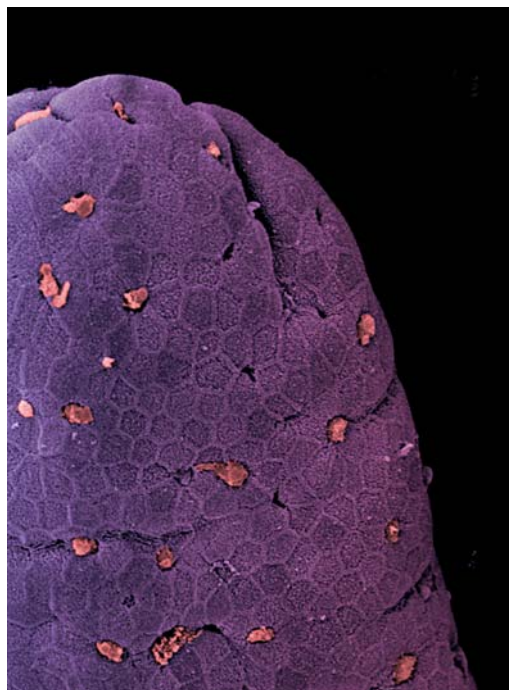


Clinical nutrition

— physiology and treatment of intestinal failure

By Nicola Ward, MRPharmS, MSc

Intestinal failure occurs when absorption from the gut is reduced below critical levels. The first article in this month's special feature looks at the physiological changes involved and gives an overview of how to manage the condition, including the use of parenteral and enteral nutrition



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A jejunal villus: removal of sections of bowel, hence villi, can make it hard to absorb enough fluid and nutrients

Intestinal failure occurs when absorption from the gut is reduced to the extent that nutrient, water and electrolyte supplements are needed to maintain health and growth.¹ The condition can be either acute (ie, temporary) or chronic, and result from a wide variety of causes, which are set out in Panel 1 (p10). Severe cases will require parenteral nutrition or parenteral fluids or both, with less severe cases generally being managed by the enteral route.

Most patients with severe intestinal failure are in the peri-operative period, mainly following gastrointestinal surgery.² Intestinal failure in most of these acute cases is short-lived, with nutritional support being required for less than 14 days and patients being managed in non-specialist units.

Chronic intestinal failure is less common, with the majority of patients having a short bowel (and therefore being referred to as having "short bowel syndrome"). Short bowel syndrome generally results from either:

- Jejunocolic anastomosis (ie, patients in whom the ileum has been removed, to leave a jejunocolic anastomosis)
- Jejunostomy (ie, patients in whom some jejunum, the ileum and colon have been removed, so they are left with an end jejunostomy)

Physiology

The length of the adult intestine ranges from 275–850cm. This large range means that it is more relevant to consider the length of bowel remaining after surgery, rather than the length removed.

The key lengths of bowel remaining are 200cm and 100cm. Where less than 200cm remain, maintaining an appropriate fluid and electrolyte balance is usually the key issue. Where less than 100cm is remaining, absorbing enough nutrients is an additional problem. The latter group of patients require specialist management and are often referred to St Mark's Hospital, London, or Hope Hospital, Salford, which are the two current specialist intestinal failure units in the UK. The most common reasons for patients to have surgery resulting in less than 200cm of bowel remaining are Crohn's disease, small

bowel ischaemia or radiotherapy-induced damage.³

Resection of the small bowel results in several physiological changes, which make it difficult for the remaining bowel to digest and absorb nutrients. These are set out below:

Gastric emptying Studies have shown that the speed of gastric emptying is increased in jejunostomy patients.⁴ This is thought to result from the loss of cells secreting peptide YY, which is a hormone responsible for the ileal and colonic braking mechanism.

Small bowel transit Small bowel transit has been shown to be faster than normal after an ileal resection and slower than normal after a jejunal resection.⁵ This reflects the usually faster transit of chyme through the jejunum than through the ileum.

Gastric secretions There is limited evidence, mainly from animal studies, to suggest that in at least the first few weeks after jejunostomy formation, hypersecretion of gastric acid may occur.⁶ This contributes to the high stoma output observed in these patients.

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Panel 1: Causes of intestinal failure

Acute

- Fistula
- Obstruction
- Small bowel dysfunction
 - ileus
 - enteritis (secondary to chemotherapy or infection)
- Sepsis
- Acute pancreatitis

Chronic

- Gut resection
 - short bowel: jejunostomy or jejunum-colon
 - gastrectomy
- Gut bypass
- Small bowel dysfunction
 - enteritis (eg, from Crohn's disease or irradiation)
 - dysmotility

Gastrointestinal hormones In addition to a reduction in peptide YY, as mentioned above, glycogen-like peptide-2 (GLP-2) levels are reduced after resection of the small bowel (because the main sites producing GLP-2 will have been removed). GLP-2 otherwise stimulates small bowel villous growth.⁷

Sodium and water homeostasis The absorption of sodium and water differs between the jejunum and ileum, as shown in Panel 2. The resection of the ileum will therefore have major consequences for sodium and water homeostasis, which will be complicated further if the jejunum is also resected.

