

The large bowel—a supplementary rumen?

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The large intestine has attracted additional interest with recent evidence that diseases such as colonic cancer, ulcerative colitis and colonic diverticulosis have a lower incidence in human populations that consume a relatively-high percentage of plant fibre. Studies conducted on a variety of species have shown that the mammalian large intestine and the ruminant forestomach show some striking similarities with respect to microbial digestion, secretion and absorption (Stevens *et al.* 1980). The following discussion will demonstrate some major analogies and attempt to explain their functional significance.

The ruminant forestomach

Results from extensive studies of the ruminant forestomach are contained in a number of reviews (Sellers & Stevens, 1966; Hungate, 1968; Stevens, 1973; Bryant, 1977; Phillipson, 1977). The forestomach consists of the reticulo-rumen (a large, blind, multicompartamental sac) and the omasum. The reticulo-rumen provides a fermentation chamber which, in adult cattle, can constitute approximately 25% of the animal's body-weight. Its construction and motor activity delay transit of digesta, especially particulate matter, as well as the indigenous microbes. The omasum serves as a pump for the transfer of digesta to the remainder of the gastrointestinal tract.

Rumen microbes ferment a wide range of carbohydrates, including sugars, starches, cellulose, hemicelluloses and pectins. Under normal conditions the principle end-products are three volatile fatty acids (VFA), acetate, propionate and butyrate, plus carbon dioxide and methane. Although the pK_a of these organic acids is approximately 4.8, a pH of 5.5-7.0 is required for maintenance of microbes responsible for their production. This is accomplished by both the rapid absorption of VFA and the addition of large volumes of heavily-buffered saliva. Parotid secretions, which provide the major source, have a sodium:potassium value similar to that of plasma, high concentrations of bicarbonate and phosphate and a pH of 8.2. Approximately 60% of the Na and chloride entering the reticulo-rumen via the diet and saliva are absorbed directly from this chamber (Dobson, 1961). Na and Cl are absorbed by active transport. Cl transport appears to be partially accomplished by exchange for HCO_3^- , which provides an additional mechanism for the buffering of VFA.

Ingestion of a diet abnormally high in starch results in a fulminating production of VFA within the rumen. The marked lowering of digesta pH results in more

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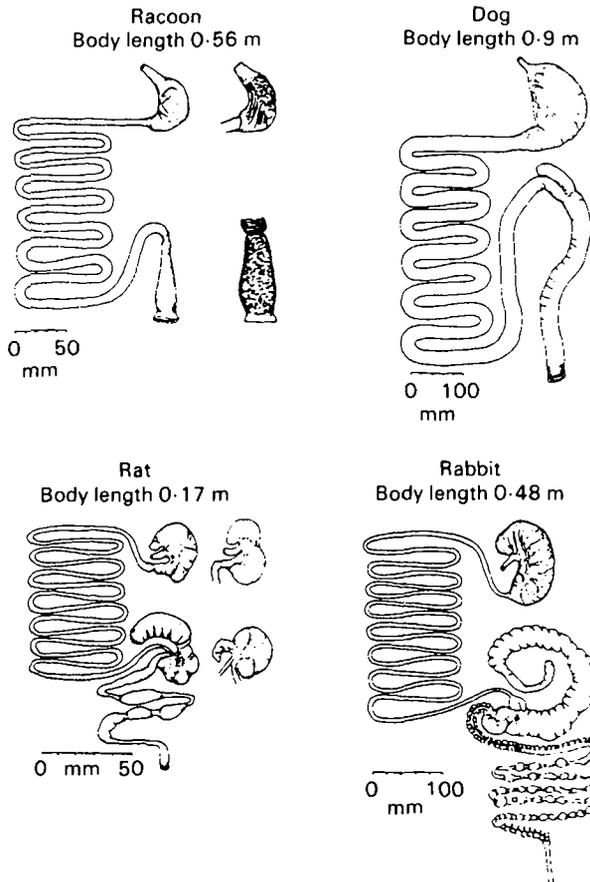


