Artificial nutrition and nutrition support and refeeding syndrome

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Abstract

Both enteral and parenteral nutrition support should be managed by a multiprofessional team to ensure the correct choice and minimize complications. Enteral tube feeding is required for patients with a functioning gastrointestinal tract unable to meet their nutritional requirements orally, and can be either intragastric or post-pyloric. Naso-enteral tubes are preferred for short-term feeding (<4 weeks); enterostomas are preferred for longer term feeding. Enteral feeding is generally safe. Complications are quite frequent, but most are minor and easily managed. Parenteral nutrition should only be used if there is intestinal failure, which can be subcategorized into three types. There is no doubt that parenteral nutrition support can be life-saving, but it is also associated with a number of serious complications. Healthcare professionals should be aware of the problems and complications that can arise, and how to prevent and deal with them.

Keywords Central venous catheter; enteral feeding; intestinal failure; MRCP; nutrition support; parenteral nutrition

Introduction

This article is aimed at ward-based clinicians dealing with the everyday issues of enteral and parenteral feeding, and is therefore intended to be a brief description of the essential clinical information to allow for safe and good practice. It assumes that nutrition screening has been completed and dietetic assessment undertaken, and that artificial nutrition support has been deemed necessary.

Patients requiring artificial nutrition support should be referred to a multiprofessional nutrition support team, which is now an essential requirement for all acute hospital trusts.[1] The team will advise the ward team on management and, with parenteral feeding, facilitate its provision.

Enteral nutrition

Enteral tube feeding is the delivery of nutritionally complete feed directly into the stomach or small intestine via a tube.

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Key points

- Enteral and parenteral feeding should be managed by a multiprofessional team
- Enteral tube feeding is required for patients with a functioning gastrointestinal tract unable to meet their nutritional requirements orally
- Enteral tube feeding can be either intragastric or post-pyloric and via nasal or enteric tubes
- Parenteral feeding is for those where the gastrointestinal tract is not working, inaccessible or absent
- Enteral feeding is generally safe. Complications are quite frequent, but most are minor and easily managed
- Parenteral feeding can be complicated most commonly by line sepsis or venous thrombosis. Liver dysfunction is usually temporary in short-term feeding but can be more significant in longer term feeding
- Refeeding syndrome should be anticipated and prevented when feeding commences

Indications

Enteral tube feeding is indicated in any patient who cannot meet their nutritional requirements by oral intake and who has a functioning and accessible gastrointestinal tract. It can be administered either into the stomach or directly into the small intestine (usually the jejunum) (Figure 1). Table 1 shows examples of when enteral feeding is indicated.

Routes

The following options are available:

- nasogastric tube (NGT)
- nasojejunal tube (NJT)
- gastrostomy:
  - percutaneous endoscopic gastrostomy (PEG)
  - radiologically inserted gastrostomy (RIG)
  - surgical
- jejunostomy:
  - endoscopic (percutaneous endoscopic jejunostomy (PEJ) or percutaneous endoscopic gastrojejunostomy (PEGJ))
  - radiological
  - surgical.

Nasogastric tubes: NGTs are recommended for individuals requiring tube feeding for no longer than 4–6 weeks. They are safe, cost-effective and less invasive than gastrostomies. There are two types of NGT: fine-bore tubes designed for administration of feed, and wide-bore tubes (e.g. Ryles' tube) designed for aspiration. The latter can cause oesophageal damage, such as ulceration and stricture, if left in for a prolonged period, and should not usually be used for feeding. Fine-bore tubes are