Jejunostomy patients can be classified as net “absorbers” or “secretors” according to their ability to maintain sodium and water balance.⁸ Classification usually depends on the residual bowel length, with the critical bowel length being 100cm (see Panel 3).

Management

Patients with a jejunostomy have a high output from their stoma, which, in a net secretor (see Panel 3), is greater after eating and drinking. This effluent largely consists of normal daily secretions produced in response to food and drink.

Providing fluids to prevent sodium and water depletion and, if necessary, clinical nutrition support are among the ways to manage the condition. Other strategies such as reducing stoma output are also important, as is considering the effects of intestinal failure on any medication needed for coexisting conditions.

Panel 2: Comparison of the absorption properties of ileal and jejunal mucosa

	Jejunal mucosa	Ileal mucosa
Permeability to water, sodium and chloride	High	Low
Sodium concentration gradient	Small	Large
Sodium absorption dependent on water movement	Yes	No
Sodium absorption dependent on glucose and amino acid absorption	Yes	No

Sodium and water depletion Each litre of jejunostomy effluent contains about 100mmol of sodium.⁸ This needs to be replaced, to prevent the patient becoming dehydrated. Oral hypotonic fluids alone cannot be used because the low concentration of sodium (<90mmol/L) in them means that there is a net efflux of sodium from the plasma into the bowel lumen until a luminal sodium concentration of 90–100mmol/L is reached. This sodium is then lost through the stoma, further increasing sodium losses.⁹ Instead an oral glucose-saline mixture containing 90mmol/L sodium (often known as “St Mark’s solution” — see Panel 4, p11) is given to sip during the day, the inclusion of glucose making the solution hypotonic and enhancing the jejunal absorption of sodium. Patients sometimes find the solution more palatable if it is chilled and sipped through a straw or if a little fruit cordial is added. Commercial oral rehydration salts (eg, Dioralyte) do not contain sufficient sodium or glucose, unless mixed as a double-strength preparation. Sodium chloride capsules have been used as an effective alternative but these can cause nausea and vomiting, and up to 14 capsules per day are required.¹⁰ If less than 100cm jejunum remains, then long-term parenteral saline will usually be required to maintain sodium and water balance.

Parenteral and enteral nutrition Most patients with less than 75cm of intact jejunum will require long-term parenteral nutrition to maintain their nutritional status. Those patients with approximately

75–100cm jejunum may manage in the long term with parenteral saline plus an enteral regimen, possibly including overnight nasogastric or gastrostomy feeding, but they might require parenteral nutrition in the acute phase of their condition until they are stabilised.

Home parenteral nutrition is a possibility for those who need a long-term parenteral regimen.¹¹ There are currently about 500 patients receiving such a service. Less than half of these patients are managed through the two UK intestinal failure units. It is essential that nutritional support for all patients who require parenteral and enteral nutrition is controlled by multidisciplinary nutrition teams (including pharmacists), with additional information and advice provided by patient support groups, such as Patients on Intravenous and Nasogastric Nutrition Therapy.

Reduce stoma output Patients who are net “secretors” (see Panel 3) will usually have the best response to drugs that reduce gastrointestinal secretions, such as histamine-2 receptor antagonists or proton pump inhibitors. Net “absorbers” (see Panel 3) will usually have better response to antimotility drugs.

Antimotility drugs such as loperamide and codeine phosphate prolong the transit time of chyme through the bowel and thus decrease water and electrolyte losses. Greatest benefits are seen when these drugs are taken 30 to 60 minutes before food. Loperamide is more effective and associated with fewer side effects than codeine phosphate,¹²

Panel 3: Classification of patients according to their ability to maintain sodium and water balance

	“Absorbers”	“Secretors”
Residual jejunal length	>100cm	<100cm
Net sodium/water balance	Absorb more from diet than take orally	Lose more from stoma than take orally
Jejunostomy output	Approximately 2kg/24h	4–8kg/24h
Relationship of jejunostomy output to food intake	Unaffected by food intake	Increases in response to food

but synergistic effects may be seen if the two drugs are taken together.¹³ High doses of loperamide may be needed (up to 12–24mg per dose) because both the enterohepatic circulation and small bowel transit are disrupted in these patients.

