Physiology and Problems of a Short Bowel

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Key Points

1. A short bowel occurs when there is an insufficient length of small intestine to absorb enough nutrition/fluid to maintain health/growth.
2. Due to large range of "normal" small intestinal length, it is important to refer to the remaining length of small bowel rather than the length resected.
3. There are two common types of patient with a short bowel. Those with jejunum anastomosed to colon (jejunum-colon or type 2) and patients with an end jejunostomy (type 1). A third less common group have had a predominantly jejunal resection [jejunum–ileum. (Type 3)], and have more than 10 cm of terminal ileum remaining, their problems are similar to the jejunum-colon patients.
4. Patients with a jejunostomy have high stomal losses of water and sodium and often have hypomagnesaemia. Fluid balance dominates their management.
5. Patients with a jejuno-colic anastomosis do not generally have fluid balance problems and the colon salvages energy from colonic fermentation. However they have a high prevalence of calcium oxalate renal stones.
6. All patient types have a high prevalence of calcium bilirubinate gallstones.
7. The absorption in patients with a preserved functioning colon improves with time; this does not occur in patients with a jejunostomy.

Background

In 1880, Koberle performed the first reported successful small intestinal resection of more than 200 cm on a 22-year-old girl with multiple intestinal strictures [1]. At the beginning of the twentieth century, a resection of more than 200 cm of small intestine, thought to be a third of the total small intestinal length, was referred to as an 'extensive' intestinal resection and was thought to be the maximum length of small intestine that could be removed and for the patient to survive [2]. In 1935, Haymond used the term 'massive' in preference to 'extensive' intestinal resection when he reviewed the literature of 257 patients, most of whom had had a resection for an intestinal volvulus (Table 1); he noted an overall survival of 67% [3].

In the 1960s, as an awareness developed that the outcome from an intestinal resection depended upon the length of small bowel remaining rather than the length resected, so the term 'short bowel syndrome' came into use. The syndrome was characterized by 'intractable diarrhoea with impaired absorption of fats, vitamins, and other nutrients, ultimately leading to malnutrition, anaemia, and continued weight loss' [4]. This description implies a slow chronic illness and is adequate to describe most patients who have a short bowel and retained functioning colon; it does not describe the acute fluid balance problems experienced by patients with a jejunostomy (end-jejunostomy syndrome). The first report of a patient surviving with a jejunostomy, 120 cm from the duodeno-jejunal flexure, was in 1963 [5].

Early work was on physiology first in animals after a large predominantly jejunal resection then work in man was initially in those with a jejunocolic anastomosis. Later work was with patients with a jejunostomy and a high output

Table 1 Reasons for a 'massive' intestinal resection in adults as published in 1935 [3]

	$n = 257$
Volvulus	76
Strangulated hernia	45
Mesenteric thrombosis	34
Tuberculosis	16
Mesenteric tumours	14
Uterine perforation	11
Adhesions/bands	7
Other	54

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stoma. The studies to understand the physiological changes in the 1990s were about motility and gastrointestinal hormones. Research since the millennium has concentrated on peptide growth factors, new hormones and the microbiome.

Length of Small Intestine

The length of the adult intestine, measured surgically, radiologically or at autopsy from the duodeno-jejunal flexure, ranges from about 275 to 1510 cm and tends to be shorter in women than in men (chapter "Normal Intestinal Anatomy and Physiology"). Congenital cases of a short bowel have been reported and are usually associated with malrotation of the gut [6, 7]. Patients who have a small intestinal length at or below the lower end of the normal range may develop the problems associated with a short bowel after relatively little small intestine has been removed. In a study of 11 patients with Crohn's disease and less than 200 cm small bowel remaining, the median original small bowel length was calculated from the lengths resected and remaining to be 240 cm (range 205–315 cm), indicating a short small bowel length before any resections [8]. A further study has confirmed that patients with Crohn's disease have a shorter total small intestinal length than controls (mean length at laparotomy in 279 Crohn's disease patients 460 cm vs. 564 cm in 77 non-inflammatory bowel disease patients) [9].

The large range of normal human small intestinal length means that it is more important to refer to the length of small bowel remaining rather than to the length removed. The term ultrashort bowel is occasionally used to refer to patients who have less than 20 or 30 cm small bowel remaining and are thus unlikely to absorb any macro or micronutrients.

Assessment of Residual Small Intestine

Anatomical Length

The remaining small bowel length is ideally assessed at surgery by measuring 10–30 cm segments of bowel along the antimesenteric border, taking great care not to over-stretch the bowel. If there is no surgical measurement available and radiographic films are available, the bowel can be measured using an opisometer, a device used for measuring distances on maps. It traces the long axis of the small bowel on a small bowel meal radiograph. This technique is relatively accurate if the total small intestinal length is less than 200 cm and if the entire small bowel is shown on one film [9, 10]. As most films are saved on a computer the small bowel length (on contrast follow through, computerized tomographic enterography [11] or magnetic resonance scans [12]) can be measured in short segments and give an a moderately accurate estimate of the remaining small bowel length. This is easier to estimate if the total small bowel length is less than 200–300 cm.

Functional Length

Citrulline is a non-essential amino acid that is almost exclusively synthesized in the enterocyte by pyrolline-5-carboxylase-synthase from glutamine. It is not derived from food or proteolysis and is not incorporated into body proteins. Some of the citrulline made by the enterocyte passes to the liver, where it is an important intermediate in the urea cycle (urea made from ammonia) and some passes into the systemic circulation. All the citrulline in the systemic circulation is derived from small intestinal enterocytes, thus plasma levels of citrulline are related to the length of the remaining functional small bowel (Fig. 1) [13–16].

Apolipoprotein AIV (Apo AIV) may be an equally effective marker of functional enterocyte mass; it is exclusively synthesized by enterocytes. Its concentration in plasma, like citrulline, mainly depends on production in the small intestine and is not affected by first-pass metabolism. Apo AIV is incorporated into the surface of nascent chylomicrons. Upon entering the blood circulation, it is rapidly dissociated from the chylomicrons and predominates in the plasma as a lipoprotein-free fraction. It shows no circadian rhythm and maintains stable physiological plasma levels. It has the advantage over citrulline of being easier to measure (smaller sample, simpler equipment and faster results) [17].

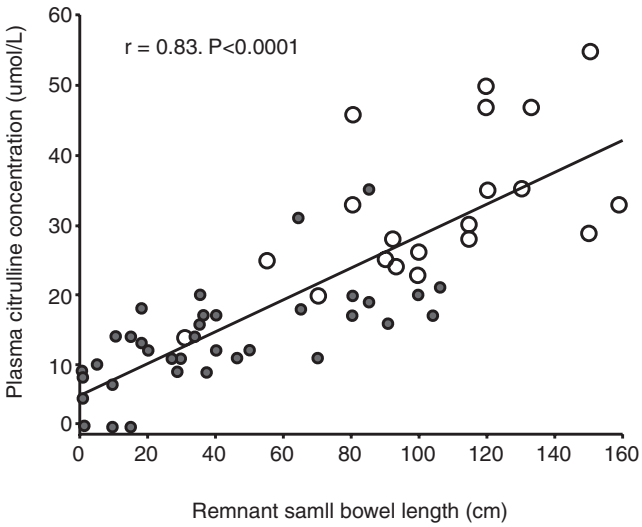

Fig. 1 Fasting plasma citrulline level and remaining small bowel length. (With permission [13])

Anatomical Considerations of Remaining Bowel

Ileum or Jejunum

A jejunal resection is better tolerated than an ileal resection. Ileal mucosa, in contrast to the jejunal mucosa, has tight intercellular junctions and thus can concentrate its contents. Gastrointestinal transit is naturally slower in the ileum than jejunum, so allowing more time for absorption [18, 19]. The terminal ileum absorbs vitamin B_{12} [20, 21] and bile salts. Ileum remaining after a small bowel resection can adapt in both structure and function to increase absorption [22–24], while the jejunum can only adapt functionally if some distal bowel remains (chapter "Intestinal Adaptation").

Ileocaecal Valve

It is traditionally considered that preservation of the ileocaecal valve is beneficial as it may slow transit and prevent reflux of colonic contents into the small bowel; however, studies of ileocaecal valve excision show no evidence that it slows transit, and small bowel peristalsis probably prevents reflux from the colon into the small bowel [18, 25] (chapter "Normal Intestinal Anatomy and Physiology").

Some reports suggest that conservation of the ileocaecal valve in children is beneficial in terms of survival and the need for parenteral nutrition [26, 27]; others show no such benefits [28, 29]. The reports proposing benefit of ileocaecal valve preservation in adults may reflect preservation of a significant length of terminal ileum.

