

Conference on ‘Malnutrition matters’

Symposium 7: Nutrition in inflammatory bowel disease Approaches to intestinal failure in Crohn’s disease

C. R. Calvert and S. Lal*

Intestinal Failure Unit, Salford Royal NHS Foundation Trust, Eccles Old Road, Salford M6 8HD, UK

Crohn’s disease is one of the leading causes of intestinal failure. The term ‘type 2’ intestinal failure is used to describe the relatively rare type of intestinal failure that occurs in association with septic, metabolic and complex nutritional complications, typically following surgical resection and/or laparostomy for intra-abdominal sepsis. A multidisciplinary approach to the management of patients with type 2 intestinal failure is crucial, and it is helpful to approach patient care in a structured manner using the ‘sepsis-nutrition-anatomy-plan’ algorithm: resolution of sepsis is required before adequate nutritional repletion can be achieved, and it is crucial to optimise nutritional status, and define intestinal anatomy before delineating a definitive medical or surgical plan. A structured approach to the management of patients with inflammatory bowel disease, who have developed type 2 intestinal failure, should reduce the likelihood of these patients developing ‘type 3’ intestinal failure, which is characterised by the need for long-term parenteral nutrition. However, Crohn’s disease is still the commonest indication for home parenteral nutrition in the UK.

Intestinal failure: Parenteral nutrition: Crohn’s disease

The term ‘intestinal failure (IF)’ has been given a variety of definitions since its original conception in 1981⁽¹⁾; the most recent, internationally agreed consensus definition suggests that IF results from ‘obstruction, dysmotility, surgical resection, congenital defect or disease-associated loss of absorption and is characterised by the inability to maintain protein-energy, fluid, electrolyte or micronutrient balance⁽²⁾. This definition can be applied to a variety of gastro-intestinal conditions that necessitate some form of fluid or nutritional support, but does not take into account the duration or severity of the disease process. To address this, IF has been further subclassified into three types (Table 1)⁽³⁾.

Potential disease aetiologies of all types of IF are, of course wide, with Crohn’s disease being one of the commonest causes of both type 2 and type 3 IF^(5,6). The objective of this review is to review the incidence and aetiology of IF in Crohn’s disease and outline a management strategy for patients with type 2 IF.

Crohn’s disease and type 2 intestinal failure

Fig. 1 outlines the causes of type 2 IF in patients referred over the last 10 years to our IF unit, which is one of only two national centres for the management of patients with severe IF in the UK. Crohn’s disease accounts for 21% of admissions to our unit and is second currently to surgical complications as the principal cause of type 2 IF in this patient cohort. In contrast, our earlier experience identified Crohn’s disease as the principal cause of type 2 IF in patients referred, accounting for 42% of all admissions in the 1980s⁽⁷⁾. Although these data represent the experience of only a single centre, it is a unit with a large national referral base and our data may therefore suggest that the incidence of type 2 IF in patients with Crohn’s disease is diminishing. Indeed, there is emerging evidence that the increased and earlier use of medications such as thiopurines, as has occurred over the last three decades in the UK, has been associated with a reduction in the need

Abbreviations: HPN, home PN; IF, intestinal failure; PN, parenteral nutrition.

***Corresponding author:** Simon Lal, fax +44 161 2065148, email simon.lal@srft.nhs.uk

Table 1. Classification of intestinal failure (IF)

Type 1 IF	Self-limiting IF that occurs following abdominal surgery, whereby patients require fluid, electrolyte, enteral and/or parenteral nutritional support for a limited period of time, before making a full recovery without complication. Type 1 IF is common in all hospitals; the recent National Confidential Enquiry into Patient Outcome and Death into the care of hospital patients receiving parenteral nutrition (PN) support, identified that 93% of patients in hospitals throughout the UK received PN for less than 30 d, with the majority of these patients needing nutritional support as a result of post-surgical complications ⁽⁴⁾
Type 2 IF	Occurs in severely ill patients, who develop septic, metabolic and nutritional complications following gastro-intestinal surgery. These patients need multidisciplinary input and nutritional support to permit recovery and, in some instances, may require transfer to a specialist IF unit for management
Type 3 IF	Chronic IF requiring long-term nutritional support. This category may include patients that have progressed from having type 2 IF in whom artificial nutrition support cannot be weaned and will therefore include patients requiring long-term, home PN (HPN)

