6.5 Parenteral nutrition

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Key points

- Parenteral nutrition (PN) should only be used when the enteral route is inaccessible or inadequate.
- PN can be given peripherally or centrally, depending on the predicted duration, availability of venous access and nutritional requirements.
- Electrolytes and micronutrients must be included to meet individual nutritional requirements.
- Detailed pre-feeding assessment and close monitoring for metabolic, infectious or mechanical complications is essential.
- Nutrition teams have an important role in ensuring quality control around the initiation, supply, monitoring and auditing of PN practice and outcomes.

Parenteral nutrition (PN) encompasses the delivery of all nutrients, electrolytes and fluid directly into a central or peripheral vein. It provides nutritional support when the gastrointestinal tract is deemed unsafe or inaccessible, or if absorption via enteral or oral feeding is inadequate to meet full nutritional requirements (NICE, 2006). Although PN is an essential and potentially life-saving therapy, it is expensive and may be associated with a high risk of serious and, occasionally, life-threatening complications, including line infections, micronutrient deficits, electrolyte disturbances, liver dysfunction, hyperglycaemia, hyperlipidaemia and cardiac failure (Austin & Stroud, 2007). Many of the complications associated with PN, highlighted in early research, may have been due to inappropriate use, inadequate line care, unbalanced formulations and significant overfeeding (Koretz *et al.*, 2001). To reduce complications, it is vital that PN be administered appropriately and monitored closely.

The British Association for Parenteral and Enteral Nutrition (BAPEN) and NICE have repeatedly recommended that patients on PN be managed by multidisciplinary nutrition support teams (NSTs) with appropriate expertise. Such teams have been shown to improve patient outcomes (Hvas *et al.*, 2014) and deliver cost savings (Kennedy & Nightingale, 2005). Despite this, a National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report in 2010 indicated that only 60% of UK hospitals had established nutrition teams. Metabolic complications were reported in 40% of patients. NCEPOD also noted unnecessary delays in recognising the need for and instituting PN, deficiencies in assessment and monitoring, inappropriate fluid administration and poor documentation of nutritional issues. They recommended that all hospitals have PN proformas to ensure a robust assessment, including indications, treatment goals, risk and precautions taken against refeeding syndrome and clinical monitoring. In addition, they recommended dedicated catheter insertion services, better education for clinical staff and that PN should not usually be started outside normal working hours.

Indications

Clinical indications

PN should only be used when nutritional needs cannot be fully met by the oral/enteral routes. Assessment of gastrointestinal function is required, ideally undertaken by an NST. Advances in enteral nutrition (EN) delivery techniques, particularly the use of post-pyloric feeding tubes, have reduced the need to give PN, e.g. surgical jejunostomy feeding after upper gastrointestinal tract surgery (Wheble *et al.*, 2012), and EN is now used in clinical conditions for which PN was previously favoured, e.g. acute pancreatitis (Tenner *et al.*, 2013). Indications for short–medium-term PN (<14–28 days) include:

- Major gastrointestinal surgery – where there is no suitable EN access or it is contraindicated, e.g. intra-abdominal sepsis or perforation.

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- Enterocutaneous fistulae – where position, volume or sepsis prevent enteral feeding.
- Gastrointestinal obstruction – where enteral access is not possible.
- Prolonged postoperative ileus.
- Severe malabsorption.
- Severe mucositis following chemotherapy.
- Multiorgan failure causing impaired tolerance to full enteral feeding.

Intestinal failure (IF) is often short term and self-limiting (see Chapter 7.4.9, Intestinal failure and intestinal resection), but more prolonged IF may result in patients remaining PN dependent for months or even permanently (Bozzetti *et al.*, 2014). This may occur in:

- Short bowel syndrome – resulting from Crohn's disease, intestinal ischaemia, surgical complications.
- Motility disorders.
- Chronic malabsorption.
- Radiation enteritis.

