *et al.* (1990)
Liver	Steers		
	Fed	20·5–20·7	Eisemann & Nienaber (1990)
	Fasted	25·2–26·4	
Liver	Steers	16·3–22·5	Reynolds *et al.* (1992*a*)
Liver	Sheep	22·0–41·0	Burrin *et al.* (1989)

* PDV, portal drained viscera.

similar to other data for fasted steers (0·07 and 0·08 MJ/d per $kg^{0.75}$, Eisemann & Nienaber, 1990), and the intercept value for animals at zero ME intake (Fig. 3) suggests a minimum rate of energy expenditure for tissue maintenance. Comparisons between diets within the same experiment suggest that this maintenance energy requirement may vary with diet composition (Reynolds *et al.* 1991*b*). In this experiment, although increases in PDV oxygen use with greater ME were similar for the two diets, PDV oxygen consumption per unit ME was always greater for heifers fed the higher fibre lucerne diet. Therefore, while the slopes of the two regressions were similar for the two diets, the intercept value was greater when heifers were fed lucerne. This may be attributable in part to increases in gut mass resulting from greater gut fill and perhaps volatile fatty acid (VFA) production and absorption (Reynolds *et al.* 1993).

High rates of liver oxygen consumption are also attributable to energy costs of ion transport and protein synthesis and degradation. In addition, other processes such as substrate cycling, free radical scavenging, glucose and urea synthesis and detoxification of phenols and other compounds all contribute to liver energy requirements. The exact costs of specific processes are difficult to ascertain, as there is considerable interplay and exchange of metabolic intermediates. For example, the ATP requirement of the urea cycle is lower when the phosphate bonds generated by fumarate metabolism in the tricarboxylic

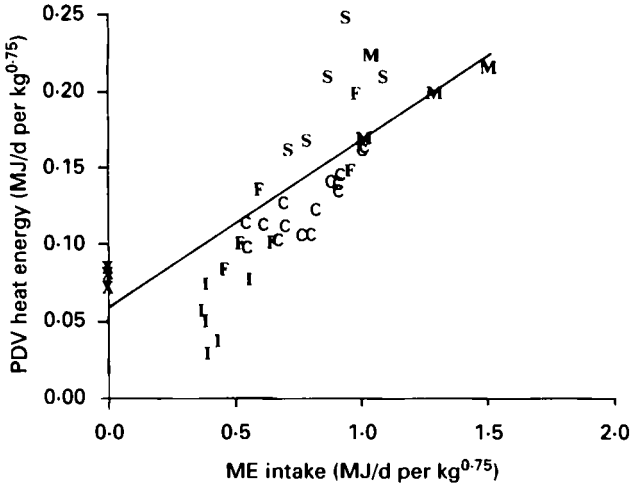

Fig. 3. The relationship between portal drained visceral (PDV) heat energy (MJ/d per $kg^{0.75}$) and metabolizable energy (ME) intake (MJ/d per $kg^{0.75}$). (F), > 50% forage diet; (C), > 50% concentrate diet; (S), ensiled forage diet; (M), ensiled forage/concentrate mixed diet; (X), fasted animals; (I), animals maintained by intragastric infusion (not included in regression analysis). Each point represents animal means from individual experiments. The equation of the regression line is $y = 0{\cdot}059 \pm 0{\cdot}109x$ ($R^2 = 0{\cdot}612$). Data are from the experiments of Harmon *et al.* (1988), Huntington *et al.* (1988), Reynolds & Huntington (1988*a*), Reynolds *et al.* (1988*a*, *b*), Eisemann & Nienaber (1990), Gross *et al.* (1990*a*, *b*), Huntington *et al.* (1990), Guerino *et al.* (1991). Reynolds *et al.* (1991*b*), Reynolds *et al.* (1992*a*, *b*) and Maltby (1993).

acid cycle are considered (Newsholme & Leach, 1983). It has long been assumed that increases in heat production of cattle resulting from excess protein intake are a direct consequence of the energy costs of urea synthesis (Tyrrell *et al.* 1970), but in a number of studies in cattle, diet-induced increases in PDV ammonia absorption and liver urea synthesis have not altered liver oxygen use (Reynolds, 1992; Maltby, 1993). However, in each of these studies other changes in PDV nutrient absorption and liver metabolism may have balanced increased oxygen requirements for ureagenesis. In this regard, a recent study found increased body oxygen use resulting from feeding excess protein to beef steers to be due to increases in both PDV and liver oxygen use (Reynolds *et al.* 1992*a*).

