ESPEN Guidelines on Parenteral Nutrition: Home Parenteral Nutrition (HPN) in adult patients

Michael Staun, Loris Pironi, Federico Bozzetti, Janet Baxter, Alastair Forbes, Francesca Joly, Palle Jeppesen, Jose Moreno, Xavier Hébuterne, Marek Pertkiewicz, Stefan Mühlebach, Alan Shenkin, André Van Gossum

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S U M M A R Y
Home parenteral nutrition (HPN) was introduced as a treatment modality in the early 1970s primarily for the treatment of chronic intestinal failure in patients with benign disease. The relatively low morbidity and mortality associated with HPN has encouraged its widespread use in western countries. Thus there is huge clinical experience, but there are still few controlled clinical studies of treatment effects and management of complications. The purpose of these guidelines is to highlight areas of good practice and promote the use of standardized treatment protocols between centers. The guidelines may serve as a framework for development of policies and procedures.

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1. Indication for home parenteral nutrition (HPN)?

1.1. 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.

Long-term PN is indicated for patients with prolonged gastrointestinal tract failure that prevents the absorption of adequate nutrients to sustain life. As it is a life-saving therapy for patients with irreversible intestinal failure, it does not require evaluation of efficacy by randomized controlled trial. Its ability to maintain quality of life and promote rehabilitation supports the use of home treatment.

Comments: Intestinal failure is defined as a condition with reduced intestinal absorption to the extent that macronutrient and/or water and electrolyte supplements are needed to maintain health and/or growth. Intestinal failure is severe when parenteral...
<table>
<thead>
<tr>
<th>Subject</th>
<th>Recommendations</th>
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<tr>
<td><strong>Indications</strong></td>
<td>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.</td>
<td>B</td>
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<td>Incurable cancer patients may enter a HPN program if they are unable to meet their nutritional requirements by oral or enteral route and there is a risk of death due to malnutrition. HPN is not recommended for patients with incurable disease and a short life-expectancy.</td>
<td>C</td>
<td>1.2</td>
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<tr>
<td><strong>The nutrition support team in HPN</strong></td>
<td>The expertise of a nutrition support team (NST) is recommended for HPN.</td>
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<td><strong>Prescription of HPN</strong></td>
<td>The electrolyte composition of the HPN regimen should reflect fluid losses.</td>
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<td>The total calories should normally be 20–35 kcal/kg per day.</td>
<td>C</td>
<td>3.1.1</td>
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<td>The non-protein energy provision should be 100–150 kcal for every gram of nitrogen in the HPN.</td>
<td>C</td>
<td>3.1.3.1</td>
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<td></td>
<td>The unstressed adult HPN patient will require 0.8–1.0 g amino acids/kg per day.</td>
<td>C</td>
<td>3.1.4.1</td>
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<td>For long-term HPN treatment (&gt; 6 months) the provision of intravenous lipid should not exceed 1 g/kg per day. Essential fatty acids should be supplied.</td>
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<td>3.1.6.1</td>
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<td><strong>Intravenous catheters and devices</strong></td>
<td>Tunneled central catheters are used, as permanent access is required for long-term parenteral nutrition. Implanted ports are an acceptable alternative. PICC-lines are intended for shorter-term use and cannot be recommended for HPN patients. Cyclic administration of parenteral nutrition is recommended.</td>
<td>C</td>
<td>4</td>
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<tr>
<td><strong>Improving prognosis in HPN</strong></td>
<td>The use of infusion pumps is recommended, but is not practiced in all European countries.</td>
<td>B</td>
<td>4.3</td>
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<td>Prognosis in HPN is mainly governed by the underlying disease, but poor outcomes related to the HPN itself come from problems with catheters and the associated vessels. It is important to preserve lines and to protect the vessels as best possible. Reference should be made to the ESPEN guidelines on central venous catheters. In line sepsis in HPN a conservative approach with antibiotics is normally advocated before removing the catheter.</td>
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<tr>
<td><strong>Education and training</strong></td>
<td>There should be a formal teaching program for the patient and/or carer. The teaching program should include catheter care, pump use, and preventing, recognizing and managing complications. Experienced nurses are usually best placed to take responsibility for the teaching program.</td>
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<td>The use of specific brochures or videotapes for teaching, and affiliation with national support organizations, are associated with better outcomes.</td>
<td>C</td>
<td>5.1</td>
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<tr>
<td><strong>Monitoring</strong></td>
<td>Training is usually carried out in an in-patient setting, but training at home can be considered in selected patients. Electrical and anthropometric measurements should be measured at all visits; measurement of trace elements and vitamins are recommended at intervals of 6 months. Bone mineral density assessment by DEXA scanning is recommended at yearly intervals.</td>
<td>C</td>
<td>5.2</td>
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<td><strong>Liver disease in HPN</strong></td>
<td>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.</td>
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</tr>
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<td><strong>Intestinal transplantation in HPN patients</strong></td>
<td>Aluminum contamination of HPN should be less than 25 μg/l.</td>
<td>B</td>
<td>8.1</td>
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<td></td>
<td>The amount of sodium should be no more than required, to avoid sodium induced hypercalcemia. The amount of sodium in HPN should be no more than required, to avoid sodium induced hypercalcemia.</td>
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<td>8.2</td>
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<td>The calcium, magnesium and phosphate content of the HPN should maintain normal serum concentrations and 24-h urinary excretion.</td>
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<td>The recommended intravenous dose of vitamin D is 200 IU/day. Consider vitamin D withdrawal in patients with low bone mineral density (BMD), low serum parathyroid hormone, and 1,25-dihydroxyvitamin D concentrations associated with normal 25-hydroxyvitamin D. Reducing infusion rates may decrease hypercalcemia. Bisphosphonates (such as clodronate 1500 mg iv or pamidronate 20 mg iv every 3 months) may maintain BMD in patients with osteopenia.</td>
<td>C</td>
<td>8.3</td>
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<td>The indication for intestinal transplantation is irreversible, benign, chronic intestinal failure associated with life-threatening complications of HPN. Present data do not support direct referral for intestinal transplantation of patients with high risk of death due to underlying disease, chronic dehydration or significantly impaired quality of life. In all patients an individual case-by-case decision is required.</td>
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<td>The timing of patient referral is key to obtaining best graft and patient survival. Early referral is recommended to minimize mortality from HPN related complications whilst on the waiting list. The highest survival rates are observed among younger individuals, those at home rather than in hospital, and in patients managed in experienced transplant centers. There has been steady improvement in patient and graft survival.</td>
<td>C</td>
<td>11.2</td>
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Incurable cancer patients may enter a HPN program if they are unable to meet their nutritional requirements by oral or enteral route and there is a risk of death due to malnutrition. It is not a contraindication for HPN that oncologic treatment has been stopped.

