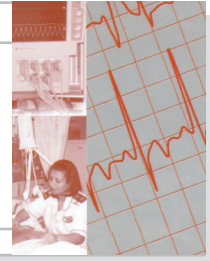


Enterocyte protection – a new goal in ICU nutrition



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Enterocytes are among the most metabolically active cells in the body but are the least well supplied with blood even under resting conditions.¹ Maintaining function of enterocytes has benefits that are becoming apparent in terms of improved outcomes from such diverse diseases as colorectal cancer² and pneumonia.³

Basic enterocyte physiology

Enterocytes are either secretory or absorptive. Secretory function is reduced in times of physiological stress such as critical illness but the basal metabolic activity of both types of cells still requires a supply of nutrients. Seventy per cent of the nutrition required by enterocytes is obtained from the gut lumen. As critical illness is almost invariably accompanied by a period of starvation, this source of nutrition is markedly diminished.⁴

Not only are luminal nutrients reduced, but the blood supply to the splanchnic circulation is also reduced in critical illness as blood flow is diverted to vital organs such as the heart, kidneys and brain.⁵ Blood flow to the enterocytes is intended for absorption rather than delivery of nutrients so is sluggish even under resting conditions. Under stress, flow is markedly diminished.⁴

The challenge of maintaining enterocyte integrity is therefore to provide luminal nutrients and maintain splanchnic blood flow. Maintenance of blood flow is central to many other therapeutic approaches in ICU so this review will concentrate on maintenance of luminal nutrient levels.

Minimise pre-operative starvation

One of the major bones of contention between the anaesthetic and surgical teams in many hospitals is the period of fasting prior to surgical procedures. Keeping patients 'nil per mouth' (NPM) arose from the findings of Mendelson⁶ that obstetric patients undergoing mask anaesthesia were at risk of regurgitation and aspiration. Fasting has been advocated to reduce the risk of aspiration during anaesthetic induction, prior to airway control, and emergence from anaesthesia. A simple formula is advocated by the American Society of Anesthesiologists (ASA), the 2/4/6/8 rule (Table I).⁷

Table I.

Period of fasting prior to anaesthesia related to food consumed

| Food consumed | Period of fasting (hours) |
|--|---------------------------|
| Large, fatty meal | 8 |
| Solid food (including dairy) | 6 |
| Breast milk/formula | 4 |
| Clear fluid (including black tea/coffee) | 2 |

This rule has a number of caveats, firstly regarding the timing of emergency surgery in relation to fasting status.⁸

- Patients who have undergone recent trauma or received opioids remain at risk irrespective of fasting period.
- Patients may have metabolic (diabetes, pregnancy) or mechanical (gastric or bowel obstruction) reasons that will result in risk irrespective of fasting period.

Patients in the groups above should be anaesthetised with necessary precautions to prevent aspiration, including awake intubation or rapid sequence induction with application of cricoid pressure.

The second group of caveats relates more specifically to the maintenance of the enterocytes:

- Patients SHOULD receive clear fluids up to 2 hours before surgery.
- Patients who are in the ICU with airway control by endotracheal tube or tracheostomy do not need to be fasted UNLESS the procedure contemplated involves the gastrointestinal (GI) tract or airway. Fasting for radiological investigations IS NOT required.⁹

Pre-operative oral fluids

Fluids administered pre-operatively have a number of beneficial effects depending on their constituents:⁹

- Water: maintains hydration and reduces the requirement for intravenous fluids that have been implicated in the generation of postoperative oedema. Adequate hydration also improves patient comfort and satisfaction.

- Carbohydrates: reduce the catabolic response generated by starvation and surgery. Insulin sensitivity and tissue integrity are maintained.¹⁰
- Peptides: maintain enterocyte function and muscle strength.¹¹

Lipids are not recommended as lipid emulsions are unstable in the acid environment of the stomach and may become particulate with a risk of aspiration.

