

# Early enteral nutrition — principles and practice

## Abstract

This article has three major objectives: to review briefly the physiology and metabolism of the small intestinal mucosa; to summarise the evidence and recommendations regarding early enteral nutrition; and to discuss how to implement early enteral nutrition in small animal veterinary practice.

The gastrointestinal tract has a high metabolic rate and is composed mostly of cells that have a short life. Early enteral nutrition (EEN) contributes to improved gastrointestinal (GI) function, decreased GI permeability and improved patient outcomes. EEN can be delivered starting on day 1 for even critically ill patients. A transition from simple to more complex foods over time results in fewer complications.

**Key words:** nutrition, enteral, bacterial translocation, glutamate

In simplest terms, the major function of the gastrointestinal tract (GIT) is to transform ingested food into simple molecules that can be used for energy and metabolic function by all of the other cells in the body. To accomplish this, the stomach provides mixing and gross breakdown of food, the small intestine provides further breakdown of food and absorption of nutrients, and the large intestine acts as a waste compactor and water extractor. The intestinal mucosa contains the cells that actually accomplish these processes. More detail on the types of cells can be found in *Figure 1*.

A very important secondary function of the GIT is to keep the waste material, digestive enzymes and bacteria inside the intestinal lumen and away from the rest of the body. The GIT is actually the largest immune organ in the body, containing about 50% of the lymphoid cells in the body (Mellema, 2011). Failure of this barrier function can allow bacteria or other pro-inflammatory substances to enter the systemic circulation, leading to sepsis or a systemic inflammatory response.

These functions represent an immense workload. The GIT is only 5% of bodyweight but consumes 20% of the body's oxygen (Yen et al, 1989; Vaugelade et al, 1994). So,

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although it is the major role of the GIT, and enterocytes particularly, to provide glucose and amino acids to the rest of the body, the cells in the GIT have to have energy and nutrients to run their own metabolic processes.

Most cells in the body use glucose as their major energy source, but studies have shown that the enterocytes prefer the amino acid glutamate as an energy source to other amino acids or glucose. Glutamine is also used by the enterocytes, but radiotracer studies have shown that it is primarily glutamate that is used for energy production (Reeds et al, 2000). Various studies in dogs, cats, rabbits, rats, pigs and chickens have confirmed that the intestines absorb and metabolise virtually all of the available dietary glutamate themselves (Neame and Wiseman, 1957; Neame and Wiseman, 1958; Watford et al, 1979).

With this high turnover of cells, and high energy demands, it is no surprise to realise that the GIT is quite vulnerable to hypoperfusion, inflammation and interruption of nutrition. As little as 30 minutes of hypotension can cause severe destruction of the small intestinal villi (Rönn et al, 2011). Any bowel surgery also contributes to gut inflammation, mucosal injury and ileus. Impairment of the GIT barrier and immune function can lead to translocation of either bacteria or inflammatory mediators from the GIT into the systemic circulation.

## The evidence for early enteral nutrition (EEN)

Historically, clinical recommendations were not to start feeding until day 3–5 of hospitalisation. In the last 10 years, however, numerous studies have shown that EEN has significant benefits in both humans and animals. Lewis et al (2001) reviewed 11 different studies involving 837 human patients that had undergone gastrointestinal (GI) surgery. Patients were either given nothing by mouth, or received enteral feeding within 24 hours after GI surgery. Early feeding significantly reduced the risk of any type of infection by 25% ( $p = 0.036$ ) and significantly reduced the number of days in the hospital ( $p = 0.001$ ). See *Figure 2* for background information on interpreting the  $p$  values and significance of scientific results.