Nutritional indications

PN should be considered in those who are malnourished (body mass index, or BMI <18.5 kg/m^2, or >10% unintentional recent weight loss, or BMI <20 kg/m^2 and >5% unintentional recent weight loss) or are at risk of becoming so and who fit the clinical indications (NICE, 2006). It is not generally indicated in previously well-nourished patients (BMI >20 kg/m^2 and <5% recent weight loss) exposed to short periods (up to 5 days) of inadequate nutrition.

Ethical considerations

PN may not be appropriate if it prolongs survival without an improved quality of life, e.g. metastatic bowel obstruction due to advanced disease. ESPEN recommends that long-term PN be offered in those with IF due to incurable disease; if EN is insufficient, the expected survival due to tumour progression is longer than 2–3 months, and it is expected that PN can stabilise or improve performance status and quality of life (Bozzetti *et al.*, 2009). The ethical aspects of feeding should be considered before treatment is commenced, and reviewed on a regular basis (Shang *et al.*, 2006).

Treatment goals

A thorough assessment should consider goals of therapy from the outset. The overall aim should be that gastrointestinal function would recover to facilitate adequate oral/enteral feeding, although a prolonged period of PN may be required for gastrointestinal adaptation or if further surgery is required to restore gut integrity and function.

Nutrition assessment

Prior to initiating PN, a detailed nutritional assessment should be undertaken, including lean and fat mass, baseline biochemistry and hydration status, and refeeding risk (based on period of starvation, BMI, percentage weight loss and electrolyte levels) (NICE, 2006). See Table 6.5.1 for more details on the baseline assessment.

Table 6.5.1 Baseline assessment of a patient requiring parenteral nutrition

Parameter	Rationale
Indication for PN	To ensure appropriateness of treatment and why EN is not appropriate.
Goal and expected duration of treatment	Determined by considering the overall clinical picture and patient prognosis.
Access route for administration	To ensure PN is given via an appropriate route to establish whether central/peripheral PN will best meet requirements, and to reduce the risk of complications.
Nutritional assessment, i.e. weight, percentage weight loss, body mass index, anthropometry	Assessment of nutritional status, fluid balance and refeeding risk.
Previous nutritional intake	To predict the risk of refeeding syndrome when PN begins.
Clinical status – appearance, blood pressure, temperature	General condition, fluid balance, presence of infection (will affect requirements).
Drug therapy	Fluid/electrolyte content of concurrent treatment, e.g. IV fluids/medications; whether the patient is on appropriate medication to promote gut function.
Hydration status (fluid balance charts)	Fluid balance, additional gastrointestinal losses to be replaced, e.g. vomit, fistula, drain output.
Urea and creatinine	Fluid balance, renal function.
Electrolytes – sodium, potassium, calcium, phosphate, magnesium	Fluid balance, electrolyte status, refeeding risk.
Full blood count and C-reactive protein	Presence of infection and anaemia.
Albumin	Used in combination with inflammatory markers to assess catabolic state.
Coagulation parameters	Before insertion of line.

Routes of administration

PN may be administered via a central or peripheral vein, according to the condition and availability of vascular supply, nutritional requirements and anticipated PN duration.

Peripheral access routes

Peripheral catheters, normally sited in a superficial vein in the hand or forearm, may be suitable for short-term peripheral parenteral nutrition (PPN) of less than 14 days. PPN can be given via either:

- A cannula (venflon), where the smallest gauge possible should be used to allow dilution of the PN solution in the vein.
- Midline catheter, extending 10–15 cm from the insertion point at the antecubital fossa (elbow) in either the basilic or cephalic vein (Figure 6.5.1).

PPN avoids the clinical risks and costs of central venous catheters (Pittiruti *et al.*, 2009), but patients must have good peripheral venous access. Thrombophlebitis is a common problem that may be minimised by rotating the insertion site (in the case of a venflona) and by avoiding high-osmolality PN regimens (Anderson *et al.*, 2003). Specifically designed PPN solutions are available, but there are limits to the electrolyte additions that can be made, particularly potassium; PPN is therefore not suitable for patients with high requirements or those requiring a fluid restriction.