Colon

Conservation of the colon is beneficial because it absorbs water, sodium [30–34], calcium [35] and short- and medium-chain fatty acids [36–38]; it also slows gastrointestinal transit [39], stimulates small intestinal hyperplasia [40] and its bacteria manufacture some amino acids and vitamins (e.g. vitamin K, biotin, folic acid and thiamine) which can then be absorbed in the colon. Patients with an entero-colic anastomosis may survive without parenteral support with a very short [41, 42] or even no remaining jejunum [43]. Patients with a preserved functioning colon rarely need regular water and sodium supplements [32–34]. In terms of the need for parenteral nutrients, preservation of at least half of the colon after a jejuno-ileal resection is equivalent to about 50 cm of small intestine [34].

Causes of a Short Bowel

The four most common reasons for patients to have less than 200 cm of small bowel are superior mesenteric artery thrombosis, Crohn's disease, irradiation damage and surgical complications [10, 34, 44] (Tables 2, 3 and 4). Resection of an ischaemic small intestine ultimately results in colonic pres-

Table 2 Reasons for a short bowel in adults in 1969 [44] (less than 120 cm small bowel remaining; almost all patients had a remaining functional colon)

	n = 123
Superior mesenteric artery thrombosis/embolus	49
Volvulus	24
Superior mesenteric vein thrombosis	10
Tumours	10
Non-occlusive gangrene	10
Strangulated herniae	5
Regional enteritis	1
Other	14

Table 3 Reasons for a short bowel in adults in 1992 (less than 200 cm small bowel remaining) [34]

	Jejunum–colon	Jejunostomy
Total (sex)	38 (26 F)[a]	46 (31 F)
Age (range)	46 (7–70)	42 (16–68)
Median jejunal length (cm)	90 (0–190)	115 (20–190)
Diagnosis		
Crohn's disease	16	33
Ischaemia	6	2
Irradiation	5	3
Ulcerative colitis	–	5
Volvulus	5	–
Adhesions	4	1
Diverticular disease	1	1
Desmoid tumour	1	1

[a]7 had an ileocaecal valve and 31 a jejuno-colic anastomosis

Table 4 Characteristics of 268 adult patients receiving HPN for non-malignant short bowel (less than 150 cm small bowel) from 1980 to 2006 [45]

Total (sex)	268 (139 F)
Age [mean (range)]	52.5 (18–89)
Diagnosis	
Mesenteric infarction	115 (43)[a]
Irradiation	61 (23)
Surgical complications	33 (12)
Soft tissue tumour	16 (6)
Crohn's disease	15 (6)
Volvulus and trauma	14 (5)
Chronic intestinal pseudo-obstruction	11 (4)
Other	3 (1)

[a]93 arterial and 22 venous infarction

ervation (75%) and affects an older age group (median age 57 years) [34]. Patients with Crohn's disease and jejunum in continuity with a functioning colon had undergone a median of 3 small intestinal resections (range 2–6) over a median of 14 years (range 0–29), compared with 4 resections (range 1–12) over a median of 11 years (range 1–26) in those with a jejunostomy [34]. The median time from irradiation to having a small intestinal length of less than 200 cm in 8 patients with irradiation damage (5 gynaecological cancers, 2 carcinomas of the colon and 1 seminoma) was 5 years (range 1–16) [34].

A short bowel occurs more commonly in women (67%) than in men [34, 45]; this may be because women start with a shorter length of small intestine than men.

The more recent causes of a short bowel in adults are derived from the reported aetiology of patients receiving parenteral support and additionally from those taking part in peptide growth hormone studies. There are no studies since 1992 of patients with a short bowel and not receiving HPS. The number of patients with a short bowel and Crohn's disease has reduced while the number following surgical resections, with mesenteric ischaemia and malignancy have all increased [46].

The causes of a short bowel arising in childhood and infancy usually result in colonic preservation. In infancy the causes include necrotizing enterocolitis, multiple jejuno-ileal atresia, gastroschisis, mid-gut volvulus and congenital [26–29, 46–49] (chapters "Peritoneal Adhesions and Encapsulating Peritoneal Sclerosis" and "Acid-Base Disturbances in Intestinal Failure"). In children trauma, post-operative complications, cancer and motility disorders dominate [46]. As the management and thus the survival of these children improves [27–29], they are being cared for as adults.

Types of Patient with a Short Bowel

There are three types of patient with a short bowel (Fig. 2):

1. *Jejunum–colon*. (Type 2) Patients in whom the ileum has been removed, often with the ileocaecal valve, to leave a jejuno-colic anastomosis (jejunum–colon); patients who have less than 10 cm of terminal ileum are included in this group.
2. *Jejunostomy*. (Type 1) Patients in whom some jejunum, the ileum and colon have been removed, so they are left with an end-jejunostomy.
3. *Jejunum–ileum*. (Type 3) Patients who have had a predominantly jejunal resection, and have more than 10 cm of terminal ileum and the colon remaining (jejuno-ileal) [10, 34, 50]. This last group is not common (2 of 86 patients [34]); since the residual ileum can adapt both structurally and functionally, these patients rarely have major problems and they are not specifically discussed in this chapter.

Patients with a jejunostomy can be classified according to the results of balance studies as net 'absorbers' or net 'secretors'. The 'absorbers' in general have more than 100 cm of residual jejunum and absorb more water and sodium from their diet than they take orally (usual daily jejunostomy output about 2 kg); they can therefore be managed with oral sodium and water supplements, and parenteral fluids are not needed. The 'secretors' usually have less than 100 cm residual jejunum and lose more water and sodium from their stoma than they take by mouth (the usual daily stomal output may be 4–8 kg). 'Secretors' cannot convert from negative to positive water and sodium balance by taking more orally, and so they need long-term parenteral supplements [51]. These requirements change very little with time [34]. The jejunostomy output from a net 'secretor' increases during the daytime in response to food and decreases at night; any drug therapy that aims to reduce the output is therefore given prior to food. The change from a net secretory state, in terms of water and sodium balance, to a net absorptive state occurs at a jejunal length of about 100 cm (chapter "Management of a High Output Stoma, Jejunotomy or Uncomplicated Enterocutaneous Fistula").

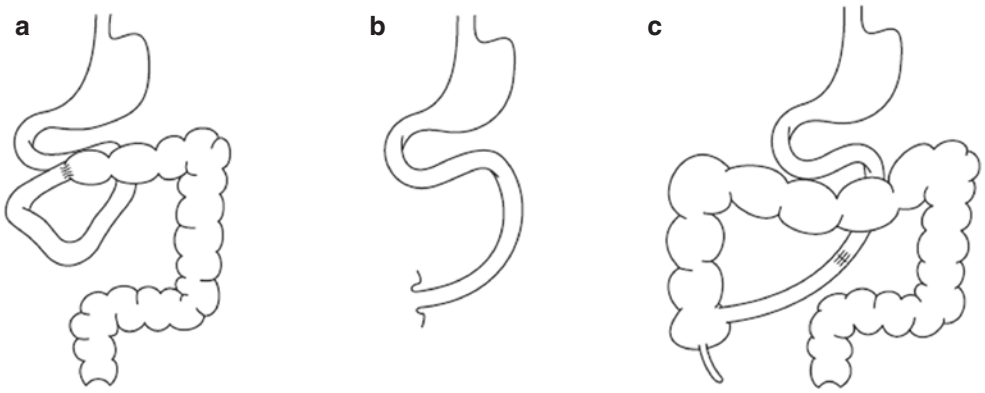

Fig. 2 The three types of patient with a short bowel. Patients with a jejuno-colic anastomosis or a jejunostomy are most commonly encountered. (**a**) Jejuno-colic anastomosis; (**b**) Jejunostomy; (**c**) Jejuno-ileal anastomosis

Bowel Length and Fluid/Nutritional Support

- *Jejunum–colon*. While it is possible for a patient with no remaining jejunum to survive without parenteral nutrition, quality of life is poor [42]. A patient with 100–200 cm of normally functioning jejunum in continuity with a functioning colon may need oral nutrient supplements for a few months but in the long-term would not be expected to need any supplements unless the remaining bowel was diseased. When the jejunal length is between 50 and 100 cm, some patients will need long-term parenteral nutrition (PN), if it is between 30 and 50 cm most will do so, and if it is less than 30 cm almost all patients will need PN [34, 50] (Fig. 3). Sometimes parenteral