VOLATILE FATTY ACIDS

Ruminants absorb little dietary carbon as glucose, even when diets high in starch resistant to rumen fermentation are fed (Bergman *et al.* 1970; Bergman, 1990). As products of microbial fermentation in the digestive tract, VFA are the primary form in which energy is absorbed into blood by the PDV of ruminants (Baird *et al.* 1980; Reynolds *et al.* 1988*b*). The contribution of VFA to body energy requirements is even greater when their extensive metabolism by PDV is accounted for. Direct comparisons between VFA production rates and net absorption rates into the portal vein are restricted by the limited amount of data in which both of these variables have been determined in the same animals, due mainly to the complexity of surgical procedures for the implantation of indwelling catheters, which restricts the use of rumen or intestinal cannulae. Alternative approaches must therefore be used, either based on data for rumen VFA production rates measured in animals fed similar

Table 2. *Comparison between rumen volatile fatty acid production rates and net portal absorption rates (moles/d)*

Animal	Diet	Rumen production rate			Portal absorption rate			Reference
		A	P	B	A	P	B	
Lambs	Infusion*	3·53	1·94	0·32	1·88 (0·53)†	1·29 (0·66)	0·08 (0·28)	Gross *et al.* (1990*b*)
		3·27	1·16	0·31	1·97 (0·60)	0·81 (0·69)	0·08 (0·26)	
		3·53	0·47	0·33	1·57 (0·44)	0·32 (0·67)	0·08 (0·26)	
Lambs	Infusion	3·59	1·11	0·44	1·64 (0·45)	0·85 (0·77)	0·11 (0·25)	Gross *et al.* (1990*a*)
		3·94	1·21	0·48	1·59 (0·40)	0·63 (0·52)	0·07 (0·14)	
		4·69	1·44	0·58	2·49 (0·53)	1·12 (0·78)	0·15 (0·26)	
Sheep	Infusion		1·86	—	—	1·06 (0·57)	-	Weekes & Webster (1975)
			2·99	–	—	1·79 (0·59)		
Sheep	Forage	3·3	0·9	0·6	2·3 (0·69)	0·44 (0·49)	0·05 (0·08)	Bergman (1990)
Cattle	Concentrate	16·9	6·1	4·8	9·5 (0·56)	4·2 (0·69)	1·1 (0·23)	Harmon *et al.* (1988)
Steers	Concentrate	23·7[a]	20·2	0·9	10·20 (0·43)[b]	8·14 (0·40)	0·6 (0·66)	[a]Sharp *et al.* (1982) [b]Huntington & Reynolds (1983)
Steers	Forage	15·75	4·25	—	7·56 (0·48)	1·26 (0·30)	0·31	Seal *et al.* (1992)
	Concentrate	13·25	4·75	–	6·89 (0·52)	1·41 (0·30)	0·25	
Steers	Forage	7·74	3·22	—	7·40 (0·96)	1·69 (0·52)		Seal & Parker (1993*a*)
	+ Propionate	8·86	3·72		6·52 (0·74)	2·09 (0·56)	—	
	+ Propionate	7·65	4·16	—	5·80 (0·76)	2·44 (0·58)	—	
Steers	Concentrate	—		1·58	—		0·74 (0·47)	Krehbiel *et al.* (1992)
	+ Butyrate	-	–	2·78	—		0·86 (0·31)	
			—	3·98	—	—	1·34 (0·34)	
			—	5·18		-	1·63 (0·32)	
			—	6·38	—	—	1·90 (0·30)	
		—		7·58	–		2·23 (0·29)	

* Intragastric infusion.
† Values in parentheses, proportion of rumen production rate.
A, Acetate; P, Propionate; B, Butyrate.
—, value not determined.

diets in different experiments, or on theoretical production rates calculated from organic matter digestibilities and observed molar proportions of VFA in rumen fluid. For individual VFA their rate of metabolism by rumen tissue *in vitro* increases with chain length (Stevens & Stettler, 1966). The main products of this metabolism are ketone bodies, CO_2 and to a lesser extent lactate. Propionate may also be converted into alanine (Bergman, 1990) and, as shown in the rabbit hind gut, acetate carbon may appear in aspartate and glutamate used in protein synthesis (Vernay, 1989). Table 2 shows that 0·31–0·60 of acetate, 0·22–0·7 of propionate and 0·34–0·92 of butyrate produced in the rumen do not appear in the portal vein. Portal appearance rates, however, not only reflect metabolism within the rumen and across the rumen wall, but also include the metabolism of VFA by tissues of the MDV. In sheep, unidirectional absorption of acetate, measured isotopically, represented 0·7 of acetate produced in the rumen and presumably absorbed; however, net PDV absorption of acetate, which includes utilization of arterial acetate, was only 0·5 of rumen production (Bergman & Wolff, 1971). These relationships were also observed in sheep maintained by intragastric infusion (Table 2) and cattle receiving intraruminal acetate (Huntington *et al.* 1983). Fermentation of residual carbohydrate flowing to the hind gut may contribute significant quantities of VFA to the portal drainage via the ileocaecal vein (Faichney, 1969; DeGregorio *et al.* 1984). This latter point is particularly important for the siting of

