Parenteral nutrition

Introduction

Many patients in hospital are malnourished, either as a consequence of their disease or as its proximal cause. Various modalities are available for nutritional support, most of which use the enteral route (*Table 1*). Occasionally this is either not available or inadequate.

Parenteral nutrition refers to the administration of nutrients via the intravenous route. It is not mutually exclusive with enteral feeding, and can be used to supplement patients tolerating such feeds in limited quantity, but if used in isolation is termed total parenteral nutrition. Opinions are frequently divided as to the relative benefits of supplemental parenteral nutrition as opposed to total parenteral nutrition, but in general a combination of parenteral nutrition plus enteral feeding is favoured as enteral feeding delivers nutrients in a more physiological manner with fewer complications and accelerated bowel recovery (Goulet et al, 2004).

Indications for parenteral nutrition

Parenteral nutrition is indicated in the following circumstances:

- Prolonged bowel obstruction or ileus, not amenable to feeding tube placement beyond the transition point
- Short bowel syndrome with severe malabsorption or fluid and electrolyte loss that cannot be controlled enterally (Nightingale and Woodward, 2006). Patients with >50 cm small bowel can often manage without long-term parenteral nutrition
- Severe dysmotility, such as pseudo-obstruction syndromes, which render enteral feeding impossible
- High output intestinal fistulae or anastomotic breakdown post-surgery (or high risk of this occurring without support)
- Patients intolerant of, or refractory to, enteral nutrition (after Van Gossum et al, 2009).

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When do you consider starting parenteral nutrition?

The decision to instigate parenteral nutrition is made on an individual patient basis, ideally in conjunction with a specialist nutrition support team. Screening should include determination of patient height, weight and body mass index, as well as formal calculation of the Malnutrition Universal Screening Tool (MUST) score (*Figure 1*) (Stratton et al, 2006).

The time into, and expected duration of, the 'intestinal failure' should be considered. Typically, parenteral nutrition should not be initiated unless the indications have persisted for greater than 3–5 days, or it is clear from the clinical scenario that they will do so, before significant improvement allows enteral feeding (National Institute for Clinical Excellence, 2006; Plauth et al, 2009).

Initial assessment should include review by a specialist dietician, and requires estimation of calorific and nutritional requirements (including nitrogen, electrolytes, trace elements and fluids). This is based upon predicted basal metabolic rates (e.g. Schofield, 1985), stress factors and severity of clinical condition.

When initiating parenteral nutrition, it is vital to assess whether the patient is at risk of refeeding syndrome (*Table 2*). This includes individuals who are below 80% of their ideal body weight and those who have had little or no nutritional intake for more than 5 days (Mehanna et al, 2008). In these circumstances, commencement of feeding must be undertaken cautiously, with the initial rate of replacement being less than 50% of the patient's energy requirements. In people at even higher risk (*Table 3*), the National Institute for Clinical Excellence suggests that the initial feeding rate should even be as low as 42 kJ/kg/24 hr (10 kcal/kg/24 hr), increasing slowly over the following days. All patients should have prior administration of vitamin B supplements (National Institute for Clinical Excellence, 2006).

Constituents and management of parenteral nutrition in hospital

Mixtures for parenteral nutrition can be customized to meet individual requirements. Modifiable factors include feed

Table 1. Possible routes of administration of enteral nutrition

Route of administration	Pros	Cons
Oral intake	Best tolerated	Requires conscious effort and normal swallowing reflex
Nasogastric, nasoduodenal or nasojejunal tube	Does not require conscious effort	May be poorly tolerated by patient; risks of tube malplacement and aspiration pneumonia
Percutaneous endoscopic gastrostomy or jejunostomy	Does not require conscious effort; tubing can be hidden under clothing; lower complication rate than nasal tubes in long term	Requires invasive procedure with associated complications; risks of infection or migration, and gastrointestinal ulceration
Surgical gastrostomy or jejunostomy	As for percutaneous endoscopic gastrostomy and percutaneous endoscopic jejunostomy	Risk of general anaesthetic; other risks as for percutaneous endoscopic gastrostomy and percutaneous endoscopic jejunostomy
Radiologically-inserted percutaneous gastrostomy	As for percutaneous endoscopic gastrostomy and percutaneous endoscopic jejunostomy, and patient does not need to undergo endoscopy or general anaesthesia	Risks of perforation and bleeding; other risks as for percutaneous endoscopic gastrostomy and percutaneous endoscopic jejunostomy

