Learning objectives:

- To identify indications for administration of parenteral nutrition;
- To appreciate the role of parenteral nutrition in different clinical situations;
- To know basic facts about intestinal failure and HPN;
- To be aware of contraindications to parenteral nutrition.

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Key Messages:

- Parenteral nutrition is indicated when nutritional support is required but needs cannot be met by enteral route for any reason;
- The indications for TPN depend partly on the availability of local knowledge and an expert nutrition team;
- Consultation with an experienced multidisciplinary nutritional-support team may reduce complications and may decrease inappropriate use of parenteral feeding method;
- There is a limited number of conditions e.g. Crohn's disease, GVHD, radiation enteritis, where parenteral nutrition can be used as a temporary route of nutritional support in order to provide a period of bowel rest while the underlying problem improves.
1. Introduction

The indications for nutritional support, comparison of parenteral and enteral nutrition in clinical practice, have been subject of many original studies, systematic reviews (1, 3, 7, 8, 9, 12, 13, 15), meta-analyses (4, 6, 10, 14, 16, 17), and guidelines from scientific societies (2, 5, 11, 18, 19, 20, 21, 22).

This text will focus mainly on evidence-based recommendations matching each type of patient management to results derived from a comparable group of patients. In the absence of clear evidence from randomised controlled studies, as a “not feeding” or starved control group would be ethically unacceptable, decisions may have to be made from clinical experience and from an understanding of the underlying pathophysiology. Because long-term starvation is associated with a high morbidity and inevitable death after 2-3 months even in previously healthy individuals, it could be construed as negligent to fail to provide artificial nutrition in such a situation.

The aim of parenteral nutrition (PN) is to administer the essential nutrients by the intravenous route to treat or to prevent malnutrition when oral or enteral nutrition is not possible – total parenteral nutrition or TPN, or is insufficient for complete nutrition – partial parenteral nutrition or PPN.

2. Indications for PN

Parenteral nutrition is indicated when:
- it is not possible to administer enteral nutrition because the gut is not functioning (e.g., perforation, obstruction, ileus or inadequate absorptive or propulsive capacity)
- the gut is not accessible (e.g., for anatomical reasons)
- tube feeding is not safe (e.g. ischaemic bowel disease) or unlikely to be effective (e.g. in patients with intractable vomiting)

2.1. PN in different clinical situations

A general recommendation is that when gastrointestinal dysfunction prevents nutritional needs being met by the oral or enteral route, the parenteral route should be used. Table 1 summarises some special conditions and situations when parenteral nutrition should be considered and this is discussed in detail in other chapters.

Table 1. Parenteral nutrition in different clinical situations

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Inflammatory bowel disease</td>
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<tr>
<td>Perioperative period</td>
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<tr>
<td>Short bowel syndrome</td>
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<tr>
<td>Critical illness</td>
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<tr>
<td>Acute renal failure</td>
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<td>Peritoneal dialysis</td>
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<tr>
<td>Haemodialysis/chronic ambulatory peritoneal dialysis (HD/CAPD)</td>
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<td>Acute liver failure</td>
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<td>Liver cirrhosis</td>
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<td>Chronic obstructive pulmonary disease (COPD)</td>
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<td>Chronic heart failure</td>
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<td>Acute pancreatitis</td>
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2.2. PN versus EN in ICU patients

The goals of nutritional support in ICU patients are:
- minimizing negative energy and protein balance and muscle loss by avoiding starvation
- maintaining tissue function, particularly of the liver, the immune system and skeletal and respiratory muscle
- improvement of the subsequent post ICU period of recovery
- modifying metabolic changes and function by using special substrates that have been shown to be beneficial

Enteral feeding is preferred to maintain immune barrier and absorptive function. Several studies have shown a better outcome when at least part of the patient’s requirement is met by the enteral route. The sooner enteral nutrition is started, the shorter the ICU stay and the better the outcome. However, this was clear only in patients who were not severely ill but required long-term parenteral nutrition to compensate for gastrointestinal dysfunction. It has not been definitively confirmed in severely ill patients, who are at risk of multiple organ failure.

The main problems of enteral nutrition in severely ill patients are: inability to cover all nutritional requirements, possible intestinal ischaemia due to decreased blood flow to proximal part of the bowel because of increased requirements, increased reflux, vomiting and aspiration.