Early postoperative enteral nutrition

Patients who undergo elective abdominal surgery do not necessarily develop an ileus requiring postoperative fasting with nasogastric drainage. Work from Copenhagen,² replicated in other centres,¹² has demonstrated that patients can undergo colonic resection with a period of fasting of only 8 - 10 hours and re-establishment of full enteral nutrition within 24 hours of surgery. This approach has become known as 'fast-track colonic surgery' and relies on a multimodal approach including:

- Clear fluids up to 2 hours pre-operatively, including carbohydrate and peptides
- Limiting intra-operative IV fluids to maintenance plus losses
- Laparoscopic dissection with specimen retrieval via Pfannenstiel incision
- NO nasogastric tube/abdominal drains
- Thoracic epidural analgesia
- Stop IV fluids on discharge from recovery room
- Commence sip feeds within 6 hours of admission to ward
- Aim for full enteral nutrition within 24 hours.

The success of programmes such as this requires a team approach with contributions from members including, but not limited to, surgeons, anaesthesiologists, intensivists, physiotherapists and dietitians. This has been supported by the ESPEN guidelines, which state that there is no reason to fast elective surgical patients postoperatively.¹

Early enteral nutrition after emergency surgery

Emergency surgical procedures involving the abdominal contents and elective operations involving the upper GI tract (including gastrectomy and pancreatectomy) do not allow for early enteral nutrition via the stomach. In these cases, a fine-bore feeding tube placed via the nose beyond the pylorus (or surgical anastomosis) into the proximal jejunum (nasojejunal tube) as part of the laparotomy may be very useful. This tube is preferable to the placement of a feeding jejunostomy as the potential for morbidity is reduced.¹³

The nasojejunal tube is extremely useful in maintaining enterocyte integrity. With the tube in place, a low dose (10 - 30 ml/h) of a semi-elemental feed may be commenced as soon as the patient arrives in the ICU. Semi-elemental feeds are absorbed in the absence of peristalsis and do not require an increase in secretory or digestive function.¹⁴ The enterocytes can thus receive nutrition without an increase in oxygen requirement.

The nasojejunal tube is not intended to provide systemic nutrition as this would require an increase in the digestive and secretory functions of the enterocytes with a resultant increase in oxygen requirements. In the early postoperative phase, splanchnic circulation may be reduced.⁵ This reduction may be exacerbated by pre-existing vascular disease or the use of inotropes, such as dopamine and adrenaline, which promote splanchnic vasoconstriction. Attempting to feed a full dose of enteral nutrition via a nasojejunal tube will result in feed intolerance, diarrhoea and even perforation of the terminal ileum. This perforation arises as a result of an increase in oxygen requirements that cannot be met by increased blood flow, as the terminal ileum lies in a watershed area between the superior and inferior mesenteric circulations, making it particularly vulnerable to ischaemia, progressing to perforation, a process with the acronym of NOMI (non-occlusive mesenteric ischaemia).¹⁵

Systemic nutrition

With enterocyte nutrition being maintained by nasojejunal feeding, systemic nutrition may be provided by the route most likely to prove successful. Systemic nutrition during the initial phase of ICU admission is most commonly confined to 5 - 10% dextrose to limit ketosis. During this phase emphasis is placed on resuscitation with restoration of circulation and oxygenation. Within 48 - 72 hours the condition of the patient should have stabilised to the extent that systemic nutrition should be considered.

A nasogastric tube will be in place so gastric feeding is also an option. Tolerance of gastric feeding is deemed to indicate that the distal ileum is no longer at risk of NOMI.¹⁵ Gastric feeding may be considered if gastric aspirate within a 6-hour period is less than 150 - 200 ml.¹⁶ The protocol followed at Addington Hospital is shown in Fig. 1.

In the early stages of ICU admission a central line is still likely to be in place. Should gastric feeding be unsuccessful, the use of parenteral nutrition should be considered at this stage. Commencing parenteral nutrition does not preclude continued attempts to feed enterally. The aim should be to establish gastric feeding with reduction of parenteral feeding as goals are met.¹⁷

Once full gastric nutrition is established, both nasojejunal and parenteral feeding can be stopped.