In animal studies, providing intra-luminal nutrients has been shown to reverse shock-induced mucosal hy-

### Figure 1. Cells in the small intestine

- The intestinal epithelium is made up of four major types of cells — enterocytes, mucous cells, enteroendocrine cells and Paneth cells. These four cell types all originate from **stem cells** located in the ‘valleys’ at the bottom of the villi, named the **crypts of Lieberkuhn**.
- Secondary digestion and absorption of nutrient molecules takes place in the small intestine through a layer of finger-like villi.
- **Enterocytes**<sup>a</sup> are simple, column-shaped epithelial cells found in the small intestine and also the colon (where they are termed colonocytes). They are also known as ‘surface absorptive cells’ and are the workhorses of the intestine. Enterocytes are continuously formed and replenished from the stem cells that are located in the crypts (valleys) between the villi. Enterocytes are ‘born’ at the bottom of the villus and take 2–5 days to slowly migrate up to the apex of the villus. Once they reach the apex, they are programmed to die (Sukhotnik et al, 2009). In contrast, red blood cells live for about 3 months in the circulation.
- Enterocytes are responsible for absorbing sugars, amino acids, water and electrolytes. They adhere tightly to each other and therefore also serve as a physical barrier that prevents food and bacteria in the intestinal lumen from migrating freely into the systemic circulation.
- Each enterocyte also forms numerous tiny folded extensions of its cell membrane, about 1 micrometer long, that are termed microvilli<sup>b</sup> or ‘striated border’. These folds increase the surface area for absorption. Enzymes located in these microvilli break down sugars and proteins into their final forms, ready for absorption and transport through the enterocyte.
- **Mucous**<sup>c</sup> cells (also known as goblet cells because of their shape) release mucin that acts as a protective barrier for the villi.
- **Enteroendocrine**<sup>d</sup> cells are scattered throughout the stomach, pancreas and small intestine. They are responsible for producing various hormones that control gastrointestinal functions, such as gastrin, cholecystokinin, insulin and glucagon.
- **Paneth cells** are the guardians of the stem cells. They can release substances that cause lysis of bacteria (Ayabe et al, 2000). Paneth cells actually live for about 3 weeks and are located in the crypts.

### Figure 2. *p*-values and significant differences

- Many scientific studies publish their results in terms of statistically significant differences. Usually, this is a difference between two kinds of treatment protocols.
- There are two steps to reading these kinds of results.
- First, the actual measured difference may be expressed in whatever units are being measured, such as % of patients that survived, or changes in a biochemical measurement, such as glucose in mmol/l. But it is sometimes hard to tell just by looking whether or not these differences actually mean anything.
- So, most results will also have a *p*-value written in parentheses, usually at the end of the sentence. The *p* stands for Probability. It is always written as a decimal number. A *p* of 0.05 or less is commonly accepted as a ‘significant difference’. In words, it means that there is less than a 5% probability that this measured difference occurred by chance. The other way to say that is ‘it is 95% certain that the difference measured was because of the treatment.’
- Studies with large numbers of patients or precise measurements can sometimes quote an even smaller *p* value, such as  $p < 0.001$ . This means that there is only one chance in a thousand that the difference between groups was not actually due to the treatment.

popperfusion and improve the GI motility in a variety of experimental animal models — sepsis, haemorrhagic shock and ischaemia-reperfusion injury (Flynn et al, 1992; Grossie et al, 2001). Another well-designed experimental study in dogs that underwent colorectal anastomosis showed that in the dogs who received full caloric intake of an elemental liquid diet starting immediately on recovery, the anastomosis had twice the bursting pressure and double the amount of collagen after 4 days, compared with those dogs who received only oral electrolytes in water ( $p < 0.001$ ) (Moss et al, 1980).

A key study in veterinary patients also showed that dogs and cats who received any sort of enteral nutrition had a significantly lower mortality rate (10%) compared with those that received only parenteral nutrition (32%) ( $p = 0.023$ ) (Chan et al, 2002).

Benefits of early nutrition, especially enteral nutrition, are reduced severity of disease, decreased complications, shorter hospital stays and better patient outcomes (McClave et al, 2009). One of the most conclusive studies showing the benefits of EEN on patient outcomes and GI function in dogs was published by Mohr. This study of 30 puppies with parvovirus, all less than 6 months old, compared the ‘proactive’ approach of feeding via a naso-oesophageal tube with the ‘conservative’ approach of ‘wait until they stop vomiting’. Half of the patients had naso-oesophageal tubes placed and began receiving a continuous infusion of a reconstituted food (Pedigree Convalescence Support) starting 12 hours after admission. The other half of the patients received nothing by mouth until they had gone for 12 hours without vomiting. After that, the second group were hand fed a solid, low-fat diet (Pedigree Canine Low-Fat Diet) every 4 hours. The naso-oesophageal dogs regained their appetite a day earlier, steadily increased their bodyweight and stopped vomiting sooner. Biochemical studies of intestinal permeability were also performed and showed that the naso-oesophageal group had better GIT integrity (Mohr et al, 2003).