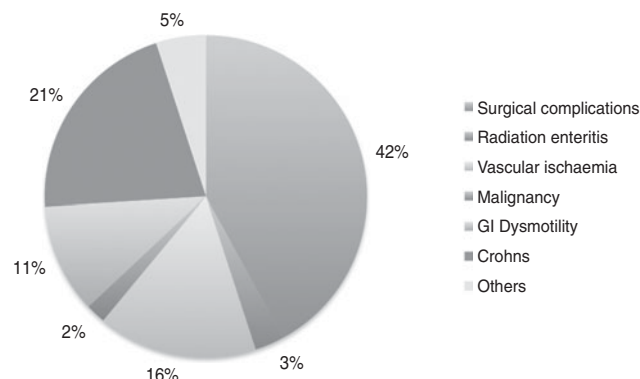


Fig. 1. Disease spectrum of patients with type 2 intestinal failure (IF) admitted to Salford Royal Infirmary, IF Unit (percentages between 1998 and 2008; *n* 453).

for surgical intervention, and therefore possibly the risk of IF, in patients with Crohn's disease⁽⁸⁾. Whether the increased use of other medical therapies such as anti-TNF- α agents, which are also associated with a reduced need for surgery in patients with Crohn's disease⁽⁹⁾, has also led to a reduction in IF in Crohn's disease is, as yet, unclear. However, any strategy that can reduce surgical intervention in patients with Crohn's disease is likely to lead to a reduction in IF, since the principal mechanism by which patients with Crohn's disease develop IF appears to be as a result of complications of surgical treatment⁽¹⁰⁾.

Management of type 2 intestinal failure in Crohn's disease

Patients with Crohn's disease, as those with many other gastro-intestinal disease groups, can develop type 2 IF as a result of intestinal resection, mechanical obstruction and/or inflammation and all of these factors may act alone or together to impair the ability of the gut to maintain protein-energy, fluid, electrolyte or micronutrient balance and so lead the patient to require artificial parenteral and/or enteral nutrition support. Furthermore, and as outlined earlier, since most patients with Crohn's disease develop IF as a result of complications of surgery⁽¹⁰⁾, it is not uncommon for these patients also to have concomitant problems relating to intra-abdominal sepsis, fistulisation and/or a high-output stoma if they have undergone an intestinal diversion procedure. It is therefore usual for

patients with type 2 IF to present with a variety of complex and interacting problems, which may include sepsis, wound dehiscence, fluid imbalance and/or malnutrition and complications relating to artificial nutrition support, such as central venous catheter infection or parenteral nutrition (PN)-associated hepatic dysfunction. Thus, given the multifaceted nature of patients' presenting problems, it is vital to adopt a structured approach to managing patients with type 2 IF and the therapeutic strategy termed as the 'sepsis-nutrition-anatomy-plan' approach provides a useful algorithmic approach to managing the various components of IF in these patients (See Fig. 2)⁽³⁾.

'Sepsis-nutrition-anatomy-plan' approach to managing type 2 intestinal failure

Sepsis. The presence of sepsis needs to be considered first in the sepsis-nutrition-anatomy-plan algorithm for two principal reasons: first, sepsis is the principal cause of death in patients with IF and, second, ongoing infection will increase metabolic demand and impair intestinal function, such that any form of nutritional support will be less effective until sepsis is investigated and treated first⁽¹¹⁾. The source of sepsis in IF can be wide, ranging from an intra-abdominal collection in a patient with an intestinal fistula following surgery, to endocarditis in a patient who has had multiple central venous catheter infections. It is important to recognise that typical features of sepsis, such as leucocytosis or pyrexia, may be absent in patients with IF^(3,12) and patients may present with other features such as hypoalbuminaemia, persistent weight loss or abnormal liver function tests. Indeed, 25% of all patients with type 2 IF referred to our unit over the last 10 years were jaundiced on admission and, of these, 67% were septic⁽¹³⁾. Clearly, other causes of abnormal liver function also need to be considered in patients with IF, such as PN-associated liver disease or drug therapy⁽¹⁴⁾, but it is vital to recognise sepsis as a potential cause of hepatic dysfunction in patients with IF since the septic patient will, of course, fare worse.