Fig. 1. Gastrointestinal tracts of the racoon (*Procyon lotor*), dog (*Canis familiaris*), rat (*Rattus norvegicus*) and rabbit (*Oryctolagus cuniculus*). Animals were fed at 12 h intervals over a 3-week period and killed 4 h after a meal. The stomach and caecum, illustrated to the right of the rat gastrointestinal tract, demonstrates the difference in size and compartmentalization in an animal killed under the same feeding conditions but immediately after a meal. Illustrations of the dog, rat and rabbit gastrointestinal tracts from Stevens (1977) and used by permission of the publisher, Cornell University Press.

rapid absorption of VFA and eventual replacement of the normal flora with lactobacillus (Dirksen, 1970). This, in turn, can result in necrosis of rumen epithelium and atony of rumen muscle as well as systemic acidosis and dehydration.

Rumen bacteria convert both protein and non-protein-nitrogen into microbial protein. Approximately two-thirds of the intact dietary protein is digested by microbial enzymes yielding peptides, amino acids and ammonia. Endogenous urea entering the reticulo-rumen in the saliva and via direct diffusion from blood is rapidly converted to NH_3 , which also may be used for protein synthesis. Microbial protein is passed on to the abomasum and small intestine and subjected to digestion and absorption of the end-products.

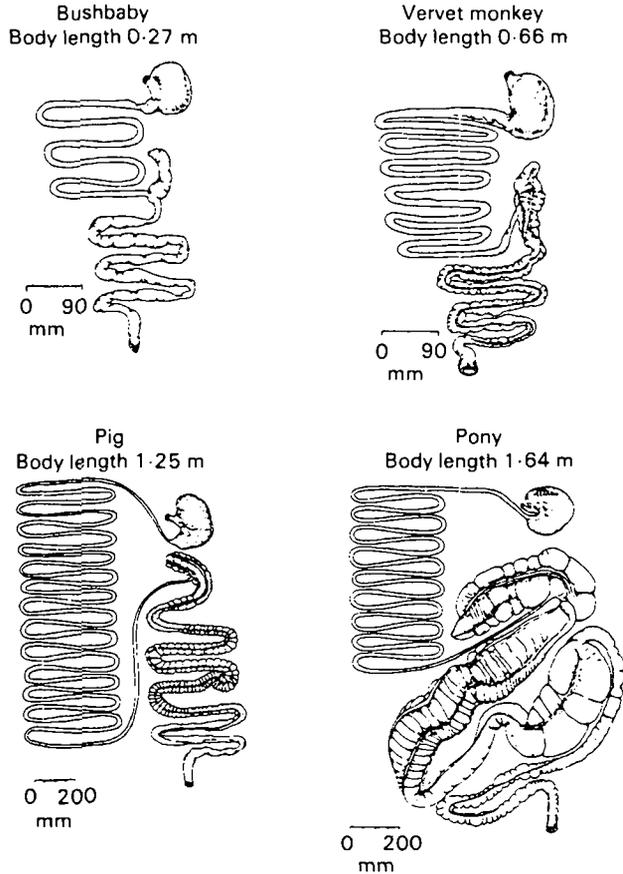


Fig. 2. Gastrointestinal tracts of the bushbaby (*Galaga crassicaudatus*), vervet monkey (*Cercopithecidae pygerrhus*), domestic pig (*Sus scrofa*) and pony (*Equus caballus*). Illustrations of the bushbaby and vervet monkey from Clemens (1981) and used by permission of the publisher, Cambridge University Press. Pig and pony illustrations from Stevens (1977) and used by permission of the publisher, Cornell University Press.

The mammalian large intestine

Species variation in structure and digesta transit. Some mammals have no distinct large intestine: these include many species of Insectivora, Chiroptera (bats), Mysticeti (baleen whales) and Odontoceti (toothed whales). Most mammals have a distinct large intestine but the relative complexity, length and volume can vary considerably even within a mammalian order. These variations tend to correlate with differences in diet or the need to conserve water (Stevens, 1981). The wide range of structural variation is indicated by the gastrointestinal tracts illustrated in Figs. 1–2.