volume, glucose, amino acids, lipids, electrolytes, essential vitamins and trace elements, although these cannot always be adjusted independently.

Individual regimens are determined in correlation with the clinical status: the critical care patient may require higher caloric intake and almost always has greater nitrogen consumption than the stable but unwell patient with small bowel obstruction, as the former is more catabolic with a higher basal metabolic rate. In essence the sicker the patient, the higher the necessary nitrogen:calorie ratio. Decisions on specific feed composition will not be required of junior doctors (although they should understand the principles), but will be determined by the dietician and pharmacist in conjunction with the nutrition team.

To ensure optimal management of the patient on parenteral nutrition, the following must be monitored closely (National Institute for Clinical Excellence, 2006; Nightingale and Woodward, 2006):

Fluid volume

This can be adjusted to ensure the patient is not over- or under-hydrated. Close attention must be paid to fluid balance, with accurate measurement and documentation of urinary and gastrointestinal tract outputs. Daily weights are helpful to identify short-term fluid shifts. Third space and insensible losses should also be estimated. In sick patients, it is often appropriate to leave some intravascular space for extra fluid that might be required in addition to feed volume.

Electrolyte concentrations

These are particularly liable to fluctuate unpredictably, especially in situations in which refeeding syndrome is a concern, where ion shifts across cell membranes may be rapid and substantial. Standard regimens of parenteral nutrition typically contain 50–80 mmol sodium, 40–60 mmol potassium, 3.3–5.0 mmol calcium, 6–10 mmol magnesium, 7.5–25 mmol phosphate and 100 µmol zinc per 24 hours. In patients with high output fistulae, stomas or diarrhoea, additional potassium or magnesium may be required.

*Figure 1. Malnutrition Universal Screening Tool. From Stratton et al (2006). *Unless detrimental or no benefit is expected from nutritional support, e.g. imminent death.*