If sepsis is suspected, then the patient should undergo standard investigations such as blood cultures (from both peripheral veins and indwelling central venous catheter), wound swabs, chest X-ray, urine cultures and/or echocardiography. Computerised tomography is the modality of choice for identifying abdomino-pelvic abscesses with a diagnostic accuracy of >95%⁽¹⁵⁾. If present, intra-abdominal collections are very unlikely to resolve with

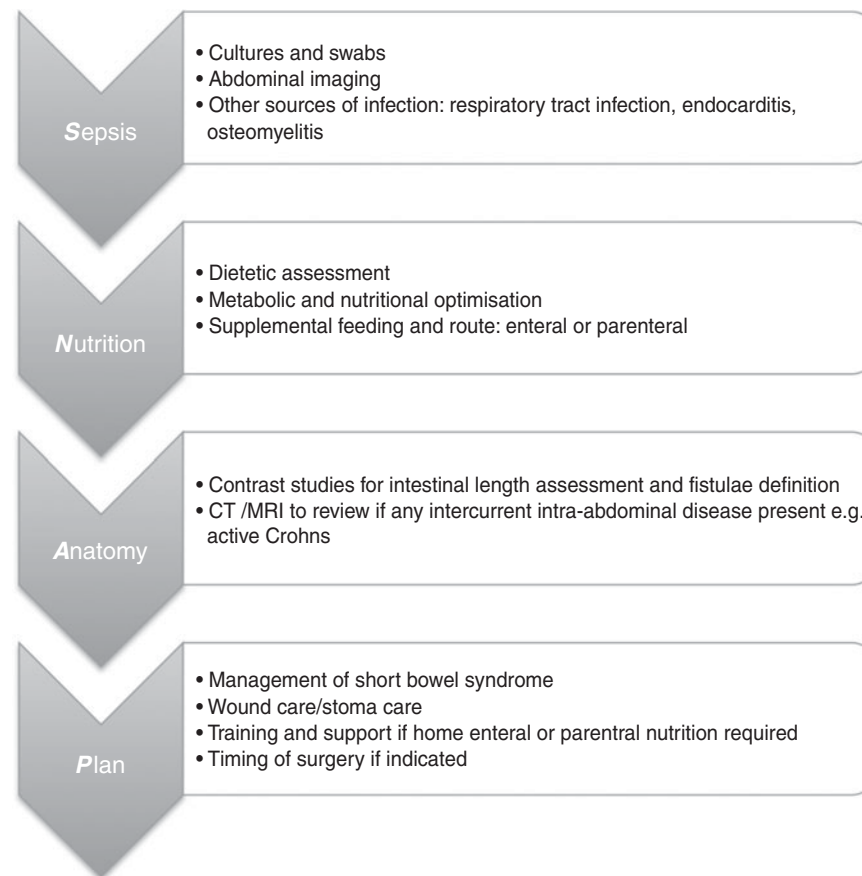


Fig. 2. The 'sepsis-nutrition-anatomy-plan' approach to the management of intestinal failure.

antibiotic therapy alone and will usually have to be drained for complete resolution; this can often be achieved by placement of a drain under computerised tomography-guidance^(16,17). Surgical drainage will sometimes prove necessary for complete resolution of an intra-abdominal abscess cavity, particularly if there are multiple interloop abscesses^(16,18). A cardinal feature of any form of surgery used to manage intra-abdominal sepsis is to avoid a primary intestinal anastomosis in the presence of sepsis, such that the intestinal ends should be exteriorised as stomas if intestinal resection is required; alternatively, drainage of an intra-abdominal collection and proximal diversion or 'defunctioning', of the gastro-intestinal tract may be more appropriate⁽¹⁶⁾. In certain situations, the abdomen may be left open post-operatively, to allow drainage of the fistulating segments, and the laparotomy wound allowed to heal by secondary intention⁽¹⁹⁾.

Nutrition

Providing nutrition can have two roles in patients with Crohn's disease: as primary therapy to treat intestinal inflammation⁽²⁰⁾ and/or as supportive therapy for the malnourished patient. Recent guidelines published by the European Crohn's and Colitis Organisation suggest that 'nutrition may be considered as primary (anti-inflammatory) therapy only if the disease is mild'⁽²¹⁾ and therefore patients with IF do not fall into this category.