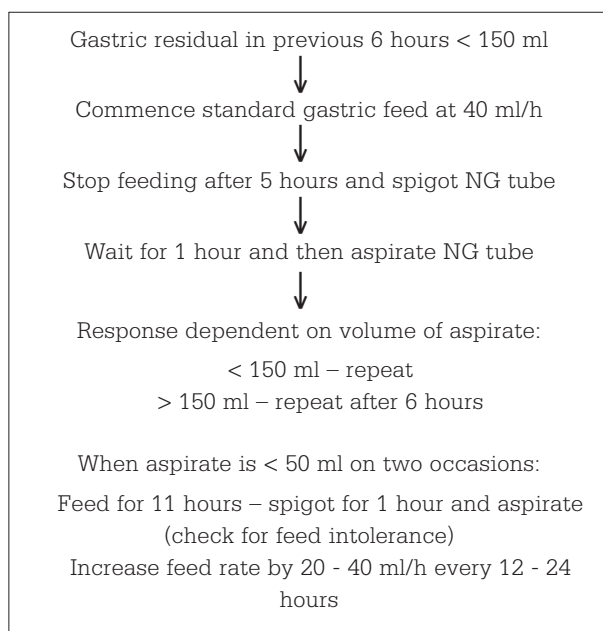


Fig. 1. Approach to gastric feeding at Addington Hospital.

Parenteral supplementation with glutamine may be continued as glutamine is avidly taken up by enterocytes, leaving limited amounts to provide systemic benefit.¹⁸

Refeeding syndrome¹⁹

Patients fed following a period of starvation exceeding 48 hours are at risk of the refeeding syndrome, the main component of which is acute hypophosphataemia. Phosphate is an essential component of all high-energy energy-transfer molecules such as adenine triphosphate (ATP). Synthesis of these compounds is reduced in starvation with increased urinary phosphate losses. On refeeding there is an increased demand for phosphate that may not be met by the slow mobilisation of phosphate from bone. It is therefore essential to check phosphate prior to and within 6 hours of commencing feeding. Phosphate is supplemented intravenously in the form of potassium-hydrogen-phosphate by the same protocol as for potassium chloride (KCl) – 40 mmol K⁺ in 200 ml 0.9% sodium chloride (NaCl)/5% dextrose. Magnesium is also a major cofactor for energy transfer that may be low in critical illness, so 2 g magnesium sulphate (MgSO₄) is added to this supplement at Addington.

Advantages of enterocyte nutrition

Early enteral nutrition does not place patients at risk of bowel perforation after surgery and bowel anastomosis. Early use of a semi-elemental feed (which does not increase enteral oxygen demand) is, by contrast, associated with a reduced rate of anastomotic dehiscence.²⁰ There is also an earlier return of bowel function and a reduced rate of both wound and pulmonary infections.²¹ The reduction in pulmonary infections led to an animal study, where mice were fed either enterally or parenterally for 2 weeks. At this stage

all animals received a similar intratracheal inoculation of *Escherichia coli*. Parenterally fed mice had a rate of subsequent pneumonia 50% greater than the enterally fed mice.²² It therefore appears that maintaining enterocyte, and thus gut-associated lymphoid tissue (GALT), function results in maintenance of barrier function at other epithelial surfaces, including the skin and respiratory epithelium.

Conclusion

Enterocytes have not commanded great attention but should be considered central to maintenance not only of bowel function, but of epithelial integrity throughout the body. Maintaining luminal nutrients will require fresh approaches to some of the 'holy cows' of peri-operative patient management, including pre-operative fasting and early enteral nutrition.

Consideration should be given to reducing pre-operative fasting and providing oral feeds as soon as possible.