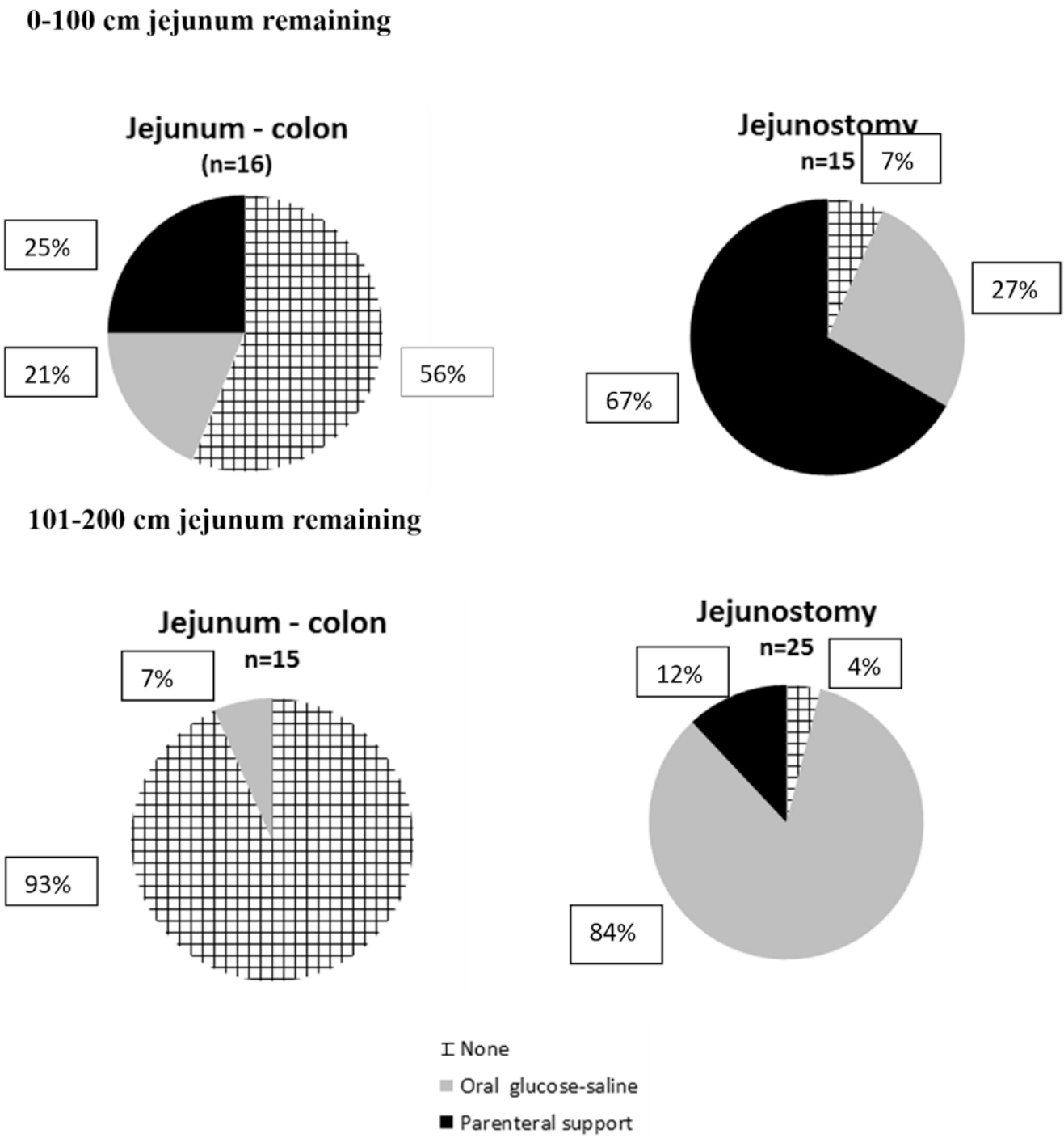

Fig. 3 Pie chart showing the parenteral and enteral sodium and water supplements given to 71 stable patients with less than 200 cm jejunum remaining. Few patients with a colon were receiving oral or parenteral sodium and water supplements, but almost all jejunostomy patients were receiving them [34]

nutrition is needed not to maintain nutritional status but to prevent the severe diarrhoea associated with eating.

- *Jejunostomy*. The survival of patients with a jejunostomy has improved since 1963 [5, 52]. If 100–200 cm normally functioning jejunum remains, oral sodium supplements (glucose–saline solution or sodium chloride tablets) are likely to be needed, often with oral nutrient solutions to which sodium chloride has been added [34, 50, 51, 53]. A patient with a jejunostomy and less than 100 cm jejunum remaining would be expected to need long-term parenteral saline. If less than 85 cm jejunum remains, long-term parenteral nutrition is likely to be required in addition to the saline. Patients usually need long-term parenteral nutrition when they absorb less than a third of their oral energy intake [51, 54].

Physiological Changes

Of the physiological changes observed after a small intestinal resection, some reflect normal and some altered physiology. Most experimental work in animals involves a predominantly jejunal resection (jejuno-ileal anastomosis); this has a better prognosis but is not a common situation in humans, in whom an ileal resection with or without a colectomy is most common.

Gastrointestinal Motility

Gastric Emptying

There are mechanisms (brakes) in the jejunum, ileum and colon that slow gastric emptying (chapter "Normal Intestinal Anatomy and Physiology"). In addition, events external to the bowel can affect gastric emptying; for example, malnutrition and many drugs (e.g. cyclizine and opiates) delay gastric emptying and parenteral nutrition delays the gastric emptying of solids [55]. Studies in animals have shown that gastric emptying of liquid is normal after a jejunal resection [56, 57].

- *Jejunum–colon*. Gastric emptying of liquids is normal in patients who have had a distal small intestinal resection that does not result in a short bowel [58]. Studies in which a dual isotope meal (liquid and solid components of the meal are labelled with different isotopes) has been given to patients with a jejuno-colic anastomosis have shown that some liquid leaves the stomach rapidly and travels quickly through the short length of remaining jejunum to reach the colon. In the colon, by a neural or hormonal mechanism, the liquid meal activates a colonic braking mechanism by which subsequent gastric emptying is slowed and overall measurements of liquid and solid gastric emptying are normal [39]. This colonic braking mechanism may be caused by the release of peptide YY from the colon [59] (Fig. 4). Infusions of peptide YY that achieve similar levels in normal subjects delay the gastric emptying of liquid [60].

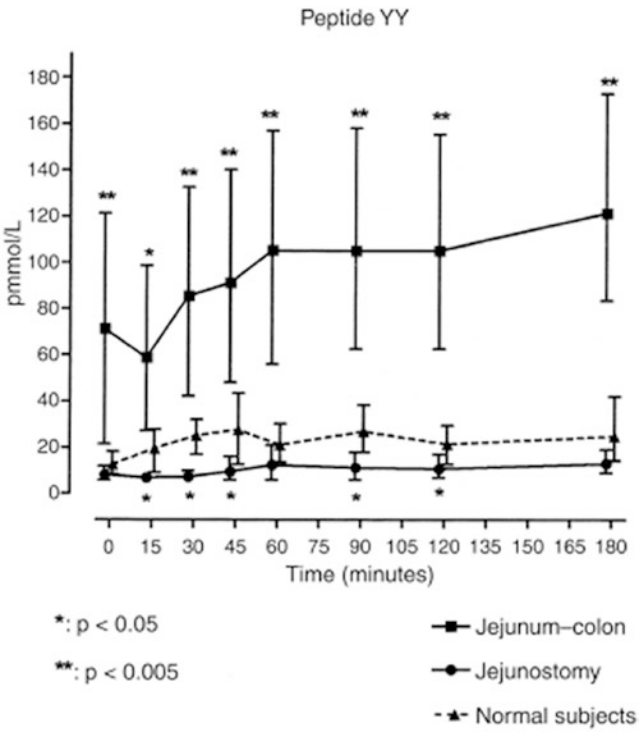

Fig. 4 Median peptide YY levels with interquartile range for 6 jejunum–colon patients, 7 jejunostomy patients and 12 normal subjects after a pancake and orange juice meal [59]

- *Jejunostomy*. The rate of gastric emptying of solids is normal in patients who do not have a short bowel but have had a proctocolectomy and distal ileal resection [61]. In patients with a jejunostomy, barium taken orally has been observed to pass rapidly into the jejunostomy bag. Dual radio-isotope studies have shown that the early rate of liquid gastric emptying is rapid and that this tends to correlate inversely with the remaining length of jejunum [39]. This is probably caused by the loss of cells secreting peptide YY in the terminal ileum and colon, and the consequent low plasma levels [59].

Small Bowel Transit

As there is normally faster transit of chyme through the jejunum than ileum [18, 19, 23, 61], it is not unexpected that small bowel transit has been shown to be fast after an ileal and slow after a jejunal resection [56, 57, 62].

- *Jejunum–colon*. The first part of a liquid meal travels rapidly from the stomach to the colon, reflecting both the

normal faster jejunal transit and the short distance it has to travel. The transit rate for solid is normal, however, suggesting that jejunal transit has been slowed by the colonic brake already activated by the prior arrival of some liquid in the colon. This effect may have been mediated by peptide YY.

- In the fasting state, in patients with a short bowel and a retained colon, the interdigestive migrating motor complex (MMC) occurs more frequently but for a shorter total time than in normal subjects, and phase 2 activity is of a shorter duration [63, 64]. The frequency and amplitude of jejunal contraction is unaffected [64].
- *Jejunostomy*. The rate of liquid and solid small bowel transit is rapid in patients with a jejunostomy. This may be due to low peptide YY levels. Six hours after a meal there is still some meal residue within the stomach, and this may result from a disorder of the MMC [39].