Pancreatitis has also traditionally been managed with ‘nil per os’ treatment, but a recent study showed that dogs that were fed through an oesophagostomy tube (starting on day 1, using low-fat commercial dog food) actually had fewer episodes of vomiting or regurgitation than dogs that received parenteral nutrition (Mansfield et al, 2011).

## Delivering EEN

Nutritional consensus guidelines in veterinary medicine have been published by the World Small Animal Veterinary Association (Freeman et al, 2011) and can serve as a broad guideline for nutritional support plans. Current consensus guidelines from the (hu-

man) Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition recommend early, proactive nutritional support in the critically ill patient (McClave et al, 2009).

There are three logical questions to answer in delivering EEN to hospitalised patients: when to start; what to give when; and what delivery method to use.

## When to start

After the patient has been adequately stabilised from any acute conditions or recovered from any surgery, this author recommends that hospitalised patients should be started on EEN within the first 24 hours, and preferably within the first 12 hours. This recommendation is supported by the evidence cited above. It is important to realise that the patient may have been anorexic for some period of time before being admitted to the clinic, which makes it even more crucial to start EEN on day 1 of hospitalisation. One study of patients admitted to a university teaching hospital showed that 54% of cats and 35% of dogs had a history of decreased food intake (Chandler and Gunn-Moore, 2004). Patients that have undergone 3–5 days of decreased food intake are at a high risk of developing malnutrition (Freeman et al, 2011).

### Figure 3. Calculating RER using the exponential formula

- Know the patient's bodyweight in kg (example: 5 kg) and get a standard hand-held calculator that has a square root key  $\sqrt{\quad}$
- Multiply the patient's bodyweight by itself 3 times (example:  $5 \times 5 \times 5 = 125$ )
- Take the square root of 125 once ( $\sqrt{125} = 11.180$ )
- Press the square root key again ( $\sqrt{11.180} = 3.343$ )
- Multiply that answer by 70 ( $3.343 \times 70 = 234$ ) to get the RER in kcal per day

- You can practice with different bodyweights and check your answers against *Table 1*.

## What to give when

**Day 1** — The small intestine returns to normal motility almost immediately after an insult such as GI surgery, but the motility of the stomach and large intestine are compromised for 24–36 hrs (Catchpole, 1989). Therefore, liquid diets or thin gruels are commonly used to begin enteral nutrition, because they require minimal mechanical digestion and are low residue (Crowe et al, 1997; Moore and Moore, 2009).

For patients that have been anorexic for more than 3 days, or that are critically ill, this author prefers to start with a dilute solution that is isotonic and that contains appropriate amounts of sodium and glucose as well

**Table 1. Resting Energy Requirements for Dogs and Cats**

Kg	Linear	Exponential	Approximate
1	<del>100</del>	70	
2	<del>130</del>	118	
2.5	<del>145</del>	139	
3	160	160	
3.5	175	179	
4	190	198	200
4.5	205	216	
5	220	234	
7.5	295	317	
10	370	394	400
12.5	445	465	
15	520	534	
17.5	595	599	
20	670	662	700
22.5	745	723	
25	820	783	
27.5	895	841	
30	970	897	900
35	<del>1120</del>	1007	
40	<del>1270</del>	1113	
45	<del>1420</del>	1216	1200
50	<del>1570</del>	1316	
55	<del>1720</del>	1414	
60	<del>1870</del>	1509	
65	<del>2020</del>	1602	
70	<del>2170</del>	1694	

Values that are crossed out should not be used. They are included for comparison purposes only.

as key amino acids such as glutamate and glutamine. Oralade (JAM Pet Foods, UK) meets all of these requirements. It also offers the advantages of being palatable and ready-mixed. Alternative solutions that can also be used are products such as Enteral Care (Kruuse UK) diluted 1:2 in water, or Royal Canin Convalescent Support powder mixed at 1/3 of normal strength.