The large intestines of the racoon and dog are relatively simple and non-voluminous. The racoon lacks a caecum and there is no anatomical evidence of an ileocolonic sphincter, both of which are present in the dog. The large intestine of the rat, other rodents and the rabbit consists of a voluminous caecum and non-

voluminous colon. The prosimian bushbaby and the vervet monkey have a caecum more voluminous than that of the dog but relatively non-voluminous in comparison with the colon. The entire colon of the vervet monkey is drawn into sacculations (haustra) by longitudinal bands of muscle in a manner similar to that of the human large intestine. Furthermore, the relative length is similar to that of the human. The colon of the pig and pony also are sacculated. However, the proximal colon of the pony is further divided into distinct compartments. This extent of colonic complexity and volume is seen only in the Perissodactyla (equids, rhinoceros and tapirs) and Proboscidea (elephants).

The rate of digesta-marker passage through the gastrointestinal tracts of the racoon (Clemens & Stevens, 1979), dog (Banta *et al.* 1979), pig (Argenzio & Southworth, 1975; Clemens *et al.* 1975), bushbaby and vervet monkey (Clemens, 1981), rabbit (Pickard & Stevens, 1972) and pony (Argenzio *et al.* 1974a) was examined under similar conditions in an attempt to determine structural-functional relationships. Retention of fluid and particulate markers tended to increase with increased complexity of the large intestine. Whereas 80% of the fluid and particulate markers were excreted in the faeces of the racoon within 24 h, over 4 d was required for excretion of the equivalent percentage by the pony and a much longer period was required for excretion of particles. The major site for retention of fluid marker by the rabbit was the caecum. However, the primary site of retention in the other species was the proximal colon and retention time increased with the extent of colonic sacculation. The mean retention time for fluid marker by the gastrointestinal tract of the vervet monkey was comparable to that reported by Hinton *et al.* (1969) for human subjects.

Microbial fermentation and synthesis of protein. Fig. 3 gives the mean concentrations of VFA measured at different sites along the gastrointestinal tract of the racoon, dog, pig, bushbaby, vervet monkey and pony over a 12-h period between meals. All were fed on a given diet at 12-h intervals for a period of 3-4 weeks before the study in order to allow the necessary time for adjustment of large-intestinal microbes (Cranwell, 1968). Despite the marked differences in diets and the rates at which digesta passed through the large intestine, VFA were the major anions in the large-intestinal contents of each species. Except for the racoon, the concentrations were equal to or greater than those seen in the rumen of cattle and sheep.

Appreciable amounts of soluble, rapidly-fermentable carbohydrate escape the small intestine of the pig and pony under normal conditions. When pigs were given a diet containing maize, 2-6% of the starch reached the large intestine (Holmes *et al.* 1973). In a separate study, less than 8% of the starch passed the terminal ileum of pigs given maize, wheat or milo, but this increased to 21% in animals given barley (Keys & DeBarthe, 1974). Up to 29% of dietary starch was shown to reach the large intestine of ponies given high levels of maize (Hintz *et al.* 1971). Endogenous substrates, such as amino acids (El Shazley, 1952a,b) and the large polysaccharide component of mucous (Vercellotti *et al.* 1978), also provide a source of VFA.