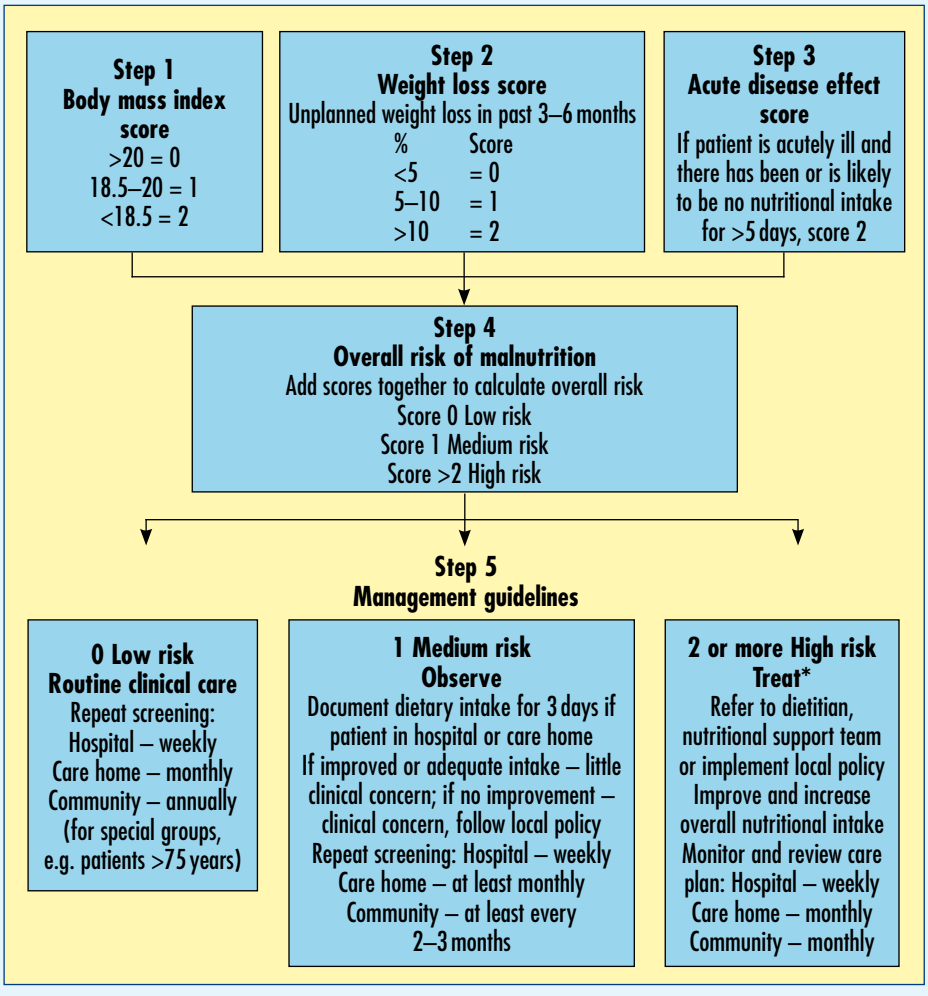

Table 2. Causes and clinical features of refeeding syndrome

Hypokalaemia	Cardiac arrhythmias including cardiac arrest
	Muscle weakness (including respiratory), paralysis, rhabdomyolysis
	Paraesthesia
	Paralytic ileus
Hypomagnesaemia	Arrhythmias
	Seizures, tremor, ataxia
	Paraesthesia
	Anorexia
Hypophosphataemia	Water and salt retention
	Paraesthesia and seizures
	Osteomalacia
	Muscle weakness (including respiratory), rhabdomyolysis
	Cardiac failure

From National Institute for Clinical Excellence (2006), Mehanna et al (2008)

Table 3. Patients at high risk of refeeding syndrome

One or more of the following	Minimal or no nutritional intake for >10 days
	>15% unintentional weight loss in the previous 3–6 months
	Low electrolyte (K^+, Mg^{2+}, PO_3^-) before refeeding
	Body mass index <16 kg/m^2
	Anorexia nervosa
Or two or more of the following	History of alcohol abuse or drugs (including insulin and diuretics)
	>10% unintentional weight loss in the previous 3–6 months
	Body mass index <18.5 kg/m^2
	Minimal or no nutritional intake for more than 5 days

From National Institute for Clinical Excellence (2006), Mehanna et al (2008)

Vitamins and trace elements

The addition of vitamins (especially vitamin C and thiamine) is essential in all patients given parenteral nutrition. Requirements for vitamin C in sick patients may be five times basal (and up to 10 times basal in smokers).

The combination of malnutrition, glucose load, and shift from lipid to carbohydrate metabolism with refeeding causes a massive increase in demand for thiamine. If this is not anticipated there is a risk of permanent neurological damage (Wernicke–Korsakoff syndrome). Trace elements (particularly zinc and selenium) are also important as they function as coenzymes.

Commercial preparations generally underprovide for the vitamin demand in serious illness and malnutrition, while tending to yield amounts of trace elements in excess of requirements (especially in the case of manganese) in the longer term. Fixed combinations can make customization of administration of specific micronutrients difficult. Give multiple doses of Pabrinex (or the equivalent) when starting parenteral nutrition in any patient in whom there is doubt about adequate intake.