Gastrointestinal Secretions

Salivary Secretion

The volume of saliva produced at rest was significantly less in 7 jejunostomy patients (median 0.6 g/5 min, range 0.0–1.4) than in 13 normal subjects (median 2.2 g/5 min, range 0.9–8.7, $p < 0.005$). After stimulation of salivary flow by chewing paraffin wax for 5 min, the volume of saliva was significantly less in jejunostomy patients (median 4.6 g/5 min, range 2.2–8.2) than in normal subjects (median 9.7 g/5 min, range 7.0–20.5, $p < 0.005$). These observations are likely to reflect altered physiology, but a degree of dehydration was not excluded [65].

Gastric Secretion

In 1914, Stassoff [66] performed experiments on six dogs in which he demonstrated that if the distal half of the small intestine was removed, the chyme that emerged from a duodenal fistula was more liquid and had left the stomach more quickly than before the resection. Many studies in dogs with denervated Heidenhain pouches [67–82] and in some with innervated Pavlov pouches [76] have shown hypersecretion of gastric acid. In most studies, the colon has been retained, though in one a colectomy alone caused gastric acid hypersecretion [83]. The larger the intestinal resection, the greater is the postoperative gastric acid hypersecretion [70, 84]. The greatest rises in acid output are produced by jejunal rather than ileal resection [75, 81, 84] (with the exception of one study [72]) and by defunctioning bowel [69, 74] rather than resecting it. The increased secretion is prevented by antrectomy [74, 79, 81, 82] but not by a vagotomy and pyloroplasty [79, 82].

Fielding and Cooke showed an 8% incidence of peptic ulcer among 300 patients with Crohn's disease and they noted that resections of 60 cm or more of the small bowel caused an increase in basal and pentagastrin-stimulated acid output [85]. They related this increased gastric acid output to a previous terminal ileal resection rather than to active disease [86].

In humans, the survival of some patients with a very short bowel has been attributed to their previous gastric surgery [70, 87, 88]. The evidence for gastric acid hypersecretion in the long term in patients with a retained colon is not good. Miura et al. reported three of seven patients with a short gut and a retained colon who developed duodenal ulcers [89]. Windsor et al. described 19 patients in whom more than 300 cm of small intestine had been resected and noted in 8 patients large postoperative aspirates of gastric juice of more than 1.5 L daily which lasted for less than 14 days. The volume of aspirate did not correlate with the remaining length of small intestine. In 6 of the 19 patients the increased secretion was attributed to impaired liver function, which these researchers postulated might increase circulating histamine levels [78].

One patient with a jejunostomy 90 cm from the duodenojejunal flexure following surgery for Crohn's disease had an acidic (pH 1–6) jejunostomy output of 4.8 L daily that was reduced by gastric irradiation [72]. O'Keefe et al. showed normal pentagastrin-stimulated gastric acid secretion in nine patients with a jejunostomy (jejunal length 25–200 cm) more than a year after surgery [90].

High gastrin levels have been observed [59, 91, 92] and may result from a reduced length of small bowel being available to catabolize gastrin [93, 94]. However, gastrin may not be of major physiological importance as studies in the Rhesus monkey have shown that, 6 months after a distal small intestinal resection, basal and histamine-induced acid secretion are at their highest levels, yet serum gastrin levels have returned to normal [95]. Another reason for gastric acid hypersecretion may be the loss of a normal inhibitor of gastric acid secretion, such as neurotensin or peptide YY, from the distal small bowel/colon. In an extensive review in 1974, Buxton suggested that stasis in remaining bowel segments allowed bacterial colonization; these bacteria then either deconjugate bile salts or degrade 'protein' which directly or indirectly causes the release of gastrin or a gastrin-like hormone that causes increased gastric acid secretion [96].

Excess gastric acid in the duodenum, in addition to increasing the incidence of peptic ulceration, causes bile salt precipitation [97], reduced pancreatic enzyme function and increased jejunal motility; all of which impair nutrient absorption.

The evidence indicates that gastric acid hypersecretion, after a small intestinal resection, occurs in dogs with denervated gastric pouches and colons left in situ. It may be present for the first 2 weeks after a small bowel resection in humans, but there is no good evidence that it occurs in the

long term in patients with a short bowel with or without a colon, even though high gastrin levels are observed.

Pancreatico-biliary Secretions

If a person is undernourished [98], or if no food passes through the gut [99], pancreatic function is reduced. In seven well-nourished patients who had a mean small bowel resection of 164 cm (leaving colon) and were taking an oral diet, the post-prandial secretion of trypsin and bilirubin (measured by jejunal aspiration after a liquid meal) was the same as in normal healthy individuals [100]. However, another study in children showed reduced pancreatic volume and enzyme secretion, after an injection of secretin and cholecystokinin, in two of five patients; both of these had most of their colon remaining [101].

When more than 100 cm of terminal ileum has been resected the increased hepatic synthesis of bile salts cannot keep pace with the stool or stomal losses and thus fat malabsorption results [102]. The greatest lipid malabsorption (steatorrhoea) occurs in patients with a jejunostomy: partly because of a very reduced bile salt pool, partly due to rapid transit, and, in a few cases, due to bacterial overgrowth in the remaining bowel [103]. It has not been determined if changes occur in the volume of bile produced each day after an intestinal resection.

Gastrointestinal Hormones

There are differences in the systemic plasma gastrointestinal hormone profiles after a meal in patients with a short bowel compared to normal subjects. However, it is only as studies are performed in these patients, using the hormones, specific agonists or antagonists, that the physiological importance of the observations can be understood; until then the significance of many observations remains a matter for speculation.

Parenteral nutrition itself does not affect the gastrointestinal hormone response to food [104]. The levels of some plasma hormones (e.g. enteroglucagon, pancreatic polypeptide and somatostatin and gastric inhibitory polypeptide) before and after a meal in patients with a short bowel (with or without a colon) are the same as in normal subjects. Plasma levels of vasoactive intestinal peptide in patients with a colon were normal in one study [105], but high in another [106]. High plasma gastrin and cholecystokinin levels and low plasma neurotensin, GLP-1 and insulin levels occur in both types of patient. The plasma neurotensin levels correlate with the length of residual jejunum [59]. The high plasma cholecystokinin levels could cause satiety in some patients with a very short gut [59]. Ghrelin (the "hunger" hormone) levels have been found to be low in patients following a substantial resection (60–80% of total length) of small intestine [107].

There are differences between the two types of patient, the most significant ones being in the plasma levels of two hormones produced by the terminal ileum and colon, namely peptide YY [59, 105] (Fig. 3) and GLP-2 [108, 109] (Fig. 5). Peptide YY slows gastrointestinal transit and GLP-2 stimulates small bowel villus growth (chapter "Normal Intestinal Anatomy and Physiology"). Patients with a colon have high fasting plasma peptide YY and GLP-2 levels, and both hormone levels are low in patients with a jejunostomy [59, 108–110]. Low plasma peptide YY levels also occur in ileostomy patients who have had a colectomy [110]. High plasma motilin levels occur in patients with a jejunostomy, but this is unlikely to be of physiological importance as the highest levels occur in those with the longest lengths of jejunum remaining who do not have rapid intestinal transit [59].

Changes in Intestinal Microbiome

The faecal microbiome is becoming an increasingly researched and thus increasingly understood. Unabsorbed nutrients (especially polysaccharides) within the colon are metabolised by bacteria to form short chain fatty acids (chapter "Normal Intestinal Anatomy and Physiology") which in turn may enhance mineral absorption, promote enteroendocrine secretions, stimulate epithelial cell growth and differentiation in the small and large intestine and may also promote the motility across the ileocaecal junction [111]. Additionally the colonic microbiome manufactures (in addition to short chain fatty acids) some amino acids (especially when undernourished), micronutrients (e.g. vitamins: folate, K, biotin, thiamine, riboflavin and panthothenic acid). It may detoxify some chemicals and manufacture others that are important for messaging/that aid absorption and it may help regulate the immune system and promote intestinal adaptation [112].