This author uses a starting volume of 0.3–0.5 ml/kg/hour, delivered either as a continuous infusion



*Figure 4. Rottweiler with nasogastric tube in place.*

through a feeding tube, or in boluses given orally every 2 hours. As the patient's tolerance to feeding improves, the volume is then increased by 50% every 8–12 hours. If the patient vomits, simply wait for 2 hours and then re-start. Sometimes it is necessary to reduce the volume back to the previous level for another 8–12 hours. The caloric content of the initial solution is also increased every 24 hours by mixing the initial solution with more concentrated foods.

The key objective in the first 12–24 hours is to keep the enterocytes supplied with fuel sufficient to maintain their function and integrity. A full assessment of the patient's illness and likely nutritional issues should be performed during this period according to WSAVA guidelines (Freeman et al, 2011).

**Days 2 and 3** — The goal is to increase both volume and caloric density as the patient increases its tolerance to food. Chan et al (2006) have shown that illness alters the body's metabolic functions such that

**Table 2. Comparison of commonly used feeding tubes**

	Naso-oesophageal	Naso-gastric	Oesophagostomy	Gastrostomy
Diameter limited by size of nares	Yes	Yes	No	No
Must be placed under general anaesthesia	No	Sometimes	Yes	Yes
Can be used to suction stomach	No	Yes	No	Yes
Can deliver semi-solid food	Probably not	Probably not	Yes	Yes

full caloric requirements should be re-introduced over a 48–72 hour period. Typically, a ‘ramping-up’ period of 3 days is used to achieve delivery of full nutritional requirements. In relatively healthy patients, day 1’s target is no more than 1/3 of the caloric requirements, with day 2 at 2/3 and day 3 delivering full caloric requirements. This process may take longer in some patients.

Caloric goals are based on the resting energy requirements (RER), which are calculated by one of two formulas:

- (1) Linear formula:

$$\text{RER in kcal/day} = (30 \times \text{bodyweight in kg}) + 70$$

- (2) Exponential formula:

$$\text{RER in kcal/day} = 70 \times (\text{bodyweight in kg})^{0.75}$$

The exponential formula (2) is considered to be the most accurate because it is based on a combination of body surface area and metabolic rate. See *Figure 3* for an example of how to calculate this formula. This formula can be used for all patients, but should definitely be used for patients that weigh less than 3 kg or more than 45 kg because the linear formula overestimates RER for those bodyweights. See *Table 1* for comparison values. *Table 1* also highlights some approximate ‘index’ points of bodyweight versus RER which can be used for quick reference.

Many older textbooks suggest that the RER should be multiplied by an ‘illness factor’, ranging from 1.2 to 2.0, with the resulting illness energy requirement as the caloric goal. These multiplication factors were extrapolated from early studies in human medicine, and have not particularly been supported by studies that measure actual metabolic rates. The first goal actually should be to deliver RER. Overfeeding can result in deleterious effects such as hyperglycaemia, hypertriglyceridaemia, azotaemia, hepatic dysfunction, and altered immune function (Chan, 2009).

**Day 3 or 4** — If all has gone well, the patient should be able to tolerate full-strength Enteral Care or Royal Canin Convalescence Support. Semi-solid foods such as Hills a/d (180 kcal per 156 g tin) or Royal Canin Recovery Support (184 kcal per 165 g tin) have a caloric density of about 1.1 kcal/g and can usually be introduced at this time, if that has not already been done. As an example, a 3.5 kg cat needs the equivalent of one small (156 g) tin of a/d per day. A 30 kg Labrador needs about 5 x 156 g tins of a/d per day. Some patients, such as those with pancreatitis, may benefit from a low-fat diet such as Hills i/d (370 kcal per 370 g tin) or Royal Canin Sensitivity Control (512 kcal per 420 g tin).