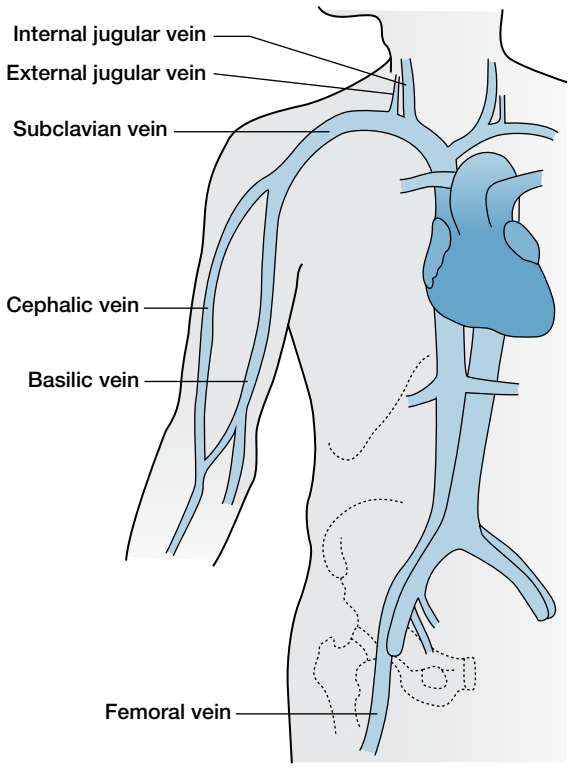

Figure 6.5.1 Access routes for parenteral nutrition (source: Dougherty & Lamb (2008); figure 10.1, p. 263. Reproduced with permission from Blackwell Publishing)

Central Access Routes

Central venous catheters (CVCs) may be placed in the jugular (neck), subclavian (chest) or femoral (groin) veins (see Figure 6.5.1). Jugular lines are easy to access but can be difficult to secure and uncomfortable. Femoral veins may increase the risk of infection due to the proximity of urine, stoma or fistulae. Guidelines for CVC management encompass insertion and subsequent care (Loveday *et al.*, 2014; Pittiruti *et al.*, 2009). Confirmation of the correct placement, tip position and the absence of insertion-related complications should be ascertained before feeding is commenced. A variety of CVCs are available for PN:

- Short-term single or multi-lumen, non-tunnelled catheters. Multi-lumen catheters may contain two to five separate lumens, where one lumen should be dedicated solely for PN use.
- Single- or multi-lumen tunnelled lines where the skin entry point is away from entry into the vein.
- Peripherally inserted central catheters (PICCs), normally inserted at the elbow (antecubital fossa), with the end advanced into a central vein.
- Implantable devices (ports); the port, attached to a catheter, sits under the skin and is accessed by piercing the skin with a needle.

A CVC should be used with the minimum number of lumens essential for the management of the patient (Loveday *et al.*, 2014). PICC are recommended for short–medium-term use, however, they can limit arm movement and can be prone to occlusion or kinking (Cowl *et al.*, 2000). For long-term feeding, a tunnelled CVC or implantable port are recommended (Pittiruti *et al.*, 2009).

Administration

To reduce infection, PN bags should only be administered by healthcare professionals, patients or carers who are assessed as competent and adhere to policies that prevent catheter-related blood stream infections (Loveday *et al.*, 2014). Most PN is administered continuously over 24 hours, but cyclical infusion may have physiological and psychological advantages, can reduce thrombophlebitis in PPN and is recommended by bodies such as NICE (2006) once the patient is biochemically stable.

Formulations

PN regimens should be formulated after the assessment of individual patient requirements. Although this usually involves a dietitian, only doctors could prescribe PN bags until recently. However, in 2016, dietitians achieved supplementary prescribing status, thereby facilitating greater autonomy. It is anticipated that this will lead to more efficient and cost-effective inpatient and home PN (HPN) patient management, and that it will contribute to improved clinical outcomes.