indwelling catheters for measurement of metabolism within the mesenteric drained viscera; if the catheter tip is sited caudal to the ileocaecal vein/mesenteric vein junction, net acetate utilization by the MDV may be masked by acetate produced in the large intestine (Seal *et al.* 1992; Seal & Parker, 1993*b*). When MDV flux of beef steers included all the post-stomach tissues of the gastrointestinal tract, net flux of acetate across MDV was positive when concentrate was fed, reflecting carbohydrate fermentation in the large intestine and caecum (Owens *et al.* 1986). When lucerne was fed, net MDV flux of acetate was negative, suggesting that any acetate absorption resulting from microbial fermentation of carbohydrate in the small intestine and caecum was exceeded by MDV utilization of arterial acetate.

Net absorption of VFA across the PDV is highly correlated with the composition of the diet and the level of feed intake (Huntington, 1983; Huntington & Prior, 1983). However, the proportions of each VFA produced in the rumen which appear in the portal vein remain constant across a wide range of different diets. Absolute absorption rates increase during lactation (Stangassinger & Giesecke, 1986) in parallel with increased feed intake, but despite the increase in gut and liver tissue mass associated with lactation (Campbell & Fell, 1970; Fell *et al.* 1972; Fell & Weekes, 1975) there is little change in the relative proportions of VFA absorbed into the portal vein. Changing rumen fermentation pattern by altering the forage:concentrate ratio of the diet or by infusions of individual VFA may alter the pattern of VFA absorbed, but the extent of metabolism of the fatty acids remains constant (Krehbiel *et al.* 1992; Seal *et al.* 1992; Seal & Parker, 1993*b*). Recent experiments from Peters *et al.* (1990) have suggested that over a wide range of rumen propionate production rates approximately 0·66 of available propionate disappeared from within the rumen (presumed to be absorbed) and 0·34 passed from the rumen to the lower tract in the liquid phase. These data suggest that at least some of the apparent shortfall in VFA appearing in the portal vein may be attributed to metabolism within abomasal and omasal tissues in addition to that lost across the rumen wall.

Excluding acetate, the liver removes 85–100% of VFA appearing across PDV on a net basis (Reynolds *et al.* 1988*b*). Therefore, acetate is the only VFA present in peripheral blood in substantial quantities and represents an important energy substrate for peripheral and PDV tissues. Net acetate flux across liver is usually slightly positive, but net measurements can mask simultaneous unidirectional uptake and release of acetate by the ruminant liver (Bergman & Wolff, 1971), which are perhaps due to zonal heterogeneity of liver metabolism as described for non-ruminants (Katz, 1992). In the liver, VFA removed contributes carbon for glucose and 3-hydroxybutyrate synthesis, and precursors of acetyl-CoA provide carbon which can enter a number of metabolic pathways. In the fed state the ruminant liver removes acetoacetate and produces 3-hydroxybutyrate, with *n*-butyrate contributing 26–48% of carbon in the 3-hydroxybutyrate produced (Lomax & Baird, 1983; Reynolds *et al.* 1988*b*, 1991*a*). Other sources of carbon for 3-hydroxybutyrate release include acetoacetate produced by PDV (Heitmann *et al.* 1986) and the oxidation of non-esterified fatty acids extracted from portal vein and arterial blood (Bell, 1979). In fasted animals the liver flux of acetoacetate switches from removal to release, and the contribution of *n*-butyrate to ketone body production decreases and its absorption by PDV and the contribution of non-esterified fatty acids to liver ketone body production rises (Heitmann *et al.* 1986). As for acetate, 3-hydroxybutyrate is a source of oxidizable substrate for extrahepatic tissues.

Propionate is the principal source of carbon for glucose synthesis in liver, which meets 85–90% of body glucose requirements in sheep (Bergman *et al.* 1970). Assuming a maximal use of propionate removed by liver for glucose synthesis, propionate accounts for 32–73% of liver glucose release (Table 3). Theoretical calculations addressing carbon randomization

Table 3. *Maximal net contributions of precursors removed to glucose released (mmol/h) by ruminant liver*