The faecal bacteria composition is different from healthy individuals in that anaerobic bacteria are reduced (e.g. bacteroidetes). Firmicutes (includes the lactobacillus and chlostridium geni) are the most abundant phylum, Proteobacteria is second, followed by Bacteroidetes, and lastly by Actinobacteria (includes bifibacterium). The lactobacilli are the largest genus and are responsible for manufacturing L and D lactic acid which in some patients may accumulate in the stool. This may be promoted by lactate-consuming bacteria (Veillonellaceae, Bacteroidaceae, Sutterellaceae, and Acidaminococcacea) being under-represented [113, 114]. When the D isomer dominates then D-lactic acidosis can result. Healthy individuals do not accumulate faecal lactate as it is readily absorbed or metabolised by other commensal

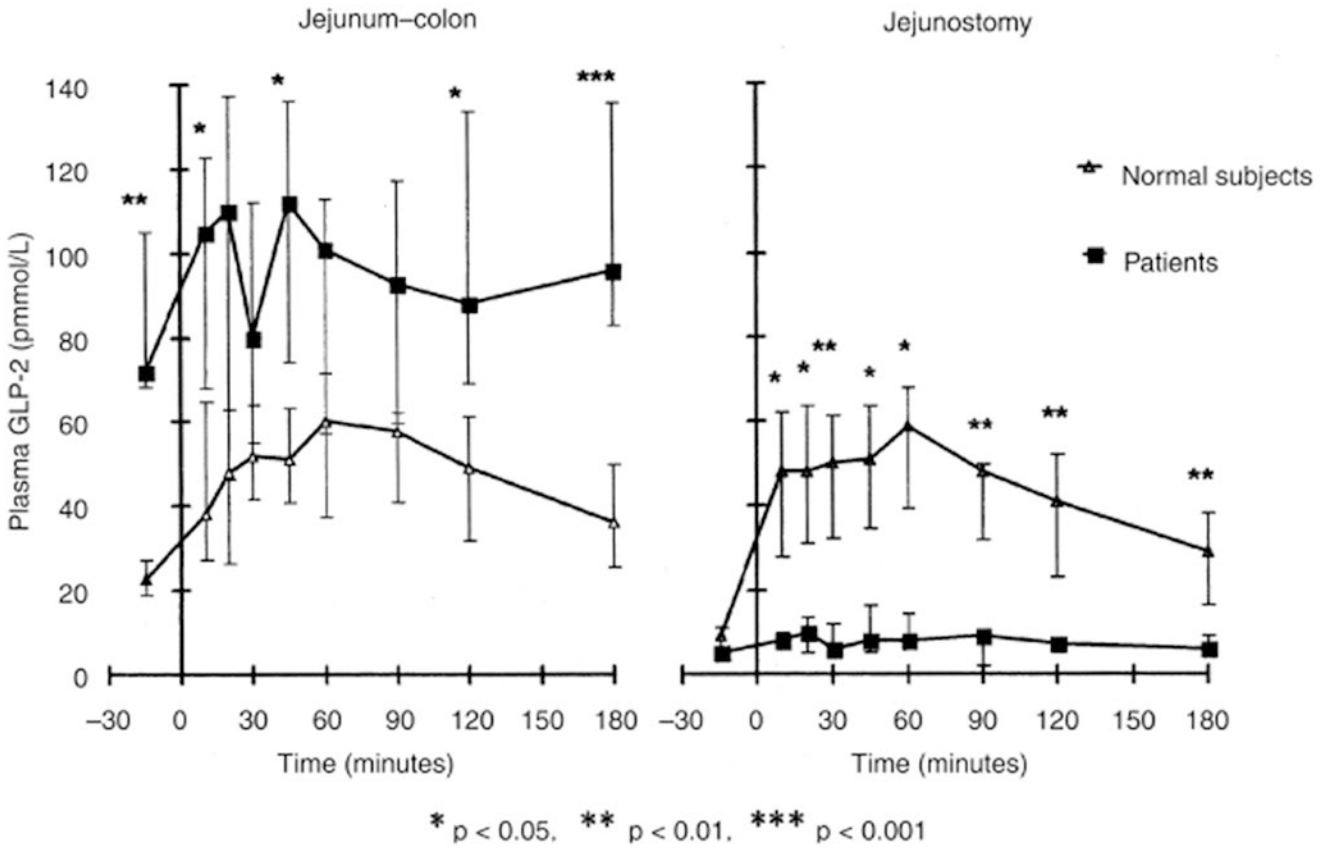

Fig. 5 Median GLP-2 levels with interquartile range in 7 jejunum–colon patients, 7 jejunostomy patients and 7 normal subjects after a continental breakfast [108, 109]. Courtesy of P. Jeppesen and P.B. Mortensen

bacteria or converted to other metabolites (e.g. SCFAs) [115]. It has been suggested that patients with jejuno-colonic anastomosis are stratified according to the presence or absence of lactate in their faeces [114].

A lack or reduction of the Gram-negative anaerobic bacterium *Oxalobacter formigenes* which both interacts with the *colonic mucosa* to induce active secretion of endogenously produced oxalate and also degrades oxalate in the intestinal tract may be partly responsible for the high prevalence of calcium oxalate renal stones in patients with a short bowel and a retained colon [116, 117] (chapter "Nephrolithiasis and Nephrocalcinosis").

The changes in bacterial content of patients with a jejunostomy or indeed an ileostomy are poorly investigated and due to a fast transit time may not be of major significance.

Changes in Absorption

In addition to absorption of nutrients, there are some specialist functions that are particular to the ileum. The ileum has the unique functions of absorbing vitamin B_{12} and bile salts. Vitamin B_{12} deficiency is likely to occur if more than 60 cm of terminal ileum has been resected [20, 62]. If more than 100 cm ileum has been removed, the enterohepatic circulation will be disrupted and diarrhoea is likely to be due to steatorrhoea [102]. If less than 100 cm has been resected, diarrhoea may result from unabsorbed deoxybile salts (secondary bile acids) causing colonic sodium and water secretion [102].

Clinical Problems and Their Treatment

The problems experienced by patients with a short bowel depend upon the type and length of remaining small bowel and the presence or absence of a functioning colon (Table 5). Most of these problems are dealt with in specific chapters and only a brief summary follows here.

Presentation

The presentation and long-term outcome from a resection can be predicted from knowledge of the remaining small bowel length and the presence or absence of a functioning colon. In both types of patient, treatment is aimed first at maintaining fluid balance. Nutritional supplements are usu-

Table 5 Problems of a short bowel

	Jejunum–colon	Jejunostomy
Presentation	Gradual, diarrhoea and undernutrition	Acute fluid losses
Water, sodium and magnesium depletion	Uncommon (in the long-term)	Common
Nutrient malabsorption	Common[a]	Very common
D(-) lactic acidosis	Occasionally	None
Renal stones (calcium oxalate)	25%	None
Gallstones (pigment)	45%	45%
Adaptation	Functional adaptation	No evidence
Social problems	Diarrhoea	High stomal output
		Dehydration
		Dependency on treatment

[a] Bacterial fermentation of carbohydrate salvages some energy, but D(-) lactic acidosis can occur if the diet is high in mono- and oligosaccharides

ally started 24–48 h after the surgery, to prevent loss of lean body mass. This may entail a period of parenteral nutrition, which is gradually reduced as the patient takes more food orally.

- *Jejunum–colon*. These patients are often deceptively well after the resection except for diarrhoea/steatorrhoea, but in the succeeding months they may lose weight and present as severely undernourished (classical 'short bowel syndrome').
- *Jejunostomy*. These patients have immediate problems after surgery due to the large volume of stomal output, which increases with food and drink. This high-volume output results in patients rapidly becoming depleted in water and sodium. Recognition of this high output means that clinicians are often aware that nutritional problems will follow; hence nutritional care is often addressed at a much earlier stage than in patients with a retained colon. Jejunostomy patients are highly dependent on treatments to compensate for water and sodium losses. If they miss their treatment for 1 day they are likely to become unwell from sodium and water depletion. Their requirements for water and sodium supplements change little with time (chapter "Intestinal Adaptation").

Undernutrition

Loss of muscle leads to weakness and early fatigue. Loss of body fat results in feeling cold, a gaunt facial appearance, dry and wrinkled skin, and dull hair. These features, together with a stooped posture, give an impression of premature ageing. Patients may dislike looking in the mirror and weighing themselves, and may avoid company because they are selfconscious about their wasted appearance. Apathy, depression and irritability associated with undernutrition may stop the patient from being motivated to recover (chapter "Consequences of undernutrition and dehydration"). Short bowel patients who can be maintained on an oral diet need to consume more energy than normal subjects because as much as 50% of the energy from the diet may be malabsorbed. Patients can achieve this by eating more high-energy food, having oral sip-feeds, or receiving high-energy enteral feeds at night through a nasogastric or gastrostomy tube. Once weight is regained, the daily energy requirements may decrease, especially in those with a retained colon. Only if these measures fail and the patient continues to lose weight, or fails to regain lost weight, is parenteral nutrition given. Even then, parenteral supplements may be needed for only a limited period of weeks or months, and thereafter oral supplements may be adequate.

In the long term, parenteral nutrition is needed if a patient absorbs less than one-third of the oral energy intake [51, 54], if there are high energy requirements and absorption is about 30–60%, or if increasing the oral/enteral nutrient intake causes a socially unacceptably large volume of stomal output or diarrhoea. In addition to consumption of a high-energy diet, the dietary advice given to the two types of patient is different (chapter "Dietary Treatment of Patients with a Short Bowel").