## What delivery methods to use

In many patients, a feeding tube will provide the most reliable and efficient means of providing nutritional



*Figure 5. Nasogastric tube correctly positioned in stomach.*

support. Voluntary intake in hospitalised patients is not a reliable method of providing nutritional support. This was shown in a multi-centre study of four veterinary schools, with 276 dogs and 821 hospital days. The RER was met only 27% of the time, and food refusal was the most common reason, occurring in 44% of the dogs (Remillard et al, 2001).

A brief analysis of tube-feeding strategies is given here (see *Table 2* also), but a full description of various tube-feeding methods is beyond the scope of this article. Excellent teaching resources on placing feed-



*Figure 6. Oesophagostomy tube in a cat.*

## Key points

- The gastrointestinal tract has high energy and oxygen requirements in proportion to its weight.
- The cells that make up the absorptive surface of the intestine prefer amino acids such as glutamate and glutamine as their energy source rather than glucose.
- The evidence for the benefits of early enteral feeding is strong. 'Nil per os' after gastrointestinal surgery or as a management strategy in pancreatitis or parvo is no longer recommended.
- Enteral nutrition should be started within the first 12–24 hours of a patient's hospital stay using elemental or easily digested diets.
- Placing a feeding tube early in the patient's treatment will provide a more reliable method of delivering nutrients and calories.
- A 4 kg cat needs about 200 kcal per day, and a 30 kg dog needs about 900 kcal per day.

ing tubes are available on the Veterinary Information Network ([www.vin.com](http://www.vin.com)), and as a DVD from Mila International (<http://milainternational.com/mila-products.html>).

Naso-oesophageal tubes are ideal for short-term feeding after relatively minor GI surgery such as enterotomies or intestinal anastomosis, or mild abdominal disease such as pancreatitis. A 5 Fr tube is the smallest useful diameter.

Naso-gastric tubes are ideal for patients with parvovirus, severe pancreatitis, peritonitis or post-operative gastric dilation-volvulus (*Figure 4*). Again, 5 Fr is the minimum diameter, and 8 Fr or larger is preferable. In larger dogs, it will be necessary to have a length of 110–120 cm in order to reach the stomach, which will require a tube that has a wire stylette for stiffness during placement. Nasogastric tubes have an advantage over naso-oesophageal tubes in some patients, because they can be used to monitor gastric residual volume (*Figure 5*). By aspirating any stomach fluid every 2–4 hours, and recording the volume, it is possible to judge very accurately the time when the stomach has regained its motility. Nasogastric tubes are also very effective at reducing nausea, since the volume of stomach contents can be monitored and kept to a minimum.

Oesophagostomy tubes are ideal for patients with head or jaw injuries, and are particularly useful in cats (*Figure 6*). In fact, mastering the placement of oesophagostomy tubes is considered essential in the

management of critically ill cats (Chan, 2009). A 14 Fr is the minimum useful diameter and can be placed in virtually all adult cats.

Gastrostomy tubes are most appropriate for cats and dogs in situations involving a non-functional upper GIT. Examples would include dogs with neuromuscular impairment such as tetanus, myasthenia gravis, or paralysis due to toxin exposure.

Jejunostomy or nasoduodenal tubes require specialist expertise and equipment to place.

## Conclusion

Early enteral nutrition has been repeatedly shown in both human and animal patients to reduce patient recovery times and complications. EEN can safely be used, and in fact should be used, in support of patients who have undergone GI surgery — post-operative fasting of patients is no longer recommended. The GIT itself has high metabolic demands and enteral feeding solutions that support its particular requirements should be used whenever possible. Tube feeding is a valuable tool in delivering EEN and its use is to be encouraged.

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### Images of small intestinal cells can be found at the following links:

<sup>a</sup>Enterocytes — Boston University: <http://www.bu.edu/histology/p/1120310a.htm>

<sup>b</sup>Microvilli — Journal of Illustrated Science: <http://journalofillustratedscience.com/?p=18>

<sup>c</sup>Mucous cells — <http://www.bu.edu/histology/p/1170610a.htm>

<sup>d</sup>Enteroendocrine cells — <http://www.bu.edu/histology/p/1160410a.htm>

- To answer the CPD questions on this article visit [www.theveterinarynurse.com](http://www.theveterinarynurse.com) and enter your own personal login.

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