Animal	Diet	Glucose release	Percentage of net glucose release: Propionate	Amino acids	L-Lactate	Reference
Mature sheep	Lucerne	21·7	40·3	29·0		Bergman *et al.* (1970); Bergman & Wolff (1971); Wolff & Bergman (1972)
Growing steers	Concentrate	180	72·8	12·1	13·1	Huntington & Eisemann (1988)
Growing steers	Fescue hay	147	46·3	21·4	10·9	Harmon *et al.* (1991*b*)
Growing steers	Concentrate					
	Low intake, saline	123	58·5	11·6	10·7	Reynolds *et al.* (1992*b*);
	Low intake + GRF	105	56·1	5·8	14·2	Reynolds *et al.* (1992*a*)
	High intake, saline	245	53·9	15·1	1·4	
	High intake + GRF	237	67·3	13·2	1·6	
Growing steers	Concentrate: hay	116	52·6	28·4	44·0	Krehbiel *et al.* (1992)
Growing steers	Lucerne	227	42·5	19·6	15·0	Harmon *et al.* (1993)
Mature steers	Concentrate	190	32·2	20·0	9·9	Reynolds *et al.* (1992*c*)
Growing heifers	Lucerne					
	Low intake	119	52·2	32·4	7·0	Reynolds *et al.* (1991*b*);
	High intake	263	59·9	35·3	9·3	Reynolds *et al.* (1993*b*)
	Concentrate					
	Low intake	116	46·6	23·9	9·1	
	High intake	285	59·8	24·6	1·9	
Mature heifers	Forage	192	75·8	26·0	8·2	Reynolds & Tyrrell (1991);
	Concentrate	214	59·6	23·5	6·6	Reynolds *et al.* (1991*a*)
Lactating cows	*Ad libitum*	392	52·8		22·9	Baird *et al.* (1980)
Lactating cows	*Ad libitum*	325	46·0		16·0	Lomax & Baird (1983)
Dry cows	Restricted	240	56·6		10·6	
Lactating cows	*Ad libitum*	713	55·4	16·5	17·5	Reynolds *et al.* (1988*b*)

GRF, growth hormone releasing factor.

during isotope transfer studies suggest that almost all of the propionate removed by liver is used in glucose synthesis (Armentano, 1992).

AMINO ACIDS AND PEPTIDES

Mechanisms for the uptake and transport of amino acids and peptides have been extensively reviewed (Webb & Bergman, 1991; Webb *et al.* 1992), and these have received added attention with the use of improved analytical techniques for the determination of free amino acids and low molecular weight peptides in plasma. Although limited by the number of animals used in the experiment, Tagari & Bergman (1978) clearly demonstrated that the quantity of amino acids appearing in the portal blood of sheep did not balance the amount disappearing from the intestinal lumen, and this report and various others since have suggested that between 30 and 80% of amino acids disappearing from the lumen do not appear in the portal vein. In steers given postruminal casein (Guerino *et al.* 1991) only 28% of the casein nitrogen infused abomasally appeared in the portal blood as α-amino nitrogen. Piccioli Cappelli *et al.* (1993*b*) similarly demonstrated that up to 48% of [^{13}C]leucine infused directly into the duodenum of sheep could not be recovered in the portal vein when measured on a net transfer basis. However, if the sequestration of arterial ^{13}C tracer by the gut tissues is taken into account, recovery of [^{13}C]leucine administered to the small intestine may be nearer 70% (MacRae *et al.* 1993). High rates of protein turnover

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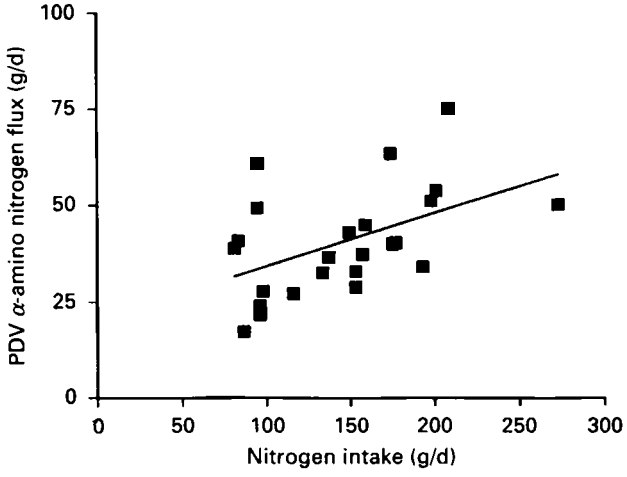

Fig. 4. The relationship between portal drained visceral (PDV) flux of α-amino nitrogen in whole blood (g/d) and nitrogen intake (g/d). Each point represents animal means from individual experiments. The equation of the regression line is $y = 20{\cdot}429 \pm 0{\cdot}136x$ ($R^2 = 0{\cdot}235$). Data are from the experiments of Harmon *et al.* (1988), Huntington *et al.* (1988). Reynolds & Huntington (1988*a*), Eisemann & Nienaber (1990), Guerino *et al.* (1991), Reynolds *et al.* (1991*c*), Reynolds & Tyrrell (1991), Reynolds *et al.* (1992*b*) and Harmon *et al.* (1993).