- *Jejunum–colon*. In order to increase energy absorption and to reduce the risk of renal stones, patients with a retained colon need a large total energy intake with a diet high in carbohydrate (polysaccharides) [37] but not increased in fat (long-chain triglycerides); the diet should also be low in oxalate. D(-) Lactic acidosis may occur if a diet is high in monosaccharides [118]. If oxalate is not reduced there is a 25% chance of the patient developing symptomatic calcium oxalate renal stones [34] (chapter "Nephrolithiasis and Nephrocalcinosis"). Long-term parenteral nutrition is likely to be needed if less than 50 cm jejunum remains [34].
- *Jejunostomy*. Jejunostomy patients need a diet high in energy. It does not matter whether this is as carbohydrate or lipid so long as the osmolality is kept low by using large molecules (polysaccharides, protein and triglycerides) [119, 120] and thus allowing extra sodium chloride to be added to give the meal/liquid feed a total sodium concentration of 90–120 mmol/L and an osmolality of about 300 mOsm/kg. An elemental diet has a high osmolality and little sodium and should therefore be avoided as it may increase water and sodium losses. A high-lipid diet may increase stomal calcium and magnesium losses (chapter "Dietary Treatment of Patients with a Short Bowel").

Water and Sodium Losses

Clinical Assessment/Monitoring

Deficiencies of water and sodium (most common in those without a retained colon) are common and result in a loss of extracellular fluid volume, hypotension and, if severe, prerenal failure. Daily body weight and an accurate fluid balance (to include stomal effluent) are essential measurements during the initial stages of management. Acute sodium and water deficiencies are detected by a rapid fall in body weight, postural hypotension, low urine volume and, if very severe, by a rising serum creatinine and urea. A useful guide to sodium depletion is measurement of sodium concentration in a random urine sample: lack of body sodium is suggested by a concentration of only 0–5 mmol/L. It is ideal, though not always possible, to achieve a daily urine volume of at least 800 mL with a sodium concentration greater than 20 mmol/L. In addition to relatively normal haematological and biochemical measurements, it is desirable (though again not always possible with oral medication) to have a plasma magnesium level greater than 0.6 mmol/L (chapter "Management of a High Output Stoma, Jejunotomy or Uncomplicated Enterocutaneous Fistula").

- *Jejunum–colon*. The colon has a large capacity to absorb sodium and water; thus patients with a short bowel and a preserved colon are rarely in negative water and sodium balance and rarely need water or sodium supplements [31, 34]. If sodium deficiency does develop, a glucose–saline drink can be sipped during the day, as for patients with a jejunostomy. Although the colon secretes potassium, a low serum potassium level is rare [34]. There is an exchange mechanism of chloride absorption/bicarbonate secretion in the colon; thus, if much sodium chloride is consumed, bicarbonate may be lost in the stools and give rise to a metabolic acidosis similar to that occurring in patients who have an ileo-conduit following a cystectomy.
- *Jejunostomy*. Patients with a jejunostomy have a large volume of stomal output that is greater after eating or drinking. Each litre of jejunostomy fluid contains about 100 mmol/L of sodium [51]. This high-volume output is mainly the result of loss of the normal daily secretions produced in response to food and drink (about 4 L/day) although gastric acid hypersecretion and rapid liquid gastric emptying and small bowel transit may contribute.

The effluent from a jejunostomy or ileostomy contains relatively little potassium (about 15 mmol/L) [32, 51]. Potassium balance is not often a problem, and net loss through the stoma occurs only when less than 50 cm jejunum remains [51]. A low serum potassium level may be caused by sodium depletion with secondary hyperaldosteronism and thus greater than normal urinary losses of potassium [32] or by magnesium depletion [121] (chapter "Dietary Treatment of Patients with a Short Bowel").

Treatment of Water and Sodium Depletion

Jejunostomy. Intravenous fluid is given initially while the patient takes no oral food or fluid. This will reduce the high output dramatically; food is then gradually reintroduced. Parenteral nutrition/saline is likely to be needed in the long term if less than 100 cm jejunum remains. Oral hypotonic fluids are restricted and a glucose–saline solution (sodium concentration 90–120 mmol/L) is given to sip during the day. Some clinicians suggest that liquid and solids be taken at different times although there is no published evidence that this reduces stool/stomal output [122]. Drugs that reduce gastrointestinal secretions or motility may be used; often both types of drug are administered. In general, patients who are net 'secretors' have the greatest reduction in their stomal output when drugs that predominantly reduce gastrointestinal secretions are given, for example omeprazole 40 mg daily, ranitidine 300 mg twice daily, cimetidine 200 mg every 6 h or 300 mg continuously over 6 h or, if there is insufficient gut to absorb these (less than 50 cm), subcutaneous or intravenous octreotide 50 μg twice a day. However, these treatments rarely completely alleviate the need for parenteral supplements. Patients who are net 'absorbers' have the greatest reduction when drugs that predominantly reduce gastrointestinal motility (e.g. loperamide 4 mg four times a day and codeine phosphate 60 mg four times a day) are given half an hour before food (chapter "Management of a High Output Stoma, Jejunotomy or Uncomplicated Enterocutaneous Fistula").

Magnesium and Other Micronutrients

The clinical syndrome of magnesium deficiency in man was described in 1960 [123, 124] and in the same year was reported as occurring after a massive intestinal resection [125]. It has subsequently been reported after jejuno-ileal bypass for obesity [126] and after ileal resections of more than 75 cm [127]. Its features include fatigue, depression, jerky and weak muscles, ataxia, athetoid movements, cardiac arrhythmias and, if severe, convulsions [123, 124, 128, 129]. Carpopedal spasm and positive Chvostek and Trousseau signs generally occur if there is a concomitant hypocalcaemia [124, 128, 130].

Low serum magnesium levels are more common in patients with a jejunostomy than in patients with a retained colon. Of short bowel patients who were not receiving parenteral nutrition, 11 of 27 (41%) of those with a colon were receiving magnesium or had low serum magnesium levels, compared with 19 of 28 (68%) with a jejunostomy [34].

Patients with a preserved colon require less magnesium and have higher serum values than those without a retained colon. This, together with reports that magnesium poisoning can occur after a magnesium sulphate enema, provides further evidence that the colon absorbs magnesium [131].

Most clinicians use a serum magnesium measurement of less than 0.6 mmol/L as their guide to magnesium depletion; however, urine, skeletal muscle, mononuclear cell or ionized magnesium levels [129] are more sensitive indicators.

There are several reasons for magnesium deficiency. Magnesium is normally absorbed by passive diffusion in the distal small bowel and colon. Bowel resections reduce the absorptive area and may increase stool losses [132]; however, this does not occur in an easily predictable manner and balance studies have shown that magnesium balance does not relate to the length of small bowel remaining [65]. The composition of the diet consumed may be another cause of stool losses of magnesium. Fatty acids, derived either from digestion of dietary fat or from bacterial fermentation of malabsorbed carbohydrate, combine with magnesium, calcium and zinc and prevent their absorption, increasing faecal or stomal losses [133]. A third reason, occurring particularly in patients with a jejunostomy, is stool/stomal loss of salt and water and the consequent secondary hyperaldosteronism. Aldosterone increases renal excretion of magnesium in rats and man and the faecal excretion of magnesium in rats [134, 135].

A low serum magnesium level reduces both the secretion and function of parathormone [136]. Thus parathormone cannot promote magnesium absorption in the ascending limb of the loop of Henle or activate renal 1α-hydroxylase to make 1,25-hydroxycholecalciferol. The failure to make 1,25-hydroxycholecalciferol results in reduced magnesium and calcium absorption from the gut [137]. Na^+/K^+-ATPase activity, which normally keeps potassium within a cell and sodium out, depends upon magnesium. When the serum magnesium level is low, activity of this enzyme is impaired. Potassium is therefore lost from cells and renal potassium excretion is increased, resulting overall in hypokalaemia. This hypokalaemia may not respond to the administration of oral or intravenous potassium, but does to magnesium supplementation [138].

The treatment of hypomagnesaemia is outlined in Table 6. Patient hydration and, thus, secondary hyperaldosteronism must first be corrected. Serum magnesium levels can usually be improved by oral supplements, however the data on magnesium absorption from different preparations are often derived from normal volunteer studies. Tablet dissolution and magnesium availability may be different in patients with a short bowel. Various magnesium salts have been given as oral treatment including magnesium sulphate, chloride, hydroxide, acetate, carbonate, gluconate, lactate, citrate, aspartate, pyroglutamate, oxide (magnesia) and diglycinate.