HPN is not recommended for patients with incurable disease and a short life expectancy. HPN is recommended for patients with malignant obstruction or partial obstruction of the gastrointestinal tract provided that they do not suffer from severe organ dysfunction that may significantly complicate treatment with parenteral nutrition. Patients should have a Karnofsky score of higher than 50 and normally be free from metastasis to the liver or lungs. It is important that symptoms are controlled and that patients are aware of the limitations of the treatment.

Comments: Nutritional support (including HPN as necessary) for cancer patients is generally accepted in relation to malnutrition while the patient is receiving oncologic therapy, or if the patient suffers severe complications following chemotherapy, radiation therapy or surgery. In the incurable patient with cancer the decision to embark on HPN is more a source of debate. While some clinicians will consider that medical care including nutritional support is justified through an increase in length of survival and quality of life, data to support this are often absent. Other caregivers may argue that patients will still die despite nutritional support even if small increments in life-expectancy can be obtained, and that measures such as HPN are inappropriately invasive.17

When considering which patients to include in an HPN program, incurable patients in the final phases of life should normally be excluded. Incurable patients to whom no more (oncologic) treatment will be offered can logically be included in HPN programs provided the clinical problem is under-nutrition or starvation rather than direct progression of the underlying malignant disease and that death is not imminent.18

The incurable cancer patient who is a candidate for HPN will typically have: little or no oral intake due to partial or complete obstruction of the gastrointestinal tract; relatively normal function of other vital organs; no severe, uncontrolled symptoms; and reasonable performance capacity (e.g. Karnofsky–Burchenal index >50). In clinical practice patients characteristically chosen for HPN might be those with peritoneal carcinomatosis, and slow growing tumors such as ovarian carcinoma, retroperitoneal cancers, and some intra-abdominal recurrences.