Antisecretory drugs such as proton pump inhibitors and H₂ antagonists inhibit gastric acid secretion and delay gastric emptying. They may need to be given intravenously if less than 50cm of jejunum remains. Most studies to date have involved cimetidine, ranitidine and omeprazole. Effective doses utilised vary from 40mg once to twice daily of omeprazole^{14,15} and 400mg four times a day of cimetidine.¹⁶ While these drugs will reduce jejunostomy output in net secretors they have no effect on the absorption of nutrition or electrolytes.^{14–16} Octreotide, a somatostatin analogue, is also used to reduce salivary, gastric, biliary and pancreatic secretions, and to delay gastric emptying and may prolong intestinal transit time. Usual doses are 50–100µg twice to three times a day but reductions in output are variable, with most effects in “secretors”.^{17,18} Some patients are able to reduce the volume of parenteral supplements required, but there is no evidence at present that octreotide significantly changes energy or nitrogen absorption.¹⁹ Longer-acting analogues, such as lanreotide, may also be effective. Its use is associated with significant cost implications, particularly if long-term therapy is necessary.

Mineral supplementation Magnesium deficiency is common in patients with a jejuno-colic anastomosis and jejunostomy patients, as a result of hyperaldosteronism secondary to dehydration and sodium depletion. After correction of water and sodium depletion, magnesium supplementation is often required. Most oral magnesium salts are poorly absorbed in patients with a functioning gastrointestinal tract. This is compounded by altered tablet dissolution and potentially reduced bioavailability in patients with a jejunostomy. Magnesium oxide is preferred, with doses of 12–24mmol a day usually sufficient.²⁰ Doses are best given at night when intestinal transit is slowest. Intravenous supplementation may be needed when oral absorption is insufficient. In addition, 1α-hydroxycholecalciferol at a dose of 1–9µg a day may increase intestinal and renal magnesium absorption in resistant cases.^{21,22}

Supplemental zinc and hydroxycobalamin may also be required.

Coexisting medical conditions Patients with a short bowel will incompletely absorb many medicines for other medical conditions. Only limited information is available at present, but dose increases may be required for certain drugs, for example, digoxin²³ and warfarin.²⁴ Formulation changes might also be required, such as

Panel 4: Composition of St Mark's electrolyte solution

- 20g (6 level 5ml spoonfuls) glucose
- 3.5g (1 level 5ml spoonful) salt
- 2.5g (1 heaped 2.5ml spoonful) sodium bicarbonate

Made up to 1,000ml with water

avoiding capsules and modified release preparations or by giving intravenous preparations.

Using medicines in patients requiring enteral or parenteral nutrition

As stated above, many patients with a short bowel will have problems absorbing some orally administered drugs. After careful consideration of drug therapy choices, however, many patients can receive much of their medicines by the oral route. Enteral nutrition can be complicated by administration issues, such as the potential for interactions with the feeding tube or the feed itself.²⁵ National guidelines are available to aid the safe and effective administration of drugs through feeding tubes²⁶.

As a rule, drugs should not be added to a parenteral nutrition admixture, because of the high likelihood that they will be incompatible with it. Limited data are available, however, to support the addition of certain drugs such as heparin and ranitidine. Consideration must also be given for potential interactions between orally administered medicines and parenteral nutrition. There are reports in the literature about the reduced efficacy of warfarin²⁷ and phenytoin²⁸ when administered in these circumstances. Drug-induced alterations in electrolyte levels and fluid balance are also of relevance in parenterally fed patients.

The future

As yet, intestinal transplantation in adults has not been shown to yield significant benefits over home parenteral nutrition in terms of safety and efficacy²⁹ so is reserved for carefully selected candidates in whom parenteral feeding is no longer possible due to permanent loss of access or major complications such as liver dysfunction. Research is ongoing regarding the use of GLP-2 and its analogues. Preliminary studies have shown it to reduce gastric emptying and increase energy absorption and lean body mass.³⁰

Conclusions

Intestinal failure is a complex, often life-long condition to manage. Pharmacists have a valuable role to contribute in the management of these patients. The pharmacist is an

essential member of the nutrition support team, converting calculated nutritional requirements into a stable, safe and cost-effective regimen. Pharmacists also bring expert knowledge of pharmacokinetics, drug metabolism and drug formulation to the multidisciplinary team. This knowledge is invaluable in ensuring safe and cost effective drug and formulation selection both to manage the symptoms of intestinal failure and concurrent medical conditions. Doses of medicines used are often above licensed doses and liaison with primary care when discharge is planned is essential to ensure continuation of effective treatment.

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More information about clinical nutrition

Further details about choosing the appropriate type of nutritional support for patients and details about measures intended to reduce the complications of artificial feeding, together with a fuller account of how to manage drug therapy in patients receiving parenteral or enteral nutrition, are set out in the June 2000 issue of *Hospital Pharmacist* (see reference 25). Information about the British Pharmaceutical Nutrition Group appears on p20.