Caloric intake

This depends on patient weight; a specialist medical opinion will be needed to decide on strategy in patients who are very overweight or underweight, and whether calculations should be based on actual or ideal weight (usually a point between the two will be selected). Pre-prepared formulations range from low calorie bags through to those containing up to 2500 kcal, with varying quantities of lipid and glucose. It is just as important not to 'overfeed' a patient as not to underfeed him/her, as the former can cause hepatic dysfunction and hyperglycaemia.

Critically unwell patients may have developed 'metabolic tolerance' to nutritional depletion, preventing rapid safe delivery of required calories. Furthermore, the nature of the lipid used may have an impact on clinical outcomes: ω-3 fatty acids have a much less pro-inflammatory effect than the ω-6 lipids from soya, and data support the use of fish oils in patients with the systemic inflammatory response syndrome (Singer et al, 2008).

Nitrogen requirements

In most patients, the nitrogen requirement is around 0.18 g/kg/day. This is supplied in the form of amino acids within the parenteral nutrition mixture; commercially available solutions contain varying amounts. In critically ill patients a balanced amino acid mixture should be infused at approximately 1.3–1.5 g/kg ideal body weight per day, in conjunction with adequate energy supply (Singer et al, 2009). L-glutamine, which in other circumstances is non-essential, should be included as it is rapidly consumed in such patients (Oudemans-van Straaten et al, 2001; Singer et al, 2009). The aim is to protect skeletal muscle mass, and ensure precursor availability for protein synthesis in tissues with high turnover, crucial in patients in an accelerated catabolic state in whom some tissue loss will remain unavoidable.

Blood glucose monitoring

In addition to hyperglycaemia, precipitous cessation of the parenteral nutrition infusion may provoke hypoglycaemia. Slowly tapering the rate over the last hour of the infusion reduces this risk.

Venous access

Basic parenteral nutrition regimens can be given peripherally via a simple cannula for a limited period of time (up to 48 hours typically), but it should be dedicated to purpose and inserted aseptically. Regimens using higher osmolalities should be given via central venous catheters. Subclavian access or peripherally inserted central venous catheters (PICC lines) are preferred over placement in the internal jugular or femoral veins because they have reduced contamination rates and allow easier nursing (Pittiruti et al, 2009).

Ideally only single lumen catheters should be inserted and their use restricted to delivery of nutrition. If a multi-lumen line is required, one lumen should be reserved exclusively for parenteral nutrition. Blood tests should be drawn from this site only when line infection is suspected. The use of full aseptic precautions (hand antisepsis, sterile gloves and non-touch technique) whenever the line is manipulated reduce rates of catheter-related infection (Pronovost et al, 2006). The line should be monitored daily for signs of thrombophlebitis or insertion site cellulitis.

Longer-term parenteral nutrition usually needs a tunnelled line or port. Although some guidelines advocate flushing catheters with heparin to maintain patency (Pittiruti et al, 2009), this is not essential and must not be undertaken concurrently with lipid administration as this causes precipitation within the lumen and occlusion; saline flushing is mandatory before any use of heparin in the patient receiving lipids.

Special circumstances in managing parenteral nutrition

There are a few circumstances that merit additional attention and specialist input:

Renal failure

Parenteral nutrition is often administered to such patients in the context of multi-organ failure on the intensive care unit. Specialist attention is required for fluid and nitrogen balance, as well as electrolyte disturbance (Cano et al, 2009). Patients with chronic kidney disease are particularly at risk of 'protein energy wasting', and intradialysis parenteral nutrition can be used. Some studies have shown that this improves nutritional status (Cano et al, 2007), although considerable debate remains around which patients benefit, the relative efficacy of different lipid formulations, and their potential to damage dialysis membranes (Cano et al, 2006).

Liver failure

Parenteral nutrition can be administered safely in these patients, but with careful continuing assessment for encephalopathy. In compensated patients, nitrogen restriction is not necessary and impairs adequate nutritional care. Amino acid solutions supplemented with branched chain amino acids (isoleucine, leucine and valine) have been developed and are thought to offer advantage in the encephalopathic patient (Plauth et al, 2009). Strict salt and fluid control is also crucial (Plauth et al, 2009).