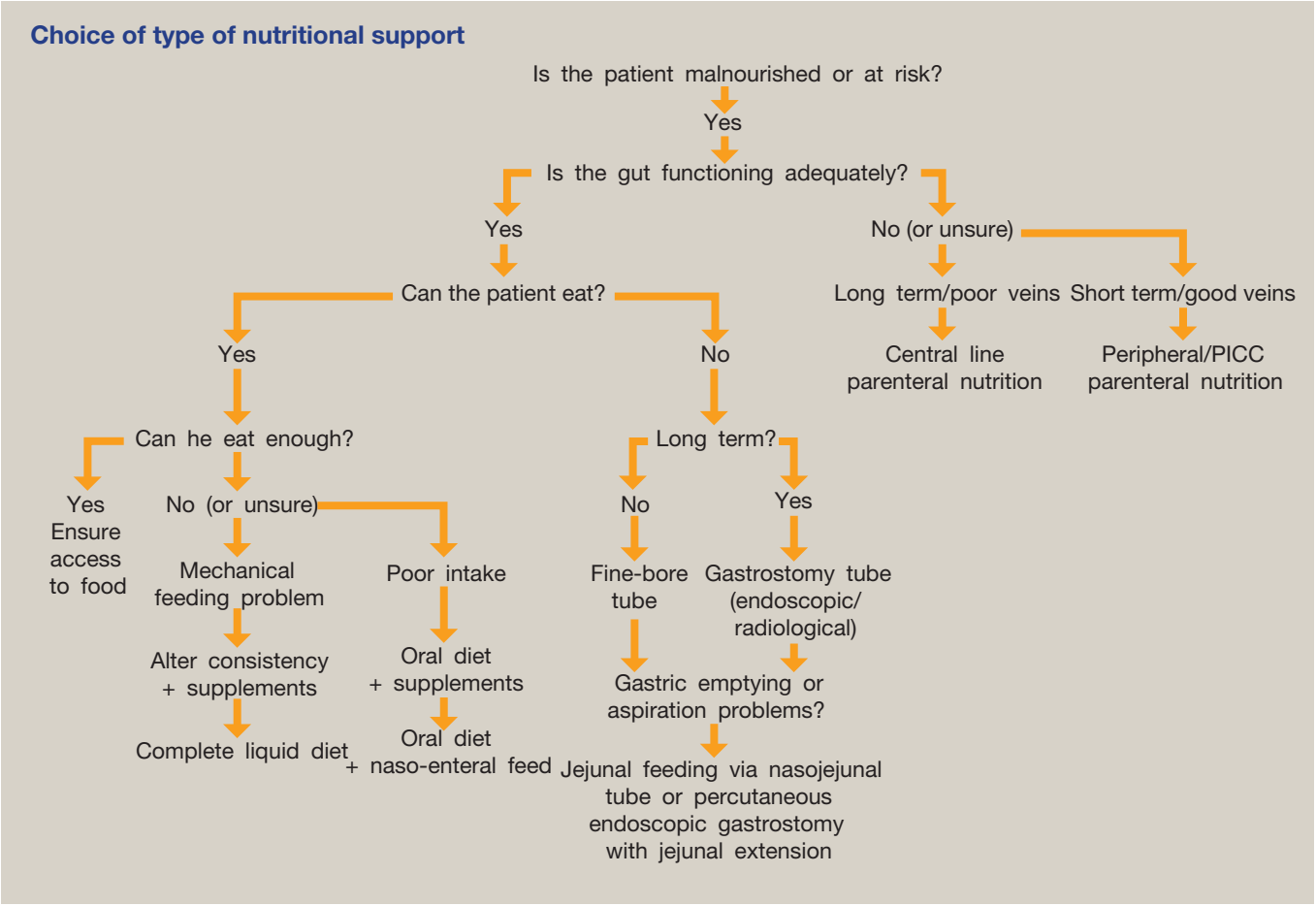

Figure 1 Adapted from McKee RF. Artificial nutrition and nutritional support and refeeding syndrome. *Medicine* 2015; **43**: 120.

Indication for enteral feeding

Patients with a functioning stomach and/or intestine:

- Impaired swallow, e.g. stroke, motor neurone disease, Parkinson's disease
- Altered level of consciousness, making oral feeding impossible
- Undergoing ventilation
- Dysphagia with oropharyngeal/oesophageal obstruction, i.e. head and neck and oesophageal cancer
- Gastric outlet obstruction: mechanical (tumour, pyloric stricture) or functional (stasis). These situations require jejunal feeding
- Severe pancreatitis (gastric or jejunal)

Supplementing inadequate oral intake:

- Cystic fibrosis
- Hypercatabolic states, e.g. burns injury, decompensated liver disease
- Facial injury
- HIV wasting
- Psychological/psychiatric reasons, e.g. anorexia nervosa

Table 1

usually easy to insert and safe, even in patients with oesophageal varices. They should not be inserted in patients with obstructive pathology in the nasopharynx or oesophagus, or in patients with basal skull fractures.