Various PN regimens are available, and local decision-making will depend on pharmacy compounding facilities, contractual arrangements and the need for specialist

feeds to suit specific patient populations, e.g. renal. The main forms of PN regimen are:

- Ready-made, multi-chamber, all in one (AIO) bags, containing carbohydrate, amino acids and fat sources in separate chambers, with or without electrolytes, to be mixed just before use. These have a long shelf life before they are mixed, but do not contain micronutrients and are not recommended unless vitamins and trace elements are added (NICE, 2006). Depending on pharmacy compounding facilities, it may be possible to make additional electrolyte additions if required.
- Tailored bespoke bags are made specifically to an individual's requirements but require adequately resourced aseptic unit facilities.

Stability is affected by the volume, proportion and formulation of different constituents. Therefore, the final volume or electrolyte content may not achieve estimated requirements, and all formulation requests should be discussed with the pharmacist. Bags with all additions should be made under full pharmacy aseptic conditions, with no subsequent tampering that might increase infection risk or compromise stability. A range of multi-chamber bags should be stocked (to suit low and high electrolyte requirements), with bespoke bags available for those patients with specific needs not met by the AIO range.

Constituents

Macronutrients

Energy and protein requirements should be estimated by standard methods (Chapter 6.1, Nutritional requirements in clinical practice). In AIO regimens, the amount and percentage of macronutrients is fixed, whereas tailored regimens offer flexibility to modify the proportions of fat, carbohydrates and amino acids, and may hence be indicated in specific circumstances, e.g. reduced fat content required to minimise hepatobiliary complications in long-term PN.

Protein

Protein is supplied as a balanced mixture of crystalline amino acids, or dipeptides for the less soluble heat-labile amino acids. The optimal PN amino acid profile remains unclear. Standard AIO formulations provide 5–18 g nitrogen. It may be possible to exceed this amount in tailored regimens, depending on stability limits. Glutamine is not present in most commercially available amino acid solutions due to its instability. However, it can be added to a PN bag with other additions prior to administration.

Fat

PN lipid emulsions offer an energy-dense isotonic alternative to dextrose and normally provide <50% of non-nitrogen energy needs. Typical PN regimens provide 400–1000 kcal/day. The first commercially available solutions contained long-chain triglycerides (LCTs) from soya bean oils, rich in n-6 polyunsaturated fatty acids (PUFA). Lipid emulsions contain essential fatty acids (EFA) which maintain cell membrane integrity and immune function. In long-term totally-PN-fed patients, it is recommended that a minimal supply of 1 g/kg/week be given to prevent EFA deficiency (Pironi *et al.*, 2016). The high n-6 content of soya bean lipid may have adverse effects on immune function, particularly in critically ill patients (Furukawa *et al.*, 1999), and excessive amounts have been implicated in hypertriglyceridaemia and hepatobiliary disease. To prevent intestinal-failure-related liver disease in long-term PN-fed patients, soya bean lipid amounts should be less than 1 g/kg/day (Pironi *et al.*, 2016). Newer formulations contain mixtures of lipid sources in various combinations, e.g. monounsaturated from olive oil, medium-chain triglycerides (MCTs) from coconut oil and n-3 PUFA from fish oil. These have been shown to offer clinical benefits over soya-bean-oil-based solutions. However, studies are based on small numbers in diverse clinical situations, and the optimal lipid profile for different conditions remains unclear (Calder *et al.*, 2015).

Carbohydrate

Glucose is available in concentrations of 5–70%, and typical PN regimens provide 400–1200 kcal/day. To avoid excessive amounts, a maximum glucose oxidation rate (GOR) of 4–7 mg/kg/min has been suggested (Burke *et al.*, 1979). If a balance of both lipid and carbohydrate is given, this should not be exceeded.

Electrolytes

The electrolyte content of PN should be based on individual patient requirements, including additional amounts to cover losses (fistula, vomit, refeeding risk) or reductions (renal impairment, fluid overload). Recommendations for electrolyte requirements given intravenously differ from oral and enteral routes. When determining PN electrolyte content, it is important to consider the contribution from intravenous infusions and medications and to discuss with the medical team whether these will continue once PN starts.

Electrolyte additions should be modified according to serum trends rather than single levels (see Table 6.5.2). If PN electrolyte additions cannot meet requirements, supplementary electrolytes may need to be infused separately.