within the gastrointestinal tract, together with the use of amino acids as energy substrates within the mucosa, are cited as possible fates of those amino acids lost across the gut wall, substantially affecting the pattern of amino acids available to the liver and peripheral tissues (Lobley *et al.* 1980). Gut protein synthesis rates vary with feed intake and physiological state (see for example Baracos *et al.* 1991) and change during postnatal growth and development (Reeds *et al.* 1993). Glutamine, glutamate and aspartate have been shown to be important fuels in rat intestinal tissues (Windmueller & Spaeth, 1978, 1980). Unidirectional utilization of glutamate and glutamine by PDV in sheep (Heitmann & Bergman, 1981) and net extraction by PDV of cattle (Huntington, 1983; Wilton, 1989) suggests that this may also be the case in ruminant gut tissues; however, venous–arterial concentration differences for glutamine are consistently smaller in these species compared with the rat (C. J. Seal & D. S. Parker, unpublished observations). Net glutamine utilization by the MDV in forage-fed steers compared with animals fed a diet containing 50% flaked maize (Seal *et al.* 1992) and similar responses across the PDV of steers when switched from forage to concentrate diets (Reynolds & Huntington, 1988*a*) indicate that amino acid metabolism within the gut tissues alters in these different dietary situations.

Measurements of net PDV α-amino nitrogen flux over a wide range of nitrogen intakes and different diets (Fig. 4) suggest that amino acid release by PDV is not correlated with dietary nitrogen supply. Within individual experiments it has been suggested, however, that net α-amino nitrogen release by PDV is correlated with ME intake (Huntington *et al.* 1988; Huntington, 1989; Reynolds *et al.* 1991*b*), the principal determinant of microbial protein synthesis and therefore duodenal protein flow (Clark *et al.* 1992). However, comparisons between experiments again show poor correlation, perhaps due to differences between experiments in sample processing and analytical techniques (Maltby, 1993). This confirms the complex interaction between gastrointestinal tissues and the diet, which may be a direct response to changes in gut energy expenditure or patterns of rumen fermentation. Changing propionate supply by intraruminal infusion of propionic acid in steers resulted in higher circulating amino acid levels and elevated net absorption rates of amino acids

across the MDV and PDV (Seal & Parker, 1991*a*). Subsequent experiments with cannulated sheep infused with propionate (Seal *et al.* 1993*a*) showed that these responses were not associated with changes in overall nitrogen digestibility or alterations in rumen microbial metabolism and the flow of microbial nitrogen into the small intestine. Circulating amino acid levels were also increased in these animals, and the results imply that amino acid utilization within the intestinal tissues had been reduced as a direct response to increased ruminal propionate availability. In contrast, Harmon (1991) showed that increased butyrate availability in animals maintained by intragastric infusion reduced net PDV α-amino nitrogen flux. A similar response was observed in steers (Krehbiel *et al.* 1992), where increasing ruminal butyrate tended to lower PDV α-amino nitrogen flux. It was suggested that this was due to increased tissue amino acid requirements in response to the known trophic stimulus of butyrate (Sakata & Tamate, 1978).

The studies of Bergman and co-workers have demonstrated both net and unidirectional metabolism of individual amino acids by liver of sheep, as well as the impact of fasting, acidosis and hormonal manipulation on splanchnic amino acid metabolism (for reviews see Bergman & Heitmann, 1978; Bergman & Pell, 1984; Bergman, 1989). Most amino acids are removed on a net basis by the liver, reducing the availability to other body tissues of amino acids absorbed across PDV. Exceptions include the branched chain amino acids and glutamate, which are usually released by liver. These studies also identified a number of interorgan amino acid cycles for which the liver is a central player. Participants include glutamate and glutamine, glycine and alanine and also arginine, ornithine and citrulline. These cycles shuttle carbon and nitrogen between the liver – as a site of glucose, protein and urea synthesis – and peripheral tissues – as sites of glucose utilization and protein synthesis and turnover. Nitrogen arising from the catabolism of amino acids in peripheral tissues is carried to the liver as alanine, glycine or glutamine for urea synthesis, avoiding excessive release of potentially toxic ammonia into the peripheral circulation. Alanine, glycine and urea cycle intermediates serve the same function for nitrogen arising from amino acid catabolism in PDV tissues.

Metabolism of glutamine, glutamate and urea show zonal heterogeneity in non-ruminant liver, with glutamine uptake, urea synthesis and glutamate synthesis more active in periportal cells, and glutamine synthesis and glutamate uptake more active in pericaval cells (Häussinger, 1983). Simultaneous unidirectional release and uptake of glutamate and glutamine in sheep liver (Heitmann & Bergman, 1981) imply a similar zonal heterogeneity in this species, but to date studies of zonal heterogeneity have not been conducted for ruminant liver. On a net basis the ruminant liver releases glutamate and removes glutamine. Glutamate is an important source of nitrogen for liver ureagenesis, supplying one or two nitrogens in urea via aspartate, and increases in liver urea production are often associated with decreases in liver glutamate release (Reynolds, 1992).