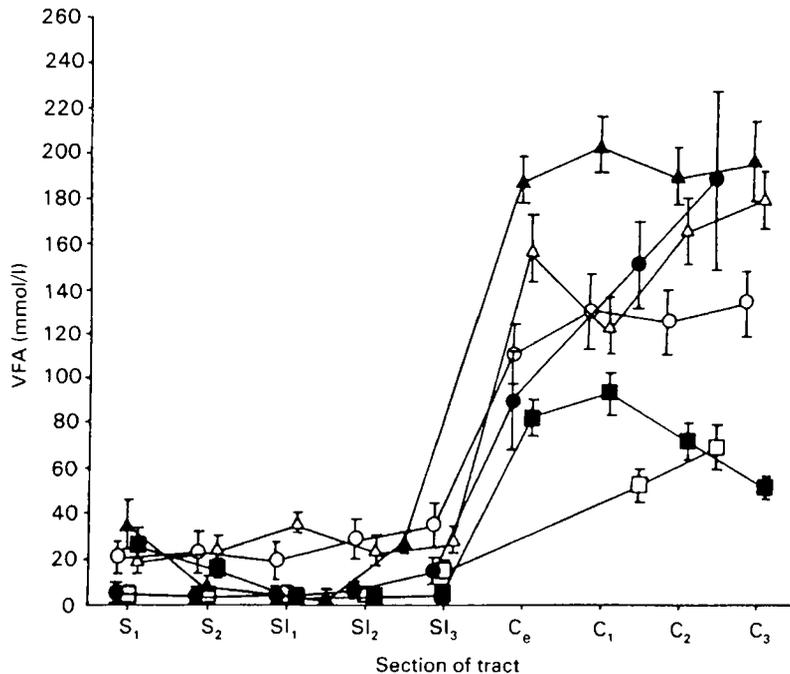


Fig. 3. Mean (with SE) values for concentrations of volatile fatty acids (VFA) along the gastrointestinal tract of (□) racoon (*Procyon lotor*), (●) dog (*Canis familiaris*), (▲) pig (*Sus scrofa*), (△) bushbaby (*Galaga crassicaudatus*), (○) vervet monkey (*Cercopithecidae pygerthrus*), (■) pony (*Equus caballus*). All animals were fed at 12 h intervals during a 3 to 4-week period before the study. Racoons, pigs and ponies were given the same diet. Each value represents the mean from twelve animals, killed in groups of three at 2, 4, 8 and 12 h after feeding. Sections of tract were oral (S₁) and aboral (S₂) halves of the stomach; two or three equal segments of small intestine (SI₁, SI₂, SI₃); caecum (C_e); and two or three segments of colon (C₁, C₂, C₃). Illustration modified from Argenzio *et al.* (1974b); Clemens *et al.* (1975); Banta *et al.* (1979); Clemens & Stevens (1979); Clemens (1981).

Over-production of VFA in the large intestine can produce results similar to those seen in the rumen. Over-feeding of grain to sheep resulted in a marked decrease in pH and an increase in the lactobacillus population of caecal digesta (Allison *et al.* 1975). Svendsen (1975) showed that VFA at low pH also could result in atony of caecal musculature in cattle. The diarrhoea associated with carbohydrate malabsorption by the small intestine has been attributed to both VFA and lactic acid. Concentrations of acetic acid similar to those found in the rumen and large intestine produced gastric ulcers in dogs (Davenport, 1964) and perfusion of the rat colon with solutions containing VFA at a low pH caused damage to the mucosa and a depression in net water transport (Bustos-Fernandez *et al.* 1976). Atony induced by VFA could produce diarrhoea through relaxation of haustra or inhibition of 'anti-peristalsis' in the proximal colon. Saunders & Sillery (1982) found that perfusion of the rat colon with lactic acid at a pH of 4.0 resulted in mucosal damage and an inhibition of water transport similar to that noted with VFA. Lactic acid may also produce an osmotic diarrhoea, as it has been shown to

be absorbed from both the rumen (Williams & MacKenzie, 1965) and rat colon (Umesaki *et al.* 1979) at only one-tenth the rate of VFA.

Carbohydrate itself may produce an osmotic diarrhoea when present in concentrations that exceed the fermentative capacity of large intestinal bacteria. Saunders & Wiggins (1981) found that administration of high levels of lactulose, mannitol or raffinose to human subjects resulted in the presence of these sugars in the stools and an increase in stool volume. A similar situation may apply to the development of microbial fermentation in newborn animals. R. A. Argenzio, H. W. Moon, L. Kemeny and S. C. Whipp (unpublished results) produced carbohydrate malabsorption by administration of corona virus to newborn pigs. This resulted in diarrhoea in pigs 3 d old, with high concentrations of lactose and low concentrations of VFA in the faeces. Pigs 3 weeks of age showed no diarrhoea, with negligible amounts of lactose and normal levels of VFA in their faeces.