In 2016, NHS Improvement issued guidance on the safe placement and position-checking of nasogastric tubes.[2] The guidance recommends testing with pH indicator paper as the first-line check (pH $\leq$ 5.5). Higher pH suggests either that the position could be wrong, i.e. it is in the respiratory tract, or the patient is on acid-suppressing therapy, such as a proton pump inhibitor. X-rays are the second-line test. All clinical areas should have protocols for checking and rechecking tube placement.

Nasojejunal tubes: these are most commonly placed endoscopically. However, specifically designed self-propelling nasojejunal tubes spontaneously cross the pylorus in 70–80% of patients with normal gastroduodenal motility; this is especially the case if a concurrent pro-motility drug, such as an intravenous bolus of metoclopramide, is given. The distal end of the NJT must be placed beyond the duodenojejunal flexure or it will invariably passes retrogradely back into the stomach. NJTs come with single, double or triple lumens. Double- or triple-lumen tubes are recommended for patients who require simultaneous gastric decompression and small bowel feeding.

Gastrostomy: a gastrostomy is usually preferred if tube feeding is likely to be required for >4–6 weeks. It can be placed endoscopically (PEG), radiologically (RIG) or occasionally surgically. There are a number of different types of PEG/RIG tube in terms of size (9–30 French gauge (FG)), internal fixator (flange, balloon) and material, including more cosmetically acceptable 'button' gastrostomies. If the anatomy prevents insertion by one method, other methods are often limited by the same problem.

PEG insertion is usually straightforward. Although it is not a sterile procedure, antibiotic prophylaxis 30 min before the procedure is recommended. Table 2 lists contraindications to PEG insertion. It should be noted that many of the 'relative contraindications' to endoscopic placement can be overcome if insertion is done under radiological guidance.

PEGs and RIGs can be easily taken out, but care is required. If removed within 2–3 weeks of insertion, a formal tract may not have formed, with consequent risk of spillage of gastric contents into the peritoneal cavity, leading to peritonitis. This also means that it is not possible to reinsert a feeding tube down the same track, as it will not find its way into the gastric lumen. Therefore if the PEG/RIG comes out in the first few weeks of insertion, the stoma site should be covered, antibiotic cover instituted and, if nutritional support is still required, an alternative, for example an NGT, used until the wound has healed.

After 2–3 weeks, removal presents little risk of peritonitis or sepsis. However, closure is rapid, so if replacement is required this must be done within 4–6 hours using a fresh PEG/RIG or, temporarily, a balloon gastrostomy or Foley catheter. Elective removal is usually undertaken endoscopically. Alternatively, the tube can be cut close to the skin, allowing the internal fixator to pass spontaneously through the gastrointestinal tract. There are a few reported incidents of obstruction, so this should not be undertaken if there is known small intestinal pathology, such as a stricture.

Contraindications to PEG insertion

Absolute	Relative
• Inability to pass endoscope because of obstructing pathology in oropharynx or oesophagus[a]	• Severe obesity (caused by technical difficulties accessing the stomach)[a]
• Obstructing gastric outflow pathology	• Uncorrected coagulopathy
• Significant ascites	• Portal hypertension/ascites
• Gastric varices	• Active gastric ulceration/ malignancy
	• Gastroparesis
	• Gastrectomy (total or partial)[a]
	• Severe kyphoscoliosis (can be difficult to access stomach)[a]
	• Impaired respiratory reserve, e.g. motor neurone disease
	• Current peritoneal dialysis

[a] Can be achieved if done under radiological guidance to locate the stomach.