Amino acids removed by liver represent important precursors for glucose and protein synthesis (Table 3). Their exact contribution to glucose synthesis has been difficult to determine precisely, in part due to the problems of label randomization in carbon exchange studies, but total gluconeogenic amino acid removal maximally accounted for 30% of liver glucose release in maintenance fed sheep (Wolff & Bergman, 1972), which is within the range of theoretical net contributions calculated from measured extraction of amino acids across the liver (Table 3). The liver has a pivotal role in the integration of body nutrient requirements with nutrient supply from the PDV. In beef steers receiving abomasal infusions of casein, increased PDV absorption of α-amino nitrogen was matched by increased liver removal such that there was little change in splanchnic release of total amino acids and a marked increase in liver urea synthesis and urinary nitrogen excretion (Guerino *et al.* 1991). However, when body nitrogen retention of beef steers was doubled by growth

hormone releasing factor injections, liver α-amino nitrogen removal was reduced, sparing absorbed amino acids for protein synthesis in peripheral tissues (Reynolds *et al.* 1992*b*). Changes in liver amino acid removal were accompanied by decreased liver urea production, a decrease in the cycling of ammonia and urea between PDV and liver, and decreased urinary nitrogen excretion. The impact of liver metabolism on the availability of absorbed amino acids was also apparent in steers fed rumen protected methionine and lysine (Maltby *et al.* 1991). Increased PDV absorption of these amino acids was matched by their liver removal and therefore there was no change in their total splanchnic release to peripheral tissues.

Speculation about the apparent loss of amino acids across the gut tissues has generated renewed interest in the possible contribution of peptide bound amino acids (PBAA) to the total α-amino nitrogen flux. The absorption of intact peptides across the gastrointestinal barrier *in vivo* is not well documented, although there is considerable *in vitro* information which supports the notion of specific transport mechanisms for the uptake of peptides into the enterocyte (Webb & Bergman, 1991). Net PDV release (positive venous-arterial concentration differences) of PBAA as measured with hydrolysed sulphosalicylic acid supernatants has been shown in steers and sheep (Koeln & Webb, 1982; Read, 1988; Webb *et al.* 1993) and in perchloric acid supernatants separated by HPLC from rat plasma (Seal & Parker, 1991*b*). Concentrations of PBAA measured in this way (4·0–6·8 mM (McCormick & Webb, 1982; Danilson *et al.* 1987); 3·3–3·9 mM (Read, 1988); 3·8–6·1 mM (Seal & Parker, 1991*b*)) exceeded plasma free amino acid concentrations two- to three-fold, and relative concentrations were different between ruminant and non-ruminant species (Seal & Parker, 1991*b*). Recent work from the Newcastle group has involved the use of molecular weight filters (Millipore Corporation, Milford, MA) to remove large proteins from plasma. Whilst the concentrations of free amino acids in filtrates were similar to those measured in acid supernatants, the corresponding PBAA levels in filtrates separated by HPLC were much lower (Seal & Parker, 1993*b*), suggesting that acid treatment of plasma samples may produce higher apparent PBAA levels, either through residual oligopeptides/small proteins remaining in supernatants or by the 'production' of small peptides through partial acid hydrolysis of labile plasma proteins. Net PBAA release across the mesenteric and portal drained viscera calculated from these data averaged 1·76 and 3·02 mmol/min respectively. PBAA release by the non-mesenteric tissues (P–M, 1·26 mmol/min) was in contrast to removal of free amino acids by these tissues (−0·99 mmol/min), suggesting net output of PBAA but not free amino acids from large intestinal, stomach and proximal small intestinal tissues. Webb *et al.* (1993) have recently suggested that ruminal and omasal epithelia incubated *in vitro* have the capacity to transport small peptides, and the same group present data showing positive non-mesenteric flux of peptides in sheep and steers. Despite numerous publications suggesting the potential of ruminant gastrointestinal tissues to absorb peptides, there is no direct evidence that luminally derived peptides are absorbed intact across the gut wall *in vivo* or that PBAA appearing in the portal drainage are solely of dietary origin – the high rates of protein turnover within gut tissues may also contribute a significant amount of peptide material to this pool. The contributions of plasma protein pools and peptides to PDV and liver nitrogen and carbon exchange need to be defined and quantified.