Studies of the pony large intestine (Wootten & Argenzio, 1975) showed that the contents underwent cyclic periods of microbial protein synthesis and disappearance in a manner similar to that of the rumen. Net production and disappearance of protein was associated with a net appearance and disappearance of urea and NH_3 . Substantial amounts of urea are secreted into the large intestine of rabbits (Regoeczi *et al.* 1965), ponies (Haupt & Haupt, 1971) and cattle (Mugerwa & Conrad, 1971). Powell (1979) estimated that 20% of the urea pool was normally secreted into the human intestine. Due to lack of evidence for active transport of amino acids or oligopeptides it is presumed that most of the N is absorbed as NH_3 and that microbial protein synthesized in the large intestine is of little nutritional value in species that do not practice coprophagia. However, digestion of microbial protein also has been demonstrated in the proximal colon of the rabbit (Bonnafeous & Raynaud, 1968) and both the large intestine of the horse (Slade *et al.* 1971) and pig (Niiyama *et al.* 1979) have been shown to absorb microbially-synthesized amino acids.

Secretion and absorption. The large intestine receives an inflow of fluid from the ileum similar to saliva in its high concentrations of Na, HCO_3 and/or PO_4 . Alexander (1965) found that the concentration of PO_4 was higher than that of HCO_3 in the dog, cat, rabbit and guinea-pig. HCO_3 was the major anion in the pig and horse (Alexander, 1962), as well as the human ileum (Fordtran, 1973). Relatively little information is available on the absorptive load normally placed on the large intestine. However, Argenzio (1975) estimated that the pony large intestine received 19 l ileal fluid/d, and large-intestinal secretions contributed a minimal addition of 12 l of fluid containing high concentrations of Na and HCO_3 . Over 95% of the Na, HCO_3 and water were absorbed before excretion in the faeces; a minimal absorptive load equivalent to over 100% of the animal's extracellular fluid volume.

Table 1 compares results from *in vivo* absorption studies of the reticulo-rumen of sheep and the large intestine of other species. Na was absorbed from the reticulo-rumen, the ventral (proximal) colon of the pony and both the pig and human colon at approximately half the rate of VFA absorption, and in association

Table 1. *In vivo* absorption or net appearance of volatile fatty acids (VFA), inorganic electrolytes and water by the isolated reticulo-rumen of sheep and the pony, pig, human, goat and dog large intestine

Species	Segment	Bathing solution*				Daily absorption or appearance (/kg body-wt)					Source	
		pH	VFA (mmol/l)	Sodium (mmol/l)	Bicarbonate (mmol/l)	Chloride (mmol/l)	VFA (mmol)	Sodium (mmol)	Bicarbonate (mmol)	Water (ml)		BMR (%)
Sheep	Reticulo-rumen	7.0	134	149	9.1	29	30	15	-15	40	23	Dobson (1959)
	Ventral colon	6.1	100	140	20	20	31	7	-12	18	33	
Pig	Proximal colon	6.4	107	122	15	15	55	26	-14	170	44	Argenzio <i>et al.</i> (1977)
	Distal colon and rectum						40	20	-9	110	32	
Human	Caecum, colon and rectum	7.4	90	120	20	40	9.8	3	-4.5	24	8.4	Argenzio & Whipp (1979)
Goat	Colon and rectum	6.0	70	100	20	30	31	29	NS	190	26	Ruppin <i>et al.</i> (1980)
Dog	Colon and rectum	6.4	90	122	27	15	7.5	8.3	NS	58	4	Argenzio <i>et al.</i> (1975)
												Herschel <i>et al.</i> (1981)

NS, not significant; BMR, basal metabolic requirement.

*Bathing solutions were isotonic to plasma of each species but varied in initial composition. In the sheep, pony, pig and human studies the VFA consisted only of acetate. The solution used in the goat study contained 60 mM-acetate and 10 mM-propionate. That used to perfuse the dog colon was an equimolar mixture of acetate, propionate and butyrate. Positive values designate net absorption and negative values net appearance within the lumen. Appearance of HCO₃ in the goat and dog colon was not significant (NS). A steady-state perfusion technique was used on all species except the sheep and pony, in which a static system was used. Contribution of VFA absorption to BMR was calculated as if all VFA were absorbed as acetate at an energetic equivalent of 875 kJ (209 kcal)/mol. Absorption of an equimolar mixture of the three VFA would provide approximately twice the energy contribution of acetate alone. Adapted from Stevens *et al.* (1980).