Where tube feeding is required, differentiation should be made between enterocyte and systemic nutrition. Low-dose, nasojejunal, semi-elemental feeds may be used for enterocytes while either gastric or parenteral feeding may be used as appropriate for systemic nutrition.²³

1. Weimanna A, Bragag M, Harsanyic L, et al. ESPEN guidelines on enteral nutrition: Surgery including organ transplantation. *Clin Nutr* 2006; 25: 224-244.
2. Soop M, Carlson GL, Hopkinson J, et al. Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol. *Br J Surg* 2004; 91: 1138-1145.
3. Kudsk KA, Li J, Renegar KB. Loss of upper respiratory tract immunity with parenteral feeding. *Ann Surg* 1996; 223: 629-635.
4. Fruhwald S, Holzer P, Metzler H. Intestinal motility disturbances in intensive care patients pathogenesis and clinical impact. *Intensive Care Med* 2007; 33: 36-44.
5. Reid CL, Campbell IT. Nutritional and metabolic support in trauma, sepsis and critical illness. *Curr Anaesth Crit Care* 2004; 15: 336-349.
6. Mendelson C. The aspiration of stomach contents into the lungs during obstetric anaesthesia. *Am J Obstet Gynecol* 1946; 52: 191-205.
7. American Society of Anesthesiologists. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. *Anesthesiology* 1999; 90: 896-905.
8. Soreide E, Ljungqvist O. Modern preoperative fasting guidelines: a summary of the present recommendations and remaining questions. *Best Pract Res Clin Anaesthesiol* 2006; 20: 483-491.
9. Martindale RG, Maerz LL. Management of perioperative nutrition support. *Curr Opin Crit Care* 2006; 12: 290-294.
10. Ljungqvist O, Nygren J, Thorell A. Modulation of post-operative insulin resistance by pre-operative carbohydrate loading. *Proc Nutr Soc* 2002; 61: 329-335.
11. Henriksen M, Hessov I, Dela F, et al. Effects of preoperative oral carbohydrates and peptides on postoperative endocrine response, mobilization, nutrition and muscle function in abdominal surgery. *Acta Anaesthesiol Scand* 2003; 47: 191-199.
12. McArdle CS, McKee RF, Finlay IG, Wotherspoon H, Hole DJ. Improvement in survival following surgery for colorectal cancer. *Br J Surg* 2005; 92: 1008-1013.
13. Davies AR, Bellomo R. Establishment of enteral nutrition: prokinetic agents and small bowel feeding tubes. *Curr Opin Crit Care* 2004; 10: 156-161.
14. Bongers T, Griffiths RD. Are there any real differences between enteral feed formulations used in the critically ill? *Curr Opin Crit Care* 2006; 12: 131-135.
15. Melis M, Fichera A, Ferguson MK. Bowel necrosis associated with early jejunal tube feeding. A complication of postoperative enteral nutrition. *Arch Surg* 2006; 141: 701-704.
16. Kreymanna KG, Berger MM, Deutz NEP, et al. ESPEN Guidelines on Enteral Nutrition: Intensive care. *Clin Nutr* 2006; 25: 210-223.
17. Sax HC, Illig KA, Ryan CK, Hardy DJ. Low-dose enteral feeding is beneficial during total parenteral nutrition. *Am J Surg* 1996; 171: 587-590.
18. Van der Hulst RR, von Meyenfeldt MF, Tiebosch A, Buurman WA, Soeters PB. Glutamine and intestinal immune cells in humans. *J Parenter Enteral Nutr* 1997; 21: 310-315.
19. Bugg NC, Jones JA. Hypophosphataemia: pathophysiology, effects and management on the intensive care unit. *Anaesthesia* 1998; 53: 895-902.
20. Mechanick JI. Practical aspects of nutritional support for wound-healing patients. *Am J Surg* 2004; 188: 52S-56S.
21. Torosian MH. Perioperative nutrition support for patients undergoing gastrointestinal surgery: Critical analysis and recommendations. *World J Surg* 1999; 23: 565-569.
22. Wu Y, Kudsk KA, DeWitt RC, Tolley EA, Li J. Route and type of nutrition influence IgA-mediated intestinal cytokines. *Ann Surg* 1999; 229: 662-667.
23. Dhaliwal R, Daren K, Heyland DK. Nutrition and infection in the intensive care unit: what does the evidence show? *Curr Opin Crit Care* 2005; 11: 461-467.