AMMONIA AND UREA

Non-protein nitrogen in the form of ammonia and urea form an important route through which nitrogen is recycled and conserved in the ruminant animal. Net PDV ammonia nitrogen flux is highly correlated with dietary nitrogen intake (Fig. 5) and especially

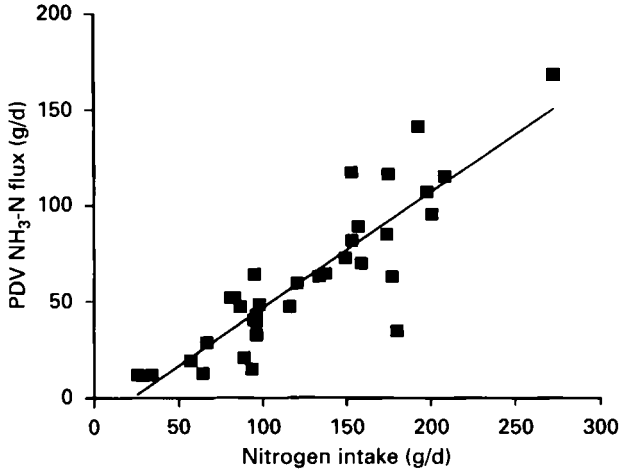

Fig. 5. The relationship between portal drained visceral (PDV) flux of ammonia nitrogen (g/d) and nitrogen intake (g/d). Each point represents animal means from individual experiments. The equation of the regression line is $y = -12{\cdot}96 \pm 0{\cdot}594x$ ($R^2 = 0{\cdot}772$). Data are from the experiments of Wolff *et al.* (1972), Sniffen & Jacobson (1975), Huntington (1983), Huntington & Prior (1983), Harmon *et al.* (1988), Huntington *et al.* (1988), Reynolds & Huntington (1988*a*), Eisemann & Nienaber (1990), Guerino *et al.* (1991), Reynolds *et al.* (1991*c*), Reynolds & Tyrrell (1991), Reynolds *et al.* (1992*b*), Seal *et al.* (1992) and Harmon *et al.* (1993).

digestible nitrogen intake (Reynolds *et al.* 1991*c*, 1992*a*); it can account for as much as 65% of nitrogen intake, and under normal circumstances is at least equal to and usually exceeds α-amino nitrogen absorption rates (Huntington, 1986). Quantities of ammonia absorbed by PDV are determined not only by intake of digestible nitrogen but also by the nature of the carbohydrate and protein consumed. All ammonia absorbed by PDV is subsequently removed by liver so that splanchnic flux is very low or negative; however, other routes of ammonia absorption from the gut have been identified (Chalmers *et al.* 1971). Ammonia removed by the liver is converted into urea or used in other synthetic pathways. Ammonia absorbed across the PDV is derived in part from urea transferred into the gut lumen, and a substantial cycling of urea and ammonia between the PDV and liver occurs in ruminants (Huntington, 1986). In growing cattle fed diets high in rumen soluble nitrogen, excessive ammonia absorption has been associated with increased net removal of amino acids by liver (Huntington, 1989; Reynolds *et al.* 1991*c*). This response has been attributed to an increase in urea cycle requirements for cytosolic aspartate and glutamate, which cannot be met by mitochondrial capture of ammonia as glutamate (Reynolds, 1992); however, recent studies have failed to repeat this effect of ammonia uptake on liver amino acid removal (Reynolds *et al.* 1992*a*; Maltby, 1993). This response has been observed primarily in younger animals at higher ME intakes, and the variability of the response across studies may relate to the interactions between protein requirements and the availability of labile protein pools (Elwyn, 1970).

GLUCOSE

Under normal dietary conditions for ruminants fed a mixed diet, the levels of glucose available for absorption in the small intestine are low, and the contribution of absorbed glucose to whole body glucose supply is minimal. When diets contain high levels of cereal grain, and in particular ground maize, there is evidence that significant quantities of starch

Table 4. *Comparison between whole body glucose turnover rate and net portal glucose utilization rate*

Animal	Diet/Treatment		mmol/h per $kg^{0.75}$ GTR*	PGU†	PGU/GTR	Reference
Sheep	Non-pregnant	Hay	1·33	0·17	0·13	Bergman *et al.* (1970)
		Concentrate	1·67	0·22	0·13	
		Fasted	1·06	0·28	0·26	
	Pregnant	Hay	2·00	0·44	0·22	
		Fasted	1·33	0·28	0·21	
Sheep		Hay	2·35	0·15	0·06	Huntington *et al.* (1980)
		Concentrate	3·79	0·40	0·11	
Sheep	Pregnant	Mixed diet	2·56	0·41	0·16	Van der Walt *et al.* (1983)
	Lactating		3·76	0·75	0·20	
Sheep	Straw based diet		1·73	0·68	0·39	Balcells *et al.* (1992)
	+0·9 mmol/h per $kg^{0.75}$ i.v. ‡		2·54	0·95	0·37	
	+1·8 mmol/h per $kg^{0.75}$ i.v.		3·70	1·49	0·40	
Sheep	Dried grass pellet diet		2·04	0·70	0·34	Piccioli Cappelli *et al.* (1993*a*)
	+1·7 mmol/h per $kg^{0.75}$ i.v.		3·09	0·91	0·29	
	+1·7 mmol/h per $kg^{0.75}$ i.d.§		3·41	1·05	0·31	
Steers	Dried grass pellet diet		3·19	0·86	0·27	Seal & Parker (1992)
	+0·5 mole propionate/d‖		3·09	0·35	0·11	
	+1·0 mole propionate/d		3·74	0·39	0·11	