Micronutrients

Vitamins and trace elements should always be included in PN prescriptions. They are normally provided by standard vitamin and trace element solutions devised for PN. However, these may be inadequate to replete body stores, and, in severe malnutrition or metabolic stress, additional amounts may be needed. As intravenous administration bypasses the normal process of selective absorption and liver processing, this may increase the risk of overdosage of some micronutrients (Buchman *et al.*, 2009). There should be local policies in place regarding the measurement and interpretation of micronutrient results, recommended frequency of testing and appropriate supplementation, as PN additions (if possible) or separately.

Table 6.5.2 Adjustments of parenteral nutrition formulations in response to monitoring

Electrolyte	Standard requirement[a] (not considering replacement of additional losses)	Usual level of adjustment[b]	Changes unlikely to be clinically significant[b]
Sodium	1.0–1.5 mmol/kg	Multiples of 40 mmol/day	±10–20 mmol
Potassium	1.0–1.5 mmol/kg	Multiples of 20 mmol/day	±5–10 mmol
Magnesium	0.1–0.2 mmol/kg	5–10 mmol/day	0–5 mmol
Calcium	0.1–0.15 mmol/kg	2.5–5 mmol/day	0–2.5 mmol
Phosphate	0.3–0.5 mmol/kg	10 mmol/day	0–5 mmol

[a] Elia (1990);
[b] Austin and Stroud (2007).

Fluid

Individual fluid requirements should be calculated in the usual way (see Chapter 6.6, Fluids and electrolytes). PN regimens commonly provide 2000–3500 mL/day. Lower and higher volumes are available, but stability issues may affect macronutrient and electrolyte contents. PN volume should always be recorded and considered when determining IV fluid requirements to prevent excess fluid delivery and clinical overload, a significant problem noted by NCEPOD (2010). Consideration should also be given to the sodium content of the fluid used (Powell-Tuck *et al.*, 2011).

Initiating Parenteral Nutrition

It is recommended that initial PN regimens aim for approximately 50% of energy requirements, unless the patient is considered to be at risk of re-feeding syndrome. In those assessed as high risk, lower initial energy intakes of 5–10 kcal/kg/day are recommended (NICE, 2006), although it may be more appropriate physiologically to restrict carbohydrate rather than total energy provision. To minimise refeeding problems, it is also vital that electrolytes and micronutrients are administered from the outset of feeding, and that serum electrolytes are monitored and proactively supplemented. As thiamin requirements are increased to support carbohydrate metabolism in the refeeding phase, additional IV B vitamin supplementation is required immediately prior to PN administration and for the first 3–10 days (depending on refeeding risk).

Monitoring

Monitoring of clinical state, nutritional requirements, anthropometry, biochemistry and line integrity is essential. Daily biochemical monitoring should generally be undertaken for the first 3 days and until levels normalise. The range and frequency of monitoring will then depend on the nature and severity of illness, degree of malnutrition and length of time on PN. Cardiac monitoring is recommended for any patients at extremely high risk of refeeding syndrome and those with pre-existing cardiac arrhythmias (Austin & Stroud, 2007).

Complications

Metabolic complications

Adaptive reductions in cellular activity and organ function in starvation are accompanied by intracellular micronutrient, mineral and electrolyte losses (Stanga *et al.*, 2008). Upon re-feeding, the greater the carbohydrate load (with associated insulin response), the more significant the cellular re-uptake and falls in serum electrolytes. Retention of sodium and fluid, hypokalaemia, hypophosphataemia and hypomagnesaemia (due to rapid intracellular uptake of potassium, phosphate and magnesium for cellular recovery and metabolic activity) may then ensue. Thiamin depletion due to increased metabolic activity and glucose and lipid metabolic abnormalities may also occur. These complications may lead to oedema, cardiac overload and failure, respiratory problems, liver function abnormalities, gastro-intestinal problems and potentially death (Crook, 2001; Stanga *et al.*, 2008; Tomlin *et al.*, 2007).