In ICU patients starvation or underfeeding is associated with increased morbidity and mortality. Since PN does not increase mortality in comparison with EN, according to the ESPEN guidelines, all patients who are not expected to be on normal nutrition within 3 days should receive PN within 24 to 48 hours if EN is contraindicated or if they cannot tolerate EN. Patients who have enteral intake less than targeted for more than 2 days should be considered for supplementary parenteral nutrition. However a recent study showed that withholding parenteral nutrition until day 8 was associated with faster recovery and fewer complications, as compared with early initiation. (30)

In the case of prolonged gastrointestinal dysfunction parenteral nutrition should be given until enteral function returns. Supplemental parenteral nutrition could also prevent onset of other nutritional deficiencies when enteral nutrition is insufficient to meet energy requirements.
2.3. PN as replacement therapy in intestinal failure

TPN is capable of maintaining life in the patient with intestinal failure for as long as needed, unless the underlying disease is progressive and fatal. It may provide a reasonable quality of life even when the prognosis is only a few months. Crohn's disease, vascular disease leading to small bowel infarction, surgical complications, radiation enteritis, GVHD, some malignant diseases of GI tract, and chronic small bowel disease from several absorption and dysmotility syndromes, are the most common underlying diseases of intestinal failure.

Short bowel syndrome represents the major "benign" indication for PN, while in some countries (sub)-obstruction due to peritoneal carcinomatosis is a frequent "malignant" indication. The role of PN in short bowel syndrome is maintenance and/or improvement of nutritional status, correction of water and electrolyte balance, and improvement in quality of life. Long-term TPN will be needed in patients with very short small bowel. Most of these patients have small bowel of less than 100 cm with a jejunostomy, or less than 50 cm with remaining colon in continuity. In patients with longer small bowel, PN is usually needed until oral/enteral intake is adequate to maintain adequate nutritional, water and electrolyte requirements.

PN is indicated in inflammatory bowel disease in patients who are malnourished and in those who are at risk of becoming malnourished and have inadequate oral intake. In Crohn's disease the specific reasons for PN are obstructed gut, and short bowel, often with a high intestinal output or an enterocutaneous fistula. In ulcerative colitis PN does not have a primary role in treatment of the underlying disease.

The evidence for the efficiency of PN as replacement therapy in GI failure relies on historical comparisons. PN for GI failure cannot be validated through RCTs because the only alternative to PN is allowing the patient to starve to death. It is therefore ethically unacceptable to have a "non-fed" control group.

2.3.1. HPN

The main indications for long-term HPN are short bowel syndrome, high-output fistula, bowel dysmotility and radiation enteropathy. It is very important to emphasise that not all patients who cannot meet their nutritional requirements by enteral intake are good candidates for HPN. Different ethical issues as well as clinical considerations should be taken into account. In order to reduce the number of complications and ensure effective and safe nutritional support, HPN should be provided through a multi-disciplinary nutritional support team with adequate expertise.

According to ESPEN guidelines, stopped oncologic treatment is not a contraindication to HPN, and incurable cancer patients, with a risk of death due to malnutrition, can enter a HPN program (Grade C). PN in cancer patients is justified if it can contribute to the improvement of function and outcome. PN is ineffective and probably harmful in non-aphagic oncological patients in whom there is no gastrointestinal reason for intestinal failure (Grade A). PN is recommended in patients with severe mucositis or severe radiation enteritis. The place of HPN in patients with incurable disease and a short life-expectancy is debatable, but usually not recommended (27).

The major issues in Home Parenteral Nutrition (HPN) for benign conditions are:

- Safety of administration, i.e. avoidance or treatment of mechanical, infectious and thrombotic complications;
- Maintaining nutritional balance of both macro- and micro-nutrients;
- Prevention of bone and liver disease.

The major problems of HPN in malignant diseases are:

- The unpredictability of the life expectancy of the patients from the primary tumour; this makes it difficult to judge the likely benefit or burden to the patient and whether the prognosis from the tumour will allow the patient to derive
significant benefit in terms of longevity and quality of life, bearing in mind that without PN the patient will die from malnutrition in 2-3 months at the most;

- It may be difficult to estimate whether and for how long HPN will maintain an acceptable quality of life. This may involve a trial of treatment for a period of time agreed with the patient and family and withdrawal of PN if it proves to be more of a burden than a benefit.