* Glucose turnover rate
† Portal glucose utilization rate.
‡ Intravenous infusion.
§ Intraduodenal infusion.
‖ Infused into the rumen.

may escape rumen fermentation and pass into the duodenum (Waldo, 1973; Armstrong & Smithard, 1979; Rooney & Pfugfelder, 1986). Despite suggestions that small intestinal starch digestion may be limited by low levels of enzyme activity and adequate access of enzymes to starch granules (Owens *et al.* 1986), substantial quantities of starch disappearing in the small intestine with digestibilities ranging from 10 to 96% have been reported (Harmon, 1992). Recovery of abomasally infused glucose and corn starch in beef steers averaged 65% of the glucose and 35% of the starch as increased glucose absorption into portal blood (Huntington & Reynolds, 1986). Kreikemeier *et al.* (1991) have also demonstrated lower recoveries of starch glucose in the portal vein from abomasal infusions of corn starch compared with equivalent infusions of glucose. A recent experiment with growing steers fed lucerne in which potato starch was infused directly into the duodenum (Seal *et al.* 1993*b*) showed that these forage-fed animals were able to hydrolyse starch very rapidly, and that plasma glucose levels were elevated within one hour of presenting starch to the intestine. Recovery of starch glucose in the portal vein averaged 84% and was not increased by the third day of a continuous starch infusion. The higher recovery of glucose may be due to differences in the chemical structure of the potato starch used in this experiment compared with previous work using corn starch (Nocek & Tamminga, 1991), but the results clearly demonstrate the capacity of the small intestine to absorb significant quantities of glucose if present in the gut lumen, despite the suggestion that during development of the enterocyte the Na^+–glucose cotransporter is regulated by the presence of sugar substrate in the lumen (Shirazi-Beechey *et al.* 1991*a*). This is in agreement with the suggestion of Mayes & Ørskov (1974) that it is the capacity to hydrolyse starch rather than to absorb glucose which is limiting in ruminants.

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Measurements of net glucose absorption by MDV and PDV in ruminants consuming forages generally show a net extraction (i.e. negative venous–arterial concentration difference) of glucose by the digestive tract compared with those fed concentrates for which net uptake may be observed (Parker, 1990). These studies do not consider the effect of glucose metabolism within the gut tissues, and reflect the overall balance of absorption and utilization across the tissue bed. Net glucose utilization rates, which reflect the metabolic requirement of intestinal tissues, determined by comparison of glucose-specific radioactivity in arterial and venous blood (Bergman *et al.* 1970), show that on average portal utilization of arterial glucose accounts for about 22% of whole-body glucose turnover (Table 4). Within individual experiments, increasing the glucose turnover rate causes a proportionate increase in glucose utilization by the PDV, except for animals receiving intraruminal propionate (Seal & Parker, 1992), where portal glucose utilization was significantly reduced by exogenous propionate. The results indicate that glucose utilization responds to increased glucose supply, and that this requirement may be met from both vascularly and luminally derived substrate (Piccioli Cappelli *et al.* 1993*a*). Manipulation of starch availability to the small intestine, and the consequences that this may have on glucose metabolism within the gut tissues and the use of other energy-yielding substrates, is clearly an area requiring further investigation.

SUMMARY

In conclusion, the splanchnic tissues have a profound impact on the supply of nutrients for maintenance and production in ruminants. Their metabolism accounts for a substantial portion of maintenance costs, but in a manner which varies with diet composition and intake level. Specific details of the quantitative and structural impact of gut and liver metabolism on absorbed nutrients and the integration of this metabolism with nutrients produced by other body tissues have resulted from *in vivo* studies utilizing multi-catheterization techniques. The judicious use of these techniques should further our quantitative understanding of how diet affects nutrient supply for productive processes such as growth or lactation. In the future, nutritionists may be able to formulate diets to meet the nutritional requirements of specific tissues, including the gut and liver. Changes in the quantity and pattern of nutrients available to the splanchnic bed influence the distribution of nutrients to the body. While it may appear that these tissues compete with other tissues for absorbed nutrients, their metabolism is in fact integrated with the metabolism of peripheral tissue and supportive of changes in requirements of all body tissues.

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