Table 6 Treatment of hypomagnesaemia

1. Correct water and sodium depletion (and thus secondary hyperaldosteronism)
2. Give oral magnesium preparation (e.g. 12 mmol magnesium oxide or 10 mmol magnesium aspartate at night)
3. Reduce lipid in diet
4. Give 1α-cholecalciferol (1–9 μg daily)
5. Give intravenous magnesium (occasionally subcutaneous or intramuscular magnesium sulphate)

Most magnesium salts are poorly absorbed and may worsen diarrhoea/stomal output. Magnesium acetate causes less diarrhoea than magnesium gluconate [139]. Magnesium oxide is commonly given and contains more elemental magnesium than the other salts. It is insoluble in water and alcohol but soluble in dilute acid. In the stomach it is converted to magnesium chloride. It is given as gelatine capsules of 4 mmol magnesium oxide (160 mg of MgO) to a total of 12–24 mmol daily or magnesium aspartate 10 mmol daily. Magnesium diglycinate (chelate) is absorbed as well as magnesium oxide as an intact dipeptide in the proximal jejunum and after an ileal resection it results in the passage of fewer stools than magnesium oxide [140]. Oral magnesium treatment is usually given at night when intestinal transit is assumed to be slowest and there is more time for absorption. This regimen does not appear to increase stomal or stool output. Magnesium may also be given as a topical spray [141]. A low-fat diet decreases stool/stomal magnesium losses, especially in patients with a retained colon [133]. If oral magnesium supplements, dietary advice and correction of water and sodium depletion do not bring the magnesium level into the normal range, oral 1α-hydroxycholecalciferol in a dose of 1–9 μg daily may improve magnesium balance [142, 143]. It may exert its effect by increasing both intestinal and renal magnesium absorption [143].

Magnesium can occasionally be given as a subcutaneous injection of 4 mmol magnesium sulphate every 2 or more days, but can cause skin ulceration. Intramuscular injection of 10 mmol/L is an alternative, but is painful. Regular intravenous infusions of 12 mmol or more can be given, usually in a litre of saline over 1–2 h, but can cause flushing.

Selenium

Patients receiving parenteral nutrition are commonly deficient in selenium [144–146] and need larger amounts of selenium than are required in the diet of normal subjects [146]. This suggests a loss of selenium from the gastrointestinal secretions. Patients with a jejunostomy also have a reduction in selenium absorption, the amount by which absorption is reduced correlating with residual jejunal length [147]. The kidney can conserve selenium but often not to a sufficient extent. Selenium deficiency is therefore common and may cause weak muscles, a tendency to infections, a dilated car-

diomyopathy and symptoms of hypothyroidism (it is a cofactor for the conversion of thyroxine to the more active triiodothyronine) [148].

Vitamin B_{12} Deficiency

Both groups of patients have had more than 60 cm of the terminal ileum removed and need long-term hydroxycobalamin injections, Traditionally 1 mg intra-muscularly every 3 months though may be longer depending on serum levels [20, 62].

Other Vitamin and Mineral Deficiencies

There may be impairment of absorption of the fat-soluble vitamins A, D, E and K and essential fatty acids. Essential fatty acid deficiency may be treated by rubbing sunflower oil into the skin [149]. Zinc deficiency is not common unless stool volumes are large, when zinc sulphate may be given (15–45 mg orally one to three times a day) [150]. In patients receiving parenteral nutrition the deficiencies depend on the regimen used, but deficiencies of iron, vitamin D and biotin [151–153] occurred with some regimens in the 1990s.

Diarrhoea (Jejunum–Colon Patients)

The oral intake determines the amount of stool passed. Diarrhoea may severely limit a patient's lifestyle; limiting food intake can reduce diarrhoea but may increase the problems of undernutrition. Rarely, a patient requires parenteral nutrition to allow him or her to eat less and so reduce the diarrhoea.

Diarrhoea may be treated with loperamide, 2–8 mg, given half an hour before food. Loperamide is usually given in preference to codeine phosphate (30–60 mg half an hour before food), as it is non-sedative and non-addictive; occasionally, however, both are needed. If tablets/capsules emerge unchanged in stool/stomal output, they can be crushed, opened, mixed with water or put on food. If less than 100 cm of terminal ileum has been resected, bile salt malabsorption may contribute to the diarrhoea. This may be helped by cholestyramine (or colesevelam) which has the additional advantage of reducing oxalate absorption but may be detrimental by reducing fat absorption and by further reducing the bile salt pool [102]. Gastric anti-secretory drugs may reduce diarrhoea shortly after surgery but are not usually effective in the long term.

Confusion

In addition to the many common general medical causes of confusion (e.g. hypoxia, hepatic, renal or cardiac failure, sepsis, hypoglycaemia, thiamine deficiency, alcohol or other drugs), other specific causes should be sought in a patient with a short bowel. Hypomagnesaemia may cause mild confusion. In patients with a preserved colon, severe confusion can result from D-lactic acidosis (in lactate accumulators), in which a metabolic acidosis with a high anion gap will be observed (chapter "Dietary Treatment of Patients with a Short Bowel"). Hyperammonaemia may cause confusion in both types of patients with a short bowel because ammonia cannot be detoxified. The small amount of intestine remaining cannot manufacture adequate citrulline to detoxify the ammonia created in the urea cycle. If there is concomitant renal impairment, the increase in blood ammonia causes a problem as the kidney will not be able to excrete the excess ammonia. Hyperammonaemia can be corrected by giving arginine (an intermediary in the urea cycle) [154, 155].

Drug Absorption

Drug absorption can be predicted from knowing the time to peak levels and the biopharmaceutical classification (chapter "Drug Absorption in the Short Bowel"). Omeprazole can be absorbed in the duodenum and upper jejunum; problems are likely to occur only if less than 50 cm jejunum remains. Warfarin [156] and thyroxine may need to be given orally in high doses. Loperamide circulates in the enterohepatic circulation, which is disrupted, and higher doses than usual may need to be given (chapter "Management of a High Output Stoma, Jejunotomy or Uncomplicated Enterocutaneous Fistula").

Adaptation

Intestinal adaptation (chapter "Intestinal Adaptation") is the process, following intestinal resection, that attempts restore total gut absorption of macronutrients, macrominerals and water to that occurring before the intestinal resection (chapter "Intestinal Adaptation").

In a classical paper in 1959, Pullan described three phases that related to the changing situations in patients after a 'massive intestinal resection' leaving a functioning colon in situ (i.e. 'short bowel syndrome') [157]. These changes reflect structural and functional adaptation.

- *Stage 1*. As intestinal motility returns in the first few days after the resection, profuse diarrhoea occurs and is maximal for the first 2–3 weeks. During this stage there may be large losses of fluid and electrolytes (up to 10 L/day). These losses have been attributed to gastric acid hypersecretion.

- Large volumes of saline (sometimes with magnesium) may be needed to maintain fluid balance, especially when the patient first starts to eat. A protein pump inhibitor or H_2 antagonist, loperamide and often codeine phosphate are empirically given. If the residual bowel length is less than 100 cm, parenteral nutrition may be started on the second postoperative day. Anal soreness and excoriations may be a problem. This phase ends as the diarrhoea lessens.
- *Stage 2*. The problem changes from that of fluid and electrolyte balance to that of progressive undernutrition requiring nutrition support. If untreated, the patient may rapidly lose weight and, despite a large oral energy intake, not absorb enough to maintain weight. Fat malabsorption is much more significant than that of carbohydrate and protein. Deficiencies of the fat-soluble vitamins A, D, E and K may occur, causing night blindness, bone pains, ataxia and bleeding respectively. Vitamin B and C deficiencies sometimes occur and cause glossitis, angular stomatitis, pellagra, psychotic changes and bleeding. Anaemia and hypoproteinaemia are rare after an uncomplicated resection.
- The patient may complain of abdominal cramps, distension and nausea. During this time the gastrointestinal transit rate slows, although a large volume of fatty stool is still passed. Carbohydrate and protein are better absorbed and a state of equilibrium is reached after 3–6 months.
- *Stage 3*. In the final stage relative equilibrium has been reached and minor adjustments are made. The dietary regimen tries to limit the lipid intake. Long-term parenteral nutrition is unlikely to be needed unless less than 50 cm jejunum remains. The beneficial effects of a proton pump inhibitor may have ceased by the end of the first year and the drug can be stopped.
- After a large resection of small intestine, improvement in absorption of macronutrients, macrominerals and water may occur by:
  - The patient eating more food than normal (hyperphagia);
  - The remaining bowel increasing in size and absorptive area (structural adaptation); and
  - Reduction in bowel transit rate to allow more time for absorption (functional adaptation).

An increased oral intake has been observed [158]. After a jejunal resection in animals, the ileal remnant undergoes structural changes which include elongation of villi, deepening of crypts, and an increase in the number of absorptive cells in a given length of villus. After a jejuno-ileal resection in man to leave a jejunocolic anastomosis, no structural adaptation (except possibly hyperplasia) has been demonstrated even though high GLP-2 levels are observed [109]. A degree of functional adaptation with slowing of liquid gastric emptying and solid small bowel transit has been demonstrated [39] and is likely to be caused by high peptide YY levels. Functional adaptation does occur, as demonstrated by the findings that there is a small reduction in faecal weight in the 3 months after a small bowel resection [159], and that there is increased jejunal absorption of water and sodium [160, 161], glucose [162] and calcium [163] with time. The intestinal calcium absorption may continue to increase for more than 2 years after a resection [163]. Restoring bowel continuity after a mesenteric infarction resulted in cessation of home parenteral nutrition in 77% within 5 years (Fig. 6) [164].