Indeed, in patients with IF of all aetiologies, the principal role of nutrition is to replenish protein, energy, vitamins and micronutrients, thus allowing for recovery before considering definitive medical and/or surgical treatment.

Careful and regular assessment of nutritional status and fluid balance is crucial to managing patients with type 2 IF. This is of particular importance in patients with stomas and/or entero-cutaneous fistulas, where daily recording of fluid input and urine, stoma and/or fistula output, as well as regular evaluation of blood and urinary electrolytes will guide patients' fluid requirements and highlight the need to intensify strategies to reduce stoma or fistula losses (see later). Nutritional status should be assessed on a week-to-week basis by nursing, medical and dietetic staff, and the specific route of nutritional supplementation in patients with type 2 IF should be tailored to the individual's needs. As with all malnourished patients, oral and/or enteral nutritional supplementation is the feeding modality of choice⁽²²⁾ in the context of a functioning gastro-intestinal tract but mucosal inflammation, a short bowel and/or intestinal obstruction may, of course, limit the delivery and utility of enteral nutrition in patients with Crohn's disease and type 2 IF. While it is important to recognise that enteral nutrition will not necessarily impair the spontaneous closure of intestinal fistulas⁽²³⁾, enteral feeding may be of limited benefit in patients with proximal small bowel fistulas or stomas and may further increase their effluent output. It may be possible to consider 'fistuloclysis' or

'distal enteral tube feeding' in such patients: this involves insertion of a feeding tube into the distal limb of an enterocutaneous fistula or loop stoma and can prove a successful means of delivering enteral nutrition, as long as there is a minimum of 75 cm of distal small intestine to allow adequate absorption⁽²⁴⁾.

Replenishing a patient's nutritional status is a dynamic process, and whatever modality chosen – oral, enteral, parenteral and/or distal enteral feeding – needs to be evaluated regularly, with appropriate adjustments if requirements are not met. Clearly, enteral nutrition is the modality of choice if the gastro-intestinal tract is functional, since this may offer the putative advantage of promoting gut barrier function and enhancing intestinal adaptation^(25,26). However, the most important feature in choosing the modality to deliver nutritional support in type 2 IF is to adopt a pragmatic approach and recognise that patients may require a varied combination of both enteral and PN, according to the degree of dysfunction of their intestinal tract, to ensure that the patient receives adequate nutritional support by whatever route necessary⁽²⁷⁾. This approach will help optimise the patient's clinical condition, as they recover from sepsis and plans are made for the definitive management of their IF. This process can take several months, and patients may require a period of parenteral and/or enteral nutritional support at home, which will allow patients to reap the benefits of being nutritionally replete with improved immune function⁽²⁸⁾, improved ability for wound healing⁽²⁹⁾ and enhanced intestinal adaptation prior to undergoing any form of reconstructive surgery.

Anatomy

It is clearly important to determine intestinal anatomy and the presence of active Crohn's disease before being able to delineate a definitive management strategy for patients with type 2 IF. Contrast-enhanced computerised tomography scanning to evaluate intra-abdominal sepsis (see earlier) will provide some information regarding intestinal anatomy, while further assessment utilising oral, per-fistula and/or enema contrast studies will allow complete assessment of the entire length of small and large intestines, including any bypassed or defunctioned segments. In general, radiologists will prefer to use water-soluble contrast agents rather than Ba in patients with type 2 IF, particularly if perforation or dehiscence is suspected, since extravasated Ba may lead to peritonitis⁽¹⁸⁾. Patients with Crohn's disease may be at additional risk of extra-intestinal fistulisation, such as urogenital and/or perineal, in which case techniques such as MRI or occasionally urography will provide a useful role.

Complete gastro-intestinal anatomical information will delineate the presence of any strictured intestinal segments, an essential piece of information prior to reconstructive surgery because distal stricturing may predispose to future anastomotic dehiscence⁽¹⁶⁾. Areas of Crohn's disease activity identified radiologically may also need to be evaluated endoscopically, and the information gleaned can be put together to determine if anti-inflammatory therapy is

appropriate before any form of reconstructive surgery that may be required.