Table 2

Jejunostomy: PEGJ tubes are 'extensions' that attach to a PEG and can be passed endoscopically beyond the duodenojejunal flexure. The PEJ technique is similar to PEG but requires a direct puncture into the small intestine. Insertion techniques are not straightforward, but in expert hands successful placement can be achieved in 70–80% of cases. For most hospitals, where such expertise may not be available, and where post-pyloric feeding is required, a surgically placed jejunostomy for post-pyloric feeding is often preferred, except in patients too unfit for a general anaesthetic.

Removal of PEGJ/PEJ tubes has similar cautions to those described for PEGs.

Delivery of enteral feed

Feed can be administered as a bolus or continuously. Continuous feeding usually occurs over 16–18 hours. Bolus feeds are typically 100–500 ml of feed over 15–60 minutes at 3–6-hour intervals. Bolus feeding into the stomach is more physiological. Although there is a perception that it predisposes to aspiration, diarrhoea, bloating and dumping syndrome compared with continuous feeding, there is no clinical evidence to indicate that this is so. With jejunal feeding, loss of the stomach reservoir means that patients with post-pyloric tubes should be fed continuously.

Complications of enteral feeding

These can be divided into: mechanical, related to the tube; gastrointestinal, related to delivery of the feed; and biochemical/metabolic, related to the content of the feed.

Mechanical:

Naso-enteric feeding tubes – inadvertent removal can be purposeful, such as when the patient withdraws consent. Alternatively, the patient might be confused, in which case re-siting might be needed; if there is repeated removal, consider a nasal loop/bridle or alternative means of nutritional support, for example a PEG.

A second complication is tube blockage. Although all types of enteral feeding tubes can become blocked, fine-bore tubes are particularly at risk. Clinical areas have protocols for flushing tubes before and after feeds and medication. If a tube becomes blocked, seek advice from the nutrition team.

Malposition in the lungs can lead to infection, effusion and empyema. Tubes are occasionally malpositioned intracranially. Correct verification of tube position should avoid this.

Localized trauma such as nasopharyngeal and oesophageal erosions and ulceration can occur, but is uncommon with fine-bore tubes.

Enterostomy feeding tubes – complications can be insertion-related or tube related. Insertion-related complications include the following:

- Pain is common within first 24 hours. If it is severe, exclude peritonitis and tube displacement into the anterior abdominal wall.
- Haemorrhage can occur but is unusual if a clotting screen is within normal limits.
- Peritonitis can develop from infection introduced during the insertion process. Pre-procedural antibiotics help prevent this.

- Pneumoperitoneum occurs because there is always some free air after PEG insertion.
- Injuries to small and large intestine, spleen and liver have been documented. They are rare, but should be considered when there is otherwise unexplained haemodynamic compromise or signs of peritonitis after insertion.

There are several tube-related complications:

- Stoma infection usually resolves with appropriate antibiotics and proper stoma care. It is not usually necessary to remove the PEG or stop feeding unless severe ulceration or wound breakdown occurs.
- Tube blockage can be minimized by flushing the tube with water before and after each feed or medication.
- A buried bumper is caused by migration of the internal fixator into the gastric or anterior abdominal wall, and leads to tube blockage.
- There have been a few case reports of neoplastic seeding along the stoma track after PEG insertion for oesophageal or oropharyngeal tumours. If the PEG has been inserted as part of palliative care, this is unlikely to be of relevance in the patient's lifetime.
- Overgranulation at the stoma site can bleed or become painful. It should be treated with corticosteroid cream or silver nitrate.

Complications relating to feed delivery:

Diarrhoea – this can be problematic and sometimes difficult to manage. The incidence can be as high as 60% in critical care. The causes are multifactorial and include concomitant medication (especially antibiotics and laxatives) and contaminated feeds.

Management should include a review and rationalization of medication, stool cultures for *Clostridium difficile* and other infective organisms, and exclusion of other causes of diarrhoea. Further treatment should concentrate on symptomatic control with loperamide and codeine. Slowing down the feed rate and using low-volume/high-caloric content feeds, changing to a different mode of delivery (continuous, bolus, etc.) and introducing fibre to the diet are sometimes successful. Consideration of parenteral feeding is appropriate only in the most severe cases.