with a net appearance of HCO_3 in the lumen. However, Na was absorbed as rapidly as VFA from the goat and dog colon, with no appearance of HCO_3 , and the same relationship was reported for the colon of sheep (Rubsaman & Engelhardt, 1979). These differences were due to variations in the rate of Na absorption. Under identical, *in vitro* conditions, the bovine rumen and the large intestinal mucosa of the pony, pig and dog showed very similar rates of VFA absorption per unit surface area of tissue (Stevens, 1978). *In vivo* studies of the pig and dog colon also showed identical rates of VFA absorption per unit surface area (Herschel *et al.* 1981). *In vitro* studies also showed that although VFA was absorbed at similar rates by the proximal and distal colon of the pony, Na was absorbed six times more rapidly by the distal colon.

Absorption of Na and VFA alone could account for the isotonic absorption of most of the water removed from the pony, pig, goat and dog colon. Therefore a slower rate of Na absorption would favour the retention of fluid necessary for efficient microbial digestion. Since the respective buffering capacities of saliva and ileal fluid are insufficient to neutralize the VFA produced in the rumen or the large intestine of the pony and pig, release of HCO_3 also would aid this process. Conversely, a more rapid rate of Na absorption would aid in the conservation of both Na and water.

Absorption of Na, VFA and water were increased with a decrease in the pH of solutions used to perfuse the rumen and the colon of the goat, pig and dog. Replacement of Na with choline reduced the rate of VFA absorption from the rat colon (Ümesaki *et al.* 1979). Replacement of VFA with Cl resulted in a reciprocal decrease in the rate of Na absorption from the colon of the goat (Argenzio *et al.* 1975) and pig (Crump *et al.* 1980). VFA replacement also reduced the rate of HCO_3 appearance in the sheep rumen and the colon of the pony, pig and rat. Mechanisms which could account for this interdependence in the absorption of Na and VFA and the release of HCO_3 were proposed by Argenzio *et al.* (1977).

Table 1 also provides an estimate of the contribution of VFA to the basal metabolic requirement of each species. Even bearing in mind the differences in pH of bathing solutions and evidence that VFA production may be the rate-limiting factor in its absorption from the pig colon (M. J. Allison and R. A. Argenzio, unpublished results), it appears that VFA could provide a substantial portion of the energy required by each species.

Summary

The rumen and the mammalian large intestine are similar in many respects. Microbial protein appears to be synthesized and degraded in the digesta of both organs in a comparable manner. The VFA end-products of carbohydrate fermentation are produced in similar concentrations. Digesta pH is maintained with buffer added by the saliva or ileal fluid, HCO_3 released into the lumen and rapid absorption of the organic acids. VFA are absorbed at equivalent rates by rumen epithelium and large intestinal mucosa. Over-production of VFA produces similar adverse effects.

There is a considerable amount of species variation in the relative length and volume as well as the extent of sacculation of the large intestine. The caecum is the primary site for retention of digesta and microbial fermentation in the large intestine of rabbits, rodents and a few other species. However, the proximal colon is the major site of retention and fermentation in most mammals.

Absorptions of Na and VFA appear to account for absorption of most of the water removed during passage of digesta through the large intestine. A relatively slow rate of Na absorption and release of HCO₃ appears to provide the fluid and buffering capacity needed for efficient microbial digestion in the rumen and in the large intestine of some species. A more rapid absorption of Na by the large intestine of other species would aid in the conservation of Na and water.

The many similarities between the large intestine and the rumen suggest that further comparison can provide additional information on both the function and diseases of these two organs. The rumen has proved to be accessible to a variety of procedures useful for the study of microbial digestive processes and its epithelium has provided a non-glandular tissue for studies of inorganic ion transport as well as the transport and metabolism of VFA. Comparative studies of the large intestine also can provide a better understanding of the functions and malfunctions of the human large intestine. The pig and some species of monkey would appear to be most suitable for examining the effects of diet and carbohydrate malabsorption. The equine large intestine provides a good system for studying events, such as those associated with the recycling of nitrogenous compounds. Furthermore, as demonstrated by comparative studies of the kidney and other organs, a great deal of information can be gained through examination of the various mechanisms that have been developed to serve similar functions.

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