Plan

It will hopefully be clear that a definitive management strategy for patients with type 2 IF can only be drawn up once sepsis has been addressed, the patient is nutritionally replete and a full and detailed anatomical assessment has taken place. All components of the 'sepsis-nutrition-anatomy-plan' algorithm require input from a multi-disciplinary team, comprising dietitians, pharmacists, biochemists, enterostomal therapists, nurses, microbiologists, radiologists, pain specialists, IF surgeons and physicians. For patients who have large laparostomy wounds with multiple entero-cutaneous fistulas that may not heal through secondary intention, additional input from a plastic surgeon may be required. In addition, it is important not to neglect the patient's psychological status; patients with IF often need a period of in-patient management of many months and this, can of course, be detrimental to psychological well-being⁽³⁰⁾, and so specialist input from a psychologist with a specific interest in IF can prove invaluable.

The multidisciplinary team will aim to progress the patient's definitive management, enabling hospital discharge. As outlined earlier, this may entail the patient receiving a period of artificial nutrition support at home before any form of definitive reconstructive surgery and/or medical management of active Crohn's disease can take place.

Medical management

Medical therapy for active Crohn's disease will entail drugs such as corticosteroids, azathioprine, methotrexate and/or biological therapies, all of which will modulate the patient's immune response and thus may be unsafe in the presence of sepsis. Hence, it may not be possible to institute any form of medical therapy in patients with type 2 IF for a considerable period of time. Standard strategies to manage 'short bowel syndrome' can be adopted to reduce diarrhoea or any excessive secretory losses from an end stoma or small-bowel fistula⁽³¹⁾; to this end, restriction of hypotonic fluid intake, encouraging the use of an oral glucose-electrolyte solution (with a Na content of 120 mmol/l) will limit intestinal Na losses⁽³²⁾; gradual introduction of anti-motility agents such as loperamide and/or codeine phosphate, as tolerated, can further reduce faecal output⁽³³⁾ and anti-secretory agents, such as omeprazole⁽³⁴⁾ can provide additional benefit, although other anti-secretory agents such as octreotide are often of limited benefit⁽²³⁾. By reducing stomal and/or fistula losses, these measures will also serve to reduce the painful wound irritation that can be associated with the corrosive nature of the effluent output in patients with abdominal laparostomy wounds.

Surgical management

It should be apparent that an essential feature of the 'sepsis-nutrition-anatomy-plan' approach relies on the

premise that any form of reconstructive surgery in patients with type 2 IF; for example, surgical repair of persistent fistulas and/or restoration of intestinal continuity in patients who have previously undergone an intestinal diversion procedure, should not be considered until the patient is free of sepsis and nutritionally replete. This process may take many months. The goal of reconstructive surgery will be to bring as much healthy bowel back into continuity as possible. The hope is that this, in tandem with medical therapy, aimed at treating any residual active Crohn's disease, will ultimately render the patient free from artificial nutrition support. There will, of course, be situations where this will not be possible, for example, if the patient does not have enough residual healthy bowel to make reconstructive surgery feasible and if this proves to be the case, then the patient may become dependent on long-term artificial nutritional support and enter the realm of having type 3 IF.

Outcome of intestinal failure in Crohn's disease

The incidence of type 2 IF in Crohn's disease is unknown, principally because there are currently limited data on the occurrence of type 2 IF in patients managed at their local hospital. This, along with the varied aetiology of type 2 IF, makes prognostic generalisations difficult. However, from our own experience as a national referral centre, about 60% of patients presenting with type 2 IF will be discharged requiring home PN (HPN)⁽³⁾. Crohn's disease is still the leading indication for HPN (type 3 IF) in the UK, accounting for 21.6% of new HPN registrations and 30.4% of established HPN cases in 2009⁽⁶⁾. Fortunately, patients with Crohn's disease have the best prognosis of all disease groups once type 3 IF is established, with a 5-year survival on HPN of 87–92%^(35,36).