Aspiration – both nasogastric and PEG feeding increase the risk of aspiration. Where possible, patients should be fed at 30–45° and for no more than 20 hours a day. Prokinetic agents can be effective. Alternative or additional management options include alteration of feed delivery (a change from bolus to continuous feeding), changing the diet to a more energy-dense one with smaller volumes delivering equivalent calories, and considering post-pyloric feeding.

Biochemical/metabolic complications:

Refeeding syndrome – this is the most common metabolic complication of nutritional support and can occur if feed is introduced at too high a rate to a malnourished patient. The anabolic drive secondary to excessive calories leads to an increased intracellular uptake of phosphate, magnesium and potassium, producing deficiencies in these electrolytes in the extracellular compartment. This can result in cardiac arrythmias, electrolyte disturbance and multiorgan failure, and is occasionally fatal.

It is difficult to give a precise definition of refeeding syndrome because many otherwise well-nourished patients, refed after only a few days' starvation, show a modest change in biochemical values, for example a fall in serum potassium and phosphate concentrations, without displaying any symptoms. There is a spectrum from such asymptomatic cases to those with severe malnutrition who are at risk of overt and even life-threatening symptoms. The cut-off point at which 'refeeding syndrome' can be said to be present is therefore somewhat arbitrary. The full-blown syndrome should be defined by the presence of symptoms. However, biochemical changes of sufficient degree to pose a potential risk should be acted upon without delay to prevent the clinical features developing.

The key features of refeeding syndrome are:

- salt and water retention leading to oedema and heart failure
- hypokalaemia caused by rapid cellular uptake of potassium as glucose and amino acids are taken up during cellular synthesis of glycogen and protein
- hypophosphataemia caused by increased phosphorylation of glucose
- rapid depletion of thiamine, a co-factor in glycolysis, leading to Wernicke's encephalopathy and/or cardiomyopathy
- hypomagnesaemia resulting from cellular uptake.

With awareness of its existence and careful management, refeeding problems, which occur primarily after feeding restarts, are usually preventable. Generous amounts of potassium, magnesium and phosphate supplements should be given alongside the initiation of feeding, which should start at around 10 kcal/kg per day in very high-risk groups.[1] Thiamine and other B vitamins must also be given intravenously, starting before any feed is commenced and continuing for at least the first 3 days of feeding.

Feeding rates can then be gradually increased over the next few days to full calorie requirements. Thereafter, regular monitoring, especially of the refeeding electrolytes (phosphate, potassium, magnesium) is essential, although the frequency required depends on the how stable the patient's condition is. A more in-depth description of the management of refeeding syndrome can be found in the Further reading list.

Other metabolic/biochemical complications – a deficiency or excess of any macro- or micronutrient can potentially be caused by enteral feeding, so monitoring of patients is essential.

Parenteral nutrition (PN)

PN should only be used if there is intestinal failure (Figure 1). Intestinal failure can be defined as the reduction of gut function to below the minimum necessary for the absorption of macronutrients and/or water and electrolytes such that intravenous supplementation is required to maintain health and/or growth.[3]

Intestinal failure can be subcategorized into types 1, 2 and 3 (Figure 2). Type 1 is self-limiting, occurring most commonly after abdominal surgery and resolving spontaneously. Type 2 intestinal failure is more prolonged, with failure of the gastrointestinal