Refeeding problems may present a greater risk in PN as it bypasses the enteral route, which limits the tolerance and absorption of nutrients. NCEPOD (2010) reported a PN metabolic complication rate of 39%, with hypophosphataemia being the most commonly recorded problem. The relative incidence of refeeding syndrome in PN, rather than oral or enterally fed patients, is not known, but it has been reported that hypophosphataemia is less common in high-risk PN-fed patients than in those on nasogastric feeds (Zeki *et al.*, 2011). Table 6.5.3 provides details of potential metabolic complications, possible causes and risk reduction guidance.

Mechanical complications

Insertion-related complications include insertion failure, pneumothorax or haemothorax, thrombosis, cardiac arrhythmias and nerve injury (Bowling, 2004). Longer-term complications include thrombus, catheter-occlusion or fracture.

Infectious complications

CVC-related infections may originate from endogenous skin flora (most common), contamination of the catheter

Table 6.5.3 Potential metabolic complications of parenteral nutrition

Complication	Possible causes	Prevention
Over-hydration, oedema	Provision of excessive or inappropriate fluid/sodium.	Detailed assessment of patient needs, including losses. Consider other concurrent sources of fluid prior to deciding on PN volume.
Hyperglycaemia	Excessive provision of glucose. Severe metabolic stress. Inappropriate insulin treatment.	Glucose oxidation rate should not be exceeded. Blood glucose should be regularly monitored. Insulin should be provided if required.
Electrolyte abnormalities, including refeeding syndrome	Inadequate electrolytes or excessive glucose, especially initially.	Detailed assessment and monitoring. Proactive supplementation according to local guidance and clinical advice.
Deranged liver function tests	Common in patients given PN, but feed is rarely the main cause (Culkin & Gabe, 2010).	Exclude sepsis, medication, underlying liver disease. Review total energy to avoid overfeeding. Consider type of fat given. Consider cyclical feeding.
Hypertriglyceridaemia	Metabolic capacity of the liver to clear fat is exceeded.	Avoid excessive lipid provision Monitor Reduce or occasionally remove lipid from PN (Llop *et al.*, 2003).

hub or contamination of the CVC from a distant site. Catheter-related sepsis is a serious concern and requires immediate treatment according to local policies. It can be prevented by strict adherence to aseptic techniques, only experienced staff being permitted to handle PN lines, using closed systems, and using dedicated lines where possible (Loveday *et al.*, 2014).

Weaning from parenteral nutrition

PN should never be stopped abruptly as rebound hypoglycaemia can occur. As IF resolves, oral or enteral nutrition should be reintroduced, accompanied by a reduction in PN infusion rate, avoiding fluid overload, overfeeding and electrolyte imbalances. This can be achieved by slowing the infusion rate or by compounding a series of individually modified bags. Supplementary PN should not impair appetite (Reifen *et al.*, 1999), although many PN patients express early satiety and may be anxious about increasing oral intake, particularly after a prolonged period of gut rest, and may need appropriate support and advice.

Home parenteral nutrition

Home parenteral nutrition (HPN) is indicated in permanent IF, or if a prolonged period of PN is required prior to further surgery to restore gastrointestinal function. Patients should be referred to specialist centres with experience in managing longer-term considerations such as hepatobiliary, metabolic and nutritional complications (e.g. micronutrient status), venous access issues and management of the underlying IF (Nightingale, 2003).

Regimens may differ significantly from inpatient regimens in terms of their composition and frequency, based on variable nutritional needs and activity levels. Infusions are commonly administered overnight to allow increased mobility during the day. To avoid hepatobiliary complications, total energy or lipid content may be reduced, and some fat-free bags may be indicated. Provided that fluid balance is maintained, some patients may not require daily feeds.

Further reading

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Internet resources

British Association for Parenteral & Enteral Nutrition (BAPEN), www.bapen.org.uk

National Confidential Enquiry into Patient Outcome and Death, www.ncepod.org.uk

Parenteral and Enteral Nutrition Group (PENG) of the British Dietetic Association, www.peng.org.uk

Patients on Intravenous & Nasogastric Nutrition Therapy (PINNT), www.pinnt.com

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