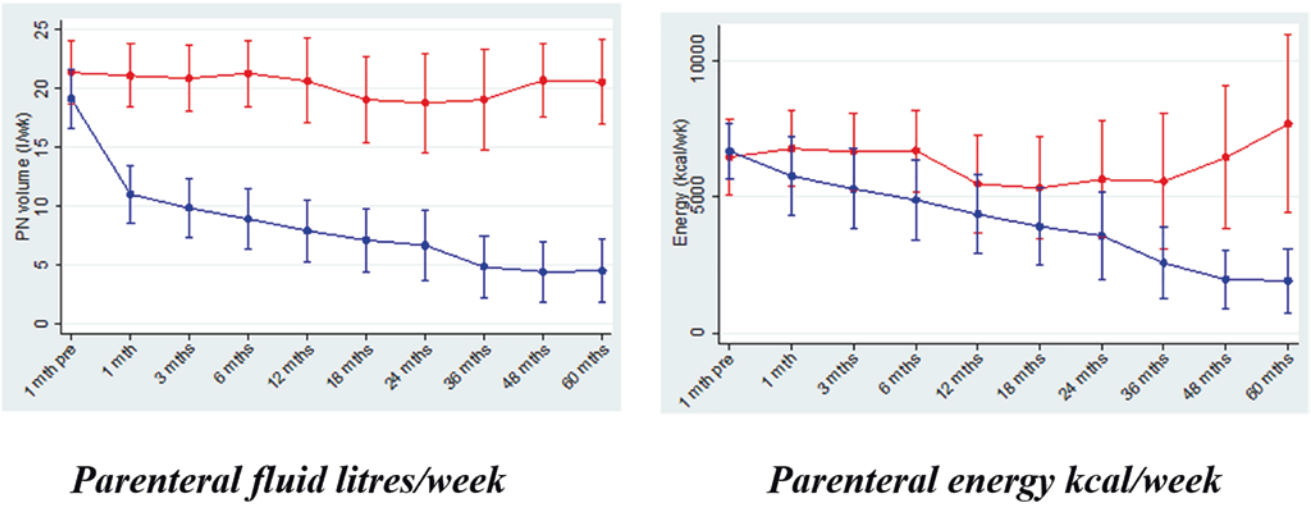

Fig. 6 Parenteral support after mesenteric infarction in patients with jejunostomy and in those following an anastomosis bringing the colon back into continuity [164]. Red top line Jejunostomy ($n = 29$) and lower blue line Jejunum-colon (re-anastomosis) ($n = 57$). There is a reduction in the need for parenteral fluid and nutrition in the 36 months (3 years) after the re-anastomosis

- Although adaptation occurs in the months after the creation of an ileostomy, there is no evidence for any structural [90] or functional [34, 165] adaptation at any time in patients with a jejunostomy.

Gallstones

Gallstones are common (45%) in both types of patient and are more common in men [34] (chapter "Gallstones in Intestinal Failure"). It was originally thought that gallstones in this circumstance resulted from deposition of cholesterol because of a depleted bile-salt pool. However, the gallstones tend to contain calcium bilirubinate. Such stones probably result from gallbladder stasis: biliary sludge develops and this subsequently forms calcium bilirubinate stones which often appear calcified on abdominal radiographs [166]. Calcium bilirubinate crystals within biliary sludge are more commonly found in men than in women [167]. Cholecystokinin injections have been used to prevent gallbladder stasis [168] and some units have advocated a prophylactic cholecystectomy [169, 170] (chapter "Gallstones in Intestinal Failure").

Social Problems

Most long-term patients with a short bowel have a body mass index within the normal range, and most are in full-time work or look after the home and family unaided [34]. Both groups of patients may have diarrhoea, which causes problems, especially if housing conditions are poor. In those with a colon the diarrhoea is malodorous and bulky due to steatorrhoea.

The effluent from a small-bowel stoma, unlike that from a colostomy, is not offensive. The large volume of fluid that emerges, however, may trouble the patient; sometimes 3 or more litres in 24 h may be passed from the stoma. The bag then has to be emptied frequently and, if it becomes overfull, the adhesive flange may separate from the skin with embarrassing leakage of fluid and with the likelihood of skin soreness.

Other and Future Treatments

New treatments are likely to be aimed at increasing the absorptive function of the remaining gut. Most are currently directed at inducing structural adaptation, for example GLP-1 or 2 analogues [171], epidermal growth factor [172, 173], colostrums or aminoguanidine [174]. Studies using growth hormone, glutamine and fibre have been disappointing [175–178]. Studies that use analogues of peptide YY have yet to be tried [179]. Cholylsarcosine is a synthetic bile acid resistant to bacterial deconjugation and dehydroxylation, that does not itself cause colonic secretion and thus diarrhoea, but does result in a variable improvement in fat and calcium absorption in patients with a short bowel, with or without a retained functioning colon [180, 181]. Attempts to replace colonic mucosa with small intestinal mucosa to increase absorption have not proved successful [182]. Tissue engineering to make small intestine over a scaffold (decellularized organ or synthetic biodegradable matrix) is difficult due to the complex structure of the small intestine (includes nerves, blood vessels, muscle and mucosa) and having to achieve a secretory, absorptive, propulsive and barrier function [183]. Another area of importance is the prevention of gallstones after an intestinal resection: trials using prophylactic antibiotics, ursodeoxycholic acid and cholecystokinin may be performed. An oral nutrient solution containing 100 mmol/L sodium and having an osmolality of 300 mOsm/kg has yet to be commercially manufactured as an ideal nutrient solution to give to patients with a jejunostomy or high-output ileostomy.

Small bowel transplantation is becoming more safe (chapter "Intestinal Transplantation") and the outcome in selected patients may be as good as that of prolonged parenteral nutrition though one set of problems may be changed for another (e.g. high output stoma, dependency on HPS for rejection/complications of immunosuppressive drugs).

Preventative Measures

Post-operative monitoring of Crohn's disease to ensure mucosal healing along with smoking cessation, immunosuppressive therapy (e.g. azathioprine, 6-mercaptopurine and methotrexate), and/or biological medication (e.g. anti-tumour necrosis factor antibodies) and balloon dilatation of strictures may reduce the need for repeated or major resections of Crohn's disease and thus the chance of developing a short bowel [184].

A small bowel embolus/venous infarction may be prevented by identification of risk factors such as atrial fibrillation, a poorly functioning myocardium, recent myocardial infarction, coagulation abnormalities or a period of hypotension. Anticoagulation therapy may be given to a patient in whom a potential source of emboli is identified. The diagnosis of a small bowel infarction can be difficult but needs to be made soon after the event. Clues to the diagnosis include the presence of the risk factors above, pain (usually of sudden onset and continuous), and usually a rise in the white cell count, amylase, phosphate, lactate and D-Dimers [185]. Ideally, contrast-enhanced computed tomography (CT) should be performed within 2–3 h of the onset of pain especially if a plain abdominal radiograph has shown no obvious abnormality [186]. If there is partial occlusive

obstruction to the mesenteric artery then percutaneous transluminal angioplasty or a surgical revascularization procedure can be performed (chapter "Mesenteric Ischaemia"). If clot is shown in the superior mesenteric artery or vein and bowel necrosis has not occurred, a bolus of a vasodilator (e.g. papaverine 60 mg or tolazoline 25 mg, phenoxybenzamine, adenosine triphosphate, glucagon or prostaglandin E) may be given into the superior mesenteric artery. If this is unsuccessful, surgery may be needed but papaverine can continue to be infused at a rate of 30–60 mg/h (1 mg/mL) [186]. Thrombolytic drugs, heparin and low molecular weight dextran may all be infused into the superior mesenteric artery or peripherally to try and halt and/or reverse the progression of the infarction or ischaemia. The outcome is best if there are no signs of peritonitis at the onset of treatment [186]. In addition nitrates, calcium antagonists or octreotide [187], may be given to try and reduce the chance of a small bowel infarction.

Experimentally, the most severe problems occur after ischaemic bowel is reperfused as the resultant toxins and cytokines can cause liver and multi-organ failure. Other drugs that may be of benefit include free-radical scavengers (e.g. superoxide dismutase, 5-aminosalicylate) or xanthine oxidase inhibitors (e.g. allopurinol) and antibiotics [188, 189]. Prostacyclin analogues may be useful when bowel is reperfused as they produce vasodilatation, reduce white cell and platelet aggregation and protect ischaemic tissues. If bowel is resected, a primary anastomosis is avoided and a temporary stoma created; often there is an elective re-exploration of the abdomen the following day and any further ischaemic bowel is resected [188, 190].

The techniques used to deliver abdominal radiotherapy have improved, with avoidance of the parallel opposed fields technique and the administration of glutamine and sucralfate (chapter "Pelvic Radiation Disease and the GI Tract"), so radiation damage may become uncommon.

Survival

The survival of patients with a short bowel is good, though there is only data on those requiring HPN in whom there is an over 50% survival at 10 years for non-malignant aetiologies [34, 45, 191–196] (chapter "Home Parenteral Support for Adults").

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