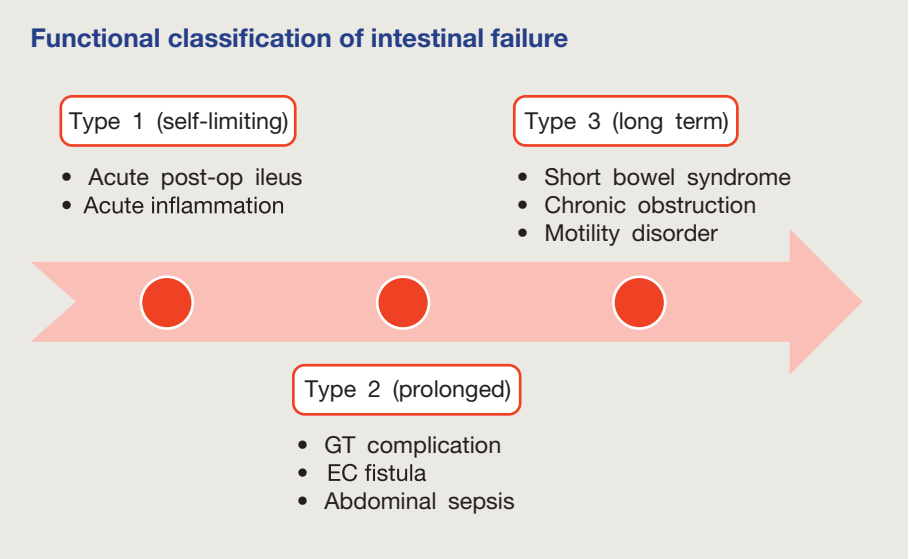

Figure 2 Source: Lal et al. Aliment Pharmacol Ther 2006; 24(1) 19-31. Pironi et al. *Clin Nutr* 2015. Apr; **34**(2): 171–80.

tract to absorb sufficient nutrients or fluid for 28 days or longer. It is associated with gastrointestinal complications such as abdominal sepsis or the development of enterocutaneous or other fistulae. Patients should be cared for in specialist centres. Type 3 intestinal failure is a long-term intestinal failure in a much more stable patient, for example patients with short bowel, chronic obstruction or motility disorders.

PN should be given via a dedicated intravenous catheter inserted for that purpose. PN is usually administered into a central vein via a peripherally inserted central catheter or a catheter that directly accesses a central vein (central venous catheter (CVC)). CVCs are non-tunnelled or tunnelled. Tunnelled CVCs tend to be used for long-term PN.

Some centres occasionally administer peripheral PN; however, the patient needs excellent veins, the cannula needs to be inserted in an aseptic manner and changed frequently, and the PN itself needs to be adjusted to have as low an osmolarity as possible. The choice of the type of venous access depends on the anticipated length of PN treatment, the availability of veins and local expertise.

The contents of the PN bag are guided by the patient's requirements for nitrogen and energy, and this is usually calculated by a dietitian. Adjustment of electrolyte content and volume is necessary in patients who need PN because of high gastrointestinal tract losses. Short-term PN can be provided using 'standard' PN bags available from commercial companies, but prolonged PN often requires a prescription designed for the individual patient.

All patients must also be given vitamins and trace elements. For stability reasons, these are not included in the multi-chamber bags so should be added in the pharmacy sterile unit before being administered to the patient.

Complications of parenteral nutrition

There is no doubt that PN can be life-saving but it is also associated with a number of serious complications.

Central venous catheter-related bloodstream infections (CRBSI): this is the most common complication,[4] and is most common in inpatients on short-term parenteral support. The reported incidence is 0.3–12 per 1000 catheter–days. The incidence of CRBSI is reduced if the hospital has a nutrition support team, in particular a dedicated nutrition nurse specialist. Care of the catheter itself is of paramount importance, and it should not also be used for blood sampling or administration of medications. An aseptic technique should be used for all connections to and disconnections from the catheter. For patients on long-term PN support who develop recurrent CRBSIs, antimicrobial locks can be used to decrease the prevalence of infective complications.

Central venous catheter thrombosis: catheter-related thrombosis can include central venous thrombosis in the vein in which the catheter is located (usually around the CVC tip) and thrombus attached to the end of the catheter (attached to a fibrin sheath). In adults, the incidence of catheter-induced central vein thrombosis is estimated at 0.03–0.06 episodes per catheter–year.[4]

The presence of a CVC is the most important risk factor for developing central venous thrombosis. Several mechanisms play a role in the development of catheter-related thrombosis, including compromised blood flow, vessel wall injury by the catheter or PN, hypercoagulable states, catheter infection and high levels of dextrose or calcium in PN solutions. In addition, a key factor is catheter tip malposition, with the tip being more proximal than the distal superior vena cava.