Summary

While type 1 IF in Crohn's disease is relatively common, types 2 and 3 IF are rarer. As outlined, once a patient has developed type 2 IF, it is important to adopt a structured, multidisciplinary approach – resolving sepsis, optimising nutritional status, defining intestinal anatomy and then formulating a definitive management plan – in order to reduce the morbidity and mortality associated with this complex condition; this may, in turn, reduce the ultimate need for long-term artificial nutritional support. However, Crohn's disease remains the commonest cause of type 3 IF in the UK; if this develops, then HPN provides the patient with the best chance of long-term survival over the current alternative of intestinal transplantation⁽³⁷⁾, while other strategies to improve intestinal absorption and reduce PN need, such as intestinal lengthening⁽³⁸⁾ and administration of growth factors⁽³⁹⁾ continue to evolve.

Acknowledgements

The authors declare no conflicts of interest. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. S. L.

conceived the ideas and structure for the article and S. L. and C. C. wrote the article together.

References

1. Fleming CR & Remington M (1981) Intestinal failure. In *Nutrition and the Surgical Patient*, pp. 219–235 [GL Hill, editor]. Edinburgh: Churchill Livingstone.
2. O'Keefe SJD, Buchman AL, Fishbein TM *et al.* (2006) Short bowel syndrome and intestinal failure: Onsenus definitions and overview. *Clin Gastroenterol Hepatol* **4**, 6–10.
3. Lal S, Teubner A & Shaffer JL (2006) Review article: Intestinal failure. *Aliment Pharmacol Ther* **24**, 19–31.
4. Stroud M, Stewart J, Mason D *et al.* (2010) Parenteral Nutrition: A Mixed Bag. London, UK: National Confidential Enquiry into Patient Outcome and Death (NCEPOD).
5. Green CJ, Mountford V, Hamilton H *et al.* (2008) A 15 year audit of home parenteral nutrition provision at the John Radcliffe Hospital, Oxford. *QJM* **101**, 365–369.
6. Smith T, Micklewright A, Hirst A *et al.* (2010) Trends in Artificial Nutrition Support in the UK 2010. A Report by the British Artificial Nutrition Survey (BANS). Redditch, Worcs.: BAPEN; available at http://www.bapen.org.uk/res_press_rel_bans_10_report.html
7. Scott NA, Leinhardt DJ, O'Hanrahan T *et al.* (1991) Spectrum of intestinal failure in a specialised unit. *Lancet* **337**, 471–473.
8. Peyrin-Biroulet L, Oussalah A, Williet N *et al.* (2010) Impact of azathioprine and tumour necrosis factor antagonists on the need for surgery in newly diagnosed Crohn's Disease. *Gut* **59**, 1200–1206.
9. Rubenstein JH, Chong RY & Cohen RD (2002) Infliximab decreases resource use among patients with Crohn's disease. *J Clin Gastroenterol* **35**, 151–156.
10. Agwunobi AO, Carlson GL, Anderson ID *et al.* (2001) Mechanisms of intestinal failure in Crohn's disease. *Dis Colon Rectum* **44**, 1834–1837.
11. Streat SJ, Beddoe AH & Hill GL (1987) Aggressive nutritional support does not prevent protein loss despite fat gain in septic intensive care patients. *J Trauma* **27**, 262–326.
12. Fry DE (1994) Noninvasive imaging tests in the diagnosis and treatment of intra-abdominal abscesses in the post-operative patient. *Surg Clin North Am* **74**, 693–709.
13. Kalaiselvan R, Singh S, Heydari S *et al.* (2009) Prognostic Indicators in Jaundiced Patients On Total Parenteral Nutrition for Intestinal Failure. *DDW Abstract No. 902*.
14. Gabe S & Culkun A (2010) Abnormal liver function tests in the parenteral nutrition fed patient. *Frontline Gastroenterol* **1**, 98–105.
15. Roche J (1981) Effectiveness of computed tomography in the diagnosis of intra-abdominal abscess: A review of 111 patients. *Med J Aust* **2**, 87–88.
16. Carlson GL (2003) Surgical management of intestinal failure. *Proc Nutr Soc* **62**, 711–718.
17. Montgomery RS & Wilson SE (1996) Intraabdominal abscesses: Image-guided diagnosis and therapy. *Clin Infect Dis* **23**, 28–36.
18. Thomas HA (1996) Radiologic investigation and treatment of gastrointestinal fistulas. *Surg Clin North Am* **76**, 1081–1094.
19. Mughal MM, Bancewicz J & Irving MH (1986) 'Laparostomy': A technique for the management of intractable intra-abdominal sepsis. *Br J Surg* **73**, 253–259.
20. Goh J & O'Morain CA (2003) Review article: Nutrition and adult inflammatory disease. *Aliment Pharmacol Ther* **17**, 307–320.