Cancer

Patients with underlying malignancy are frequently undernourished, and the enteral route may not be available. There have previously been fears that providing nutritional support may 'feed the tumour', generating poorer outcomes. These have not been substantiated in clinical practice.

Optimizing nutritional status in patients on active treatment in fact enhances their ability to complete courses of therapy and improves overall outcomes (Bozzetti et al, 2009).

There are issues concerning the invasiveness of parenteral nutrition in patients who are for palliation only, and in many nutritional support will not be appropriate. Nonetheless, a proportion will be oncologically terminal in the sense that they have exhausted or rejected active therapeutic approaches but death will not be imminent. Such individuals can benefit from parenteral nutrition with increased functional status and quality of life if their prognosis is >3 months (Bozzetti et al, 2002).

Patients requiring long-term or home parenteral nutrition

It is becoming increasingly common for patients to be discharged home on parenteral nutrition once stable (Staun et al, 2009). Tertiary level specialist hospital nutrition teams will normally supervise this. In most such patients a tunnelled central catheter or port will be used. Specialist domiciliary nursing is essential to coordinate safe, complication-free progress if the patient is unable to undertake line care and administration of the feed independently. Routine community nursing services are not normally able to undertake this responsibility.

When to stop parenteral nutrition

The need for continuing parenteral nutrition should be regularly reviewed. It will depend on the persistence or resolution of the underlying indication, whether it is possible and safe to reinstitute enteral feeding, and whether enteral nutrition is likely to prove adequate in the long term. Furthermore, even if a patient may be successfully converted to enteral nutrition, he/she may still require long-term intravenous fluid or electrolyte replacement. The transition from parenteral nutrition should therefore be conducted at a calculated pace. Central venous catheters should not be removed prematurely, and parenteral nutrition should not be completely weaned until it is clear that the patient can maintain at least 50% of his/her required nutritional intake through other routes (greater if the need has been long term) (National Institute for Clinical Excellence, 2006).

Some patients develop recurrent complications or fail parenteral nutrition. In these cases, intestinal transplant may be the only remaining viable option to achieve adequate nutrition (Bines, 2009).

Complications of parenteral nutrition

The decision to initiate parenteral nutrition is tempered by the numerous complications that may ensue. These include:

Venous catheter infection

This is almost certainly the most common complication associated with parenteral nutrition (Forbes, 2007; Pittiruti et al, 2009). Septic complications can range from mild infections, which can be treated by antibiotics with or without catheter exchange, to those with recurrent and life-threatening line sepsis from multi-resistant bacterial septicaemia or fungaemia. These latter are considered indications for subsequent intestinal transplantation in those who remain dependent on parenteral nutrition.

Venous thrombosis

As vascular access becomes progressively compromised, long-term parenteral nutrition becomes increasingly difficult to maintain. This is also an independent indication for intestinal transplantation. In patients at high risk of venous thrombosis, prophylaxis with daily subcutaneous low molecular weight heparin is necessary (Pittiruti et al, 2009).

Catheter insertion-related complications

Pneumothoraces and even cardiac tamponade can occur with central catheter insertion, hence ultrasound-guided insertion is recommended where possible (Pittiruti et al, 2009).

Liver disease

Clinically significant liver disease develops in 40–60% of infants and 5% of adults on long-term parenteral nutrition (Kelly, 2006), and up to 50% may have asymptomatic deranged serum liver enzymes. The clinical spectrum of liver disease can range from hepatic steatosis and cholestasis, through to hepatic fibrosis and even cirrhosis. Progression to cirrhosis and the development of portal hypertension and liver failure is more common in infants and neonates than in adults. In infants the pathogenesis is closely related to prematurity, low birth weight, duration of parenteral nutrition, short bowel syndrome requiring multiple laparotomies, and recurrent sepsis.