Central venous catheter occlusion and fracture: these complications are less well documented in the literature and are more relevant for long-term CVCs. CVC fractures can involved the external or internal sheath and require repair or replacement of the catheter.

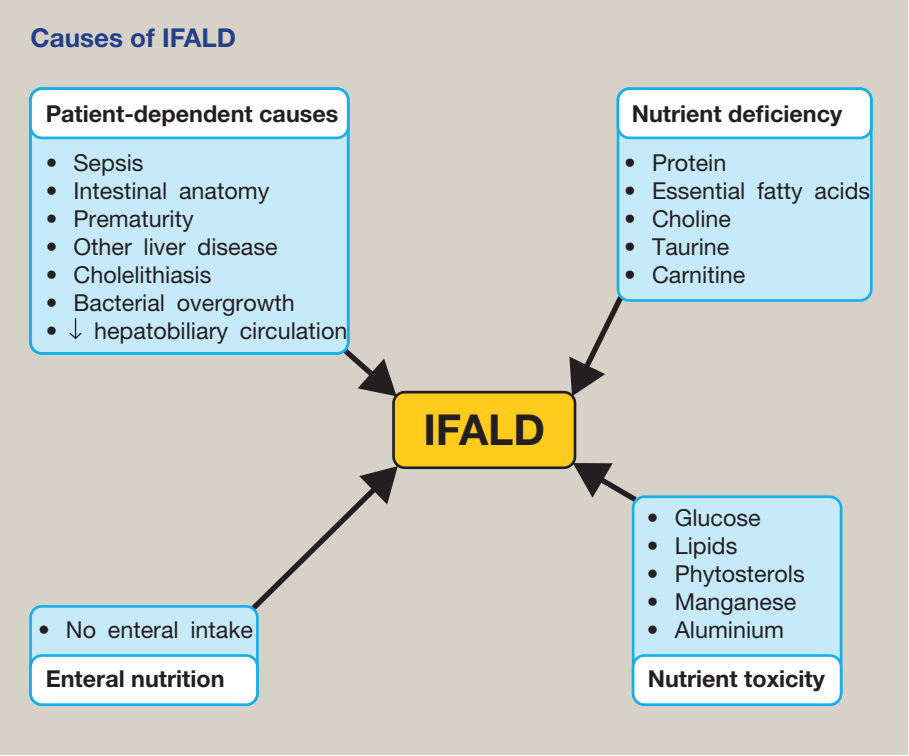

Figure 3

CVC occlusion affects 30% of long-term CVCs and can be partial or complete as well as thrombotic or non-thrombotic in aetiology. Non-thrombotic occlusions can occur from the build-up of precipitates of lipid, minerals and/or medications associated with the PN regime. Blood reflux within the catheter can occur for a variety of reasons, contributing to thrombotic occlusions within the catheter.

Intestinal failure-associated liver disease (IFALD): the prevalence of abnormal liver function tests during PN varies from 15% to 85%.[5] Liver function tests abnormalities in patients being given short-term PN are usually transient, but substantial liver damage and ultimately end-stage liver disease can occur with long-term PN. The aetiology is complex, involving a large number of patient-related and nutrition-related factors (Figure 3), but the term 'intestinal failure-associated liver disease' is more appropriate than 'PN-associated liver disease'.

In acute intestinal failure, liver enzyme abnormalities are usually mild and transient, often returning to normal when PN is stopped and an enteral or oral diet reinstated. Overall, the management of IFALD concentrates on:

- treatment of non-nutritional causes (treatment of sepsis, medication review, assessment of biliary stones)
- reinstatement of enteral or oral intake when not contraindicated
- optimization of PN (adjustment of lipids and glucose delivery, avoidance of energy overload, use of second- and third-generation lipid emulsions).

Severe IFALD can ultimately necessitate referral for small intestine and/or liver transplantation.