21. Dignass A, Van Assche G, Lindsay JO *et al.* (2010) The second European evidence-based consensus on the diagnosis and management of Crohn's disease. *J Crohns Colitis* **4**, 28–62.
22. Stroud M, Baldwin C, Bradnam V *et al.* (2006) Nutrition Support in Adults Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition. National Institution for Clinical Excellence NICE; available at <http://www.nice.org.uk/nicemedia/pdf/cg032fullguideline.pdf>
23. Lloyd DA, Gabe S & Windsor AC (2006) Nutrition and management of enterocutaneous fistula. *Br J Surg* **93**, 1045–1055.
24. Teubner A, Ravishankar H, Farrer K *et al.* (2004) Fistuloclysis can successfully replace parenteral feeding in the nutritional support of patients with enterocutaneous fistula. *Br J Surg* **91**, 625–631.
25. Braunschweig CL, Levy P, Sheean PM *et al.* (2001) Enteral compared with parenteral nutrition: A meta-analysis. *Am J Clin Nutr* **74**, 534–542.
26. Buchman AL, Moukarzel A, Bhuta S *et al.* (1995) Parenteral nutrition is associated with intestinal morphologic and functional changes in humans. *JPEN J Parenter Enteral Nutr* **19**, 453–460.
27. Woodcock NP, Zeigler D, Palmer MD *et al.* (2001) Enteral versus parenteral nutrition: A pragmatic study. *Nutrition* **17**, 1–12.
28. Penn N, Purkins L, Kelleher J *et al.* (1991) The effect of dietary supplementation with vitamins A, C and E on cell-mediated immune function in elderly long-stay patients: A randomized controlled trial. *Age Ageing* **20**, 169–174.
29. Wild T, Rahbarnia A, Kellner M *et al.* (2010) Basics in nutrition and wound healing. *Nutrition* **26**, 862–866.
30. Stern JM, Jacyna N & Lloyd DA (2008) Review article: Psychological aspects of home parenteral nutrition, abnormal illness behaviour and risk of self-harm in patients with central venous catheters. *Aliment Pharmacol Ther* **27**, 910–918.
31. Nightingale J & Woodward J (2006) Guidelines for the Management of Short Bowel Gut 55 Suppl IV, iv1–iv; available at http://www.bsg.org.uk/pdf_word_docs/short_bowel.pdf
32. Nightingale JM, Lennard-Jones JE, Walker ER *et al.* (1992) Oral salt supplements to compensate for jejunostomy losses: Comparison of sodium chloride capsules, glucose electrolyte solution, and glucose polymer electrolyte solution. *Gut* **33**, 759–761.
33. Tytgat GN, Huibregtse K, Dagevos J *et al.* (1977) Effect of loperamide on fecal output and composition in well-established ileostomy and ileorectal anastomosis. *Am J Dig Dis* **22**, 669–676.
34. Jeppesen PB, Staun M, Tjellesen L *et al.* (1998) Effect of intravenous ranitidine and omeprazole on intestinal absorption of water, sodium, and macronutrients in patients with intestinal resection. *Gut* **43**, 763–769.
35. Scolapio J, Fleming C, Kelly D *et al.* (1999) Survival of home parenteral nutrition-treated patients: 20 years of experience at the Mayo Clinic. *Mayo Clin Proc* **74**, 217–222.
36. Lloyd DA, Vega R, Bassett P *et al.* (2006) Survival and dependence on home parenteral nutrition: Experience over a 25-year period in a UK referral centre. *Aliment Pharmacol Ther* **24**, 1231–1240.
37. Pironi L, Joly F, Forbes A *et al.* (2011) Long-term follow-up of patients on home parenteral nutrition in Europe: Implications for intestinal transplantation. *Gut* **60**, 17–25.
38. Yannam GR, Sudan DL, Grant W *et al.* (2010) Intestinal lengthening in adult patients with short bowel syndrome. *J Gastrointest Surg* **14**, 1931–1936.
39. Jeppesen PB (2007) Growth Factors in short-bowel syndrome patients. *Gastroenterol Clin North Am* **36**, 109–121.