Intestinal failure

The small bowel is a marvellous organ. First, it absorbs nutrients on behalf of all the other organs of the body. This function is not entirely 'altruistic': enteric (small-bowel) epithelium is itself nourished by luminal nutrients, which explains its disproportionately severe atrophy in starvation or total parenteral nutrition. Second, it has an enormous functional reserve. In the era of jejunoileal bypass for morbid obesity, most patients with 85–90% of the small bowel taken out of circuit could still maintain a body weight above normal. Third, the fact that diarrhoea after a major enterectomy diminishes with time indicates the adaptive power of the remnant small intestine. The lining of the jejunum and ileum is normally shed every few days as cells migrate from crypt base to villus tip, yet the process can be further accelerated to compensate for loss of tissue mass.

The six articles in this symposium are based on presentations given at a conference on intestinal failure held at the Royal Society of Medicine, London, in June 2006. The articles illustrate the problems in managing a patient with insufficient small bowel to maintain health, in whom supplements of macronutrients and/or water and electrolytes are required on a temporary or permanent basis. The symposium is concerned almost exclusively with loss of small bowel (i.e. enteric) function. Panproctocolectomy has limited nutritional consequences, although ileostomists are at increased risk of dehydration. Likewise, the large intestine has very little ability to adapt to small bowel resection, although additional loss of colon (including the ileocaecal valve) will magnify its effects.

Types and causes of intestinal failure

Three types of intestinal failure are described. Type 1 failure is the temporary loss of motility that is commonly seen in the early aftermath of laparotomy (paralytic ileus) or in critical illness. Type 2 failure is the more serious loss of function that stems from intestinal disease or complications of a major abdominal operation but is still potentially reversible. Type 3 failure implies permanent loss of function; it is this chronic condition that accounts for most referrals to the two intestinal failure units in Britain. Besides the need for long-term parenteral nutrition, reasons for such referral include intractable fistulas, persistent sepsis and problems with the central venous feeding line.

The commonest causes of chronic intestinal failure in Britain are Crohn's disease and mesenteric vascular insufficiency; cancer accounts for less than 10% of specialist referrals. The situation is very different in continental Europe, Japan and the USA, where approximately 40% of patients on home parenteral nutrition programmes have cancer. The disparity reflects different attitudes to palliative care in patients with advanced malignancy. It partly accounts for the tenfold difference in the rate of accrual of patients onto such programmes between the UK (10–12 per million population per year) and the USA (120 per million).

Intestinal adaptation

Compensatory growth of the shortened bowel is manifested by increased thickness of the wall and a modest increase in length. At a cellular level the crypts become deeper and the villi taller. This process of villous hyperplasia is always greater downstream from the site of resection, and healthy ileum has a greater adaptive power than jejunum. Jejunal mucosa is accustomed to a high nutrient load and may be close to its maximum potential mass, whereas ileal chyme is usually devoid of nutrients (which are fully absorbed within the proximal bowel). Thus when the ileum is brought closer to the stomach, it can grow apace.

Luminal nutrition and pancreatobiliary secretions are not the only mechanisms to explain intestinal adaptation, however. Experimental work in models of cross-circulation and sequestered bowel segments has indicated a role for humoral factors (Bristol and Williamson, 1985), notably glucagon-like peptide 2 or GLP-2 (enteroglucagon), growth hormone and the EGF (epidermal growth factor) family of peptides.

Attempts to enhance intestinal adaptation with dietary supplements of short-chain fatty acids, triglycerides, glutamine or arginine have met with limited success. Of potentially greater interest is the GLP-2 analogue teduglutide. Whether sustained mucosal growth can be achieved beyond the level anticipated with the passage of time remains to be seen. However, the importance of the compensatory response – both structural and functional – is demonstrated by the fact that up to one half of those patients taken onto a home parenteral nutrition programme no longer need such nutritional support 1 year later.

Small bowel fistula

Even if the length of the small bowel is close to normal, the organ cannot be used to maintain proper nutrition if there is a high-output fistula to the skin, i.e. >500 ml per day. Such fistulas can arise spontaneously in Crohn's disease or radiation enteritis, but 80% develop postoperatively as the consequence of an anastomotic leak or inadvertent enterotomy (including laparoscopic accidents). The initial emphasis must be on stabilizing the patient by reversing fluid and electrolyte deficiencies, dealing with ongoing sepsis (the usual cause of death), maintaining nutritional status and controlling the site of leakage. Spontaneous closure can then be anticipated in approximately 50% of cases. If not, operative closure is more likely to succeed if the surgeon waits for at least 24 weeks.

Short bowel syndrome: medical or surgical treatment

The non-operative treatment of chronic intestinal failure (type 3) entails home parenteral nutrition unless just enough bowel remains to support independent life. Meticulous maintenance of the central venous catheter – a true lifeline – is of paramount importance, so patients and carers need thorough training. Most patients on home parenteral nutrition receive between 2–5 litres of intravenous feed for 3–7 nights per week. Serious complications include cholestasis leading to liver failure and catheter sepsis, which

can potentially be overcome without losing the line but risks central venous thrombosis.

With a 3-year survival rate of around 80%, home parenteral nutrition has become a realistic long-term option; I have encountered one such patient who went through a normal pregnancy. Nevertheless, it seriously limits the patient's lifestyle, so surgical options should be considered. Several ingenious techniques for gastrointestinal reconstruction have been designed to increase the absorptive surface of the small bowel in young children, who have usually lost their midgut as a result of antenatal volvulus: reversed bowel segments, colonic interposition, semi-obstructive valves, plication of dilated loops, longitudinal lengthening, mucosal grafting onto a seromuscular gastric flap and combinations of the above. Since failure can make a bad situation worse, they all require considerable technical expertise.

The surgical alternative to autologous reconstruction is small bowel transplantation, which carries its own substantial set of problems: early risks of infection (bacterial translocation, viral enteritis) and perforation, persistent immunogenicity with the constant threat of graft rejection, lymphoproliferative disease, and graft *vs* host disease following the transfer of donor immune cells. Nevertheless, the growing experience of small bowel transplantation with novel techniques and improved immunosuppression has now achieved good results in the paediatric population, with a 3-year survival rate of up to 80% (similar to that of home parenteral nutrition). Moreover, in children with co-existent liver disease, various types of combined graft have been used with success.

This editorial presents a few highlights from a fascinating symposium, but it is only intended as a taster. The reader is invited to read the articles that follow. **BJHM**

Robin Williamson
Consultant Surgeon, Hammersmith Hospital
Professor of Surgery, Imperial College
Emeritus Dean, Royal Society of Medicine, London

Bristol JB, Williamson RCN (1985) Postoperative adaptation of the small intestine. *World J Surg* **9:** 825–32

KEY POINTS

- Intestinal failure is either acute, usually in the context of a recent operation, or chronic, when nutritional support is needed on a long-term basis.
- The functional reserve of the small intestine and its propensity for adaptive growth mean that many patients can live independently despite extensive bowel resection.
- In one type of acute failure – enterocutaneous fistula – nutritional support alone may lead to spontaneous cure, but most fistulas that persist beyond 2 months require operative closure.
- For those with permanent intestinal insufficiency, home parenteral nutrition can be associated with prolonged survival provided scrupulous attention is paid to the central venous catheter.
- In children at least, both autologous gastrointestinal reconstruction and small bowel transplantation have now become acceptable alternatives to permanent intravenous feeding.