Other metabolic complications: these can be acute or chronic. In acute intestinal failure, metabolic complications can include hypoglycaemia, electrolyte abnormalities and refeeding syndrome (see above). For patients on long-term PN, the metabolic complications include metabolic acidosis (hyperchloraemic, lactic acidosis), mineral or vitamin deficiencies or toxicities, chronic kidney disease, renal calculi, hyperammonaemia and metabolic bone disease. Diabetic control is also much more problematic in patients on long-term PN support.

Monitoring

In the acute phase of nutritional support, there is inevitable emphasis on monitoring to detect complications. Complications of enteral tube insertion or parenteral line insertion should be excluded early after the procedures. This should be followed by daily monitoring to review fluid and electrolyte balance, glucose control and gastrointestinal or infective complications.[1] In patients on long-term enteral or parenteral support, monitoring usually occurs around 3-monthly, depending on how stable the patient's condition is. ◆

KEY REFERENCES

1 National Institute for Health and Clinical Excellence. Nutrition support in adults. 2012. Quality Standard no. 24, https://www.nice.org.uk/guidance/qs24 (accessed September 2018).
2 NHS Improvement. Initial placement checks for nasogastric and orogastric tubes: resource set. 2016, https://improvement.nhs.uk/resources/resource-set-initial-placement-checks-nasogastric-and-orogastric-tubes/ (accessed September 2018).

3 Pironi L, Arends J, Baxter J, et al. ESPEN endorsed recommendations: definition and classification of intestinal failure in adults. *Clin Nutr* 2015; **34:** 171–80.
4 Dibb M, Teubner A, Theis V, Shaffer J, Lal S. Review article: the management of long-term parenteral nutrition. *Aliment Pharmacol Ther* 2013; **37:** 587–603.
5 Klek S, Forbes A, Gabe S, et al. Management of acute intestinal failure: a position paper from the European Society for Clinical Nutrition and Metabolism (ESPEN) special interest group. *Clin Nutr* 2016; **35:** 1209–18.

FURTHER READING

Cadman A, Lawrance JAL, Fitzsimmons L, Spencer-Shaw A, Swindell R. To clot or not to clot? That is the question in central venous catheters. *Clin Radiol* 2004; **59:** 349–55.
Friedli N, Stanga Z, Sobotka L, et al. Revisiting the refeeding syndrome: results of a systematic review. *Nutrition* 2017; **35:** 151–60.
Howard L, Ashley C. Management of complications in patients receiving home parenteral nutrition. *Gastroenterology* 2003; **124:** 1651–61.
Lal S, Teubner A, Shaffer JL. Review article: intestinal failure. *Aliment Pharmacol Ther* 2006; **24:** 19–31.
Lipp A, Lusardi G. Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy. *Cochrane Database Syst Rev*, 2013. Issue 11. Art. No.:CD005571.

TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 48-year-old man had been found to have nasopharyngeal cancer, having presented with weight loss, hoarse voice and odynophagia. He was awaiting surgery followed by radiotherapy. He was not acutely unwell and, as he was self-employed, he was keen to continue working.

What is the best means to provide him with nutrition?

A Oral feed with food supplements
B Nasogastric tube with intermittent feed
C Nasojejunal tube with intermittent feed
D Insertion of percutaneous endoscopic gastrostomy
E Provision of home total parenteral nutrition

Question 2

A 60-year-old man was found to have an unsafe swallow after a large ischaemic stroke. He was started on nasogastric feeding. After 5 days, he developed severe diarrhoea, with his bowels opening >10 times a day. Three stool samples were negative on culture. The rate of delivery of feed was decreased, and codeine phosphate and loperamide were added, but without improvement.

What is the next most appropriate step in the management of his diarrhoea?

A Change to a bolus feeding regimen, and increase the codeine and loperamide
B Stop the nasogastric feed and insert an nasojejunal tube for feeding
C Stop the nasogastric feed, and insert a percutaneous endoscopic gastrostomy for feeding
D Stop the nasogastric feed, start temporary total parenteral nutrition and insert a nasojejunal tube for long-term feeding
E Stop the nasogastric feed, give intravenous fluid and after a few days reintroduce the nasogastric feed at much slower rate