Both these issues are the subject of continuing clinical investigation.

2.4. Elective PN for bowel rest

In a limited number of conditions e.g. radiation enteritis and other acute bowel problems (GVHD, mucositis) it can be a good option, if not always essential, to rest the bowel temporarily, using PN electively until the underlying problem improves. Acute radiation enteropathy (RE) is difficult to prevent, but frequently reversible and patients should be treated conservatively, with total bowel rest and TPN if necessary; while in chronic RE, PN may have a role if the RE involves large parts of the small bowel or if there is short bowel syndrome due to previous resectional surgery. In severe subacute RE, medium term PN, is indicated and may allow resolution of intestinal obstruction and help to restore oral feeding.

2.5. Comparing different intravenous substrates in parenteral nutrition

The optimal formula for PN feeds in general is the subject of much discussion and research, as are the ideal formulae for different clinical situations (e.g. fat vs. glucose, LCT vs. MCT, N-3 vs. N-6 PUFA, and amino acid substrates; standard admixtures vs. those enriched in BCAA, glutamine, arginine, etc.).

As parenterally fed patients must metabolize or excrete all infused nutrients, the composition of nutritional formulae should be adapted to nutritional requirements, metabolic capacity, metabolic disturbances and coexisting deficiencies or nutrient excess. The end-points of many investigations are often metabolic/nutritional surrogates rather than the more important goal of clinical outcome. Such studies are therefore of limited value in terms of developing guidelines, although they help to increase our understanding of the metabolic processes involved.

A major challenge in clinical nutrition is designing and carrying out further well designed studies with relevant clinical endpoints. In this respect, the diversity of the patient population, the complexity of the underlying clinical problems, and the recruitment of adequate numbers make it difficult, but not impossible for any centre to conduct studies of adequate size to achieve significance. This emphasises the need for multicentre collaborative studies, if the funding can be found for them.

3. Contraindications to parenteral nutrition

PN is not indicated if gastrointestinal tract is fully functional with adequate absorption of macro and micronutrients.

PN is not a treatment of choice when administration of PN is anticipated for less than 5 days in patients without severe malnutrition. Other relative contraindications for PN are inability to obtain venous access, cases when the risks of PN exceed the benefits and in patients with a prognosis that does not justify aggressive nutrition support. Renal and hepatic failure are not absolute contraindications but they both require careful attention regarding the use of amino acids and lipid.
4. Summary

The rationale for providing parenteral nutrition in different pathologies is discussed, emphasising the importance of evidence-based recommendations.

- PN is indicated when nutritional support is required but, for any reason, nutritional requirements cannot be met entirely by the enteral route.
- PN can be used to meet the patient's entire nutritional requirements, or used as a supplement to EN when patients can tolerate some oral feedings but cannot ingest adequate amounts of nutrients to meet their nutritional needs.
- PN, unlike EN, is a very efficient way of administering large volumes of fluid and nutrients. Therefore it is easy to administer excess nutrients and fluid, causing, for example, hyperglycaemia and salt and water overload. This may explain some of the adverse effects of PN reported in the literature and indeed some of the adverse comparisons with EN.
- Inadequate administration of PN can be prevented by the inclusion of multidisciplinary nutrition support team in hospitals.
- Accurately and precisely targeted PN is safe and effective when the right indications are present.
- Patients in ICU should be fed because starvation or underfeeding in those patients is associated with increased morbidity and mortality.
- Intestinal failure is characterized by the inability to maintain protein-energy, fluid, electrolyte or micronutrient balance, which can be improved by PN.
- Home parenteral nutrition support should be used in patients who cannot meet their nutritional requirement by enteral intake, and who are able to receive therapy outside an acute care setting.
- In a few conditions (severe enteritis, radiation enteropathy, high output GI fistulas, etc.), using PN as a means of temporarily resting the bowel may be helpful.

5. References:

2. ASPEN Board of Directors. Guidelines for the use of parenteral and enteral nutrition in adult and paediatric patients. JPEN 2002;26 (Suppl 1).