In adults, predisposing factors are age, total caloric intake, length of time on parenteral nutrition, and lipid or glucose overload. Soya-based lipid emulsions are particularly implicated, and patients should not receive more than 3000 kcal lipid/week for long periods. Liver dysfunction early (<4 weeks) after starting parenteral nutrition usually has another cause. There are no evidence-based guidelines on the frequency of monitoring of liver function tests and imaging in those patients with liver dysfunction, although clinicians should be aware of its potentially progressive nature and reversibility in early stages (Lloyd and Gabe, 2007). It is the authors' practice to perform liver function tests weekly in the early phases of establishment on parenteral nutrition but it is rarely necessary more than every 3 months in those on home parenteral nutrition.

Aberrant glycaemic control

Both hyperglycaemia and hypoglycaemia can occur in response to parenteral nutrition. Hyperglycaemic events are associated with increased cardiovascular and septic morbidity, and all-cause mortality (Cheung et al, 2005). This can almost always be avoided by the use of insulin.

Continued or exacerbated fluid, electrolyte and nutritional disturbance

There may be a multitude of reasons why these occur. Additional intravenous fluids and electrolytes may be needed in certain cases, particularly during the risk period for refeeding syndrome.

Metabolic bone disease

Osteoporosis and osteomalacia are potential complications of long-term parenteral nutrition use, in addition to associated risks with primary diseases that may have necessitated nutritional support (such as

Crohn's disease or short bowel syndrome). Guidelines recommend baseline dual energy X-ray absorptiometry scanning and weekly assessments of serum calcium and phosphate levels in such patients (Seidner, 2002).

Psychological

Patients may experience acute grief and loss reactions to surgery and bowel resection, lifestyle restrictions imposed by parenteral nutrition regimens, and altered body image. Depression is common (up to 80% of patients) but deliberate self-harm rare, although this must be considered in patients with recurrent central line infections (Stern et al, 2008).

Conclusions

Parenteral nutrition is indicated to prevent or correct malnutrition in patients unable to achieve sufficient intake via the enteral route. Although it is best managed in conjunction with a specialist nutrition support team, junior doctors will frequently be required to make referrals for its institution, monitor its administration and detect complications. An understanding of the potential hazards will allow appropriate monitoring and a proactive approach should any of these arise (*Table 4*). BJHM

Conflict of interest: none.

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Table 4. 'Do's and don'ts' for the junior doctor managing a patient on parenteral nutrition

Do:	Ask for help. Patients requiring parenteral nutrition are complex and best managed in conjunction with a specialist nutrition support team. If this service is not available, each trust will have a consultant responsible for supervising and providing support for such patients
	Make a clear assessment of whether parenteral nutrition is indicated before exposing your patient to potential risks and complications associated with its use
	Be aware of the patient who is at high risk of refeeding syndrome. Give vitamins and monitor for this proactively, and respond quickly to acute metabolic disturbances
	Maintain strict vigilance over the handling of central venous catheters
Don't:	Routinely bleed your parenteral nutrition patient every day. Although regular blood tests are necessary initially, once a patient is stable on a customised regimen this is not required. Minor fluctuations in electrolytes occur but are often of limited significance. It is the authors' practice to check twice weekly
	Ignore fluid balance. This is crucial to determining the correct regimen for your patient. When possible get daily weights as these will compensate for inaccuracies in the fluid balance charts
	Use the albumin level or weight gain as isolated nutritional measurements in patients on parenteral nutrition. Weight gain on initiation of parenteral nutrition does not indicate improvement in clinical status, but usually reflects over-prescription of sodium and/or water. Albumin is an acute phase protein and therefore does not accurately reflect nutritional status
	Use parenteral nutrition as an 'easy option'. If the gut works, use it!

KEY POINTS

- Carefully assess the risk:benefit of starting parenteral nutrition. Use the enteral route where possible.
- Monitor closely for complications and respond quickly should these arise.
- Seek support from the responsible specialist, but actively engage in the decision-making processes.