The crucial issues to consider include:

(i) An estimate of life-expectancy. HPN should not be commenced if it is probable that the patient will succumb from the underlying disease rather than from poor nutritional status. However, the negative impact of low nutritional intake must also be taken into consideration.

(ii) Communication with the patient and his/her family to balance their expectations with realistic outcomes to be expected from HPN.

(iii) Definition of the criteria for withholding and withdrawing the nutritional support if there is no effect.19,20

The survival of cancer patients on HPN depends on the severity of the malignant disease, staging and type. Median survivals in several small series ranged from 53 to 120 days, and is heavily dependent on selection criteria.21 Quality of life studies indicate that HPN benefits a limited proportion of these patients. In patients who survive for more than 3 months there is some evidence that the quality of life remains stable and fairly acceptable.22–24 The early addition of parenteral nutrition to patients with advanced cancer may improve survival and quality of life in some cases.25

Nutritional requirements are similar to those of other patients on HPN other than those with large stomal losses. Some restriction of the intravenous water supply may be appropriate given an expansion of the extra cellular fluid volume caused by cachexia. Combined with sodium (and glucose) a water load can readily precipitate ascites in patients with peritoneal carcinomatosis. Other factors operating in cancer also influence water clearance negatively, and the total amount of fluid and sodium should probably not exceed 30 ml/kg per day and 1 mmol/kg per day, respectively.26,27 Thus in general more energy dense preparations...
with high proportions of energy from fat emulsions may be considered a favorable choice for this patient group. When treatment continues for longer periods fat emulsions providing n-3 fats may be considered through extrapolation from the successful studies of oral supplements of n-3 fatty acids in cachectic cancer patients. All patients on HPN should receive micronutrients.

2. Nutritional support team for HPN

The expertise of a nutrition support team (NST) is recommended for HPN.

The core NST consists of a physician, nutrition nurse specialist, senior dietician and senior clinical pharmacist. The NST will prepare management protocols to facilitate patient education, help to minimize complications, assist cost-containment, and audit the practice.

For long-term treatment, patients and/or carers are trained to manage parenteral nutrition at home. All patients requiring this complex treatment should have coordinated care from an expert nutrition support team (NST). The NST should provide both physical and psychological or emotional support for all patients who are discharged from hospital with home parenteral nutrition (HPN).

NSTs are usually affiliated to a particular discipline – most commonly gastroenterology or surgery or both. The minimum core composition of the team should include a physician (e.g. gastroenterologist, gastrointestinal surgeon, clinical biochemist), a nutrition nurse specialist, a senior dietician and a senior clinical pharmacist.

The tasks of the team should include minimizing the complications of parenteral nutrition by ensuring adherence to management protocols (particularly catheter care) and the management and auditing of complications, including catheter complications (e.g. sepsis and central vein thrombosis) and metabolic complications (such as liver and bone disease and micronutrient imbalance). Where a national registry of HPN patients exists, the team should report to this.

The impact of a nutrition support team in the management of HPN is likely to be significant. Centers with a NST experienced in the management of intestinal failure/HPN are likely to use monitoring protocols, allowing the patient to be independent from hospital with improvement in quality of life. Adequate, careful training allows the patient to become the ‘expert’ patient, thereby reducing the frequency of catheter related complications (especially sepsis) and consequent readmissions to hospital. It is important for the NST to monitor the skills of the patient so that they recognize the symptoms of complications.

Comments: The incidence and prevalence of HPN has steadily increased over past decades. The age of patients being prescribed the treatment is increasing so they are more often dependent on carers. The NST is essential to optimize the effectiveness and safety of the treatment and it is recommended that hospitals that do not have a NST experienced in HPN should not provide this treatment.

As well as the core NST, there should be specialized support from clinical biochemistry and microbiology. When necessary there may be input from the general practitioner, community nurses and home care company nurses.

The NST needs to practice at an evidence-based level and work within a clinical governance framework; performance should be audited. The NST should be in a position to influence the purchasing of the solutions, delivery equipment, catheters and pumps. Other tasks should include:

- provision of a care plan which includes the overall aims of treatment and monitoring;
- preparation of local policies, local/national procedures and guidelines and care plans for the insertion of feeding catheters, care of the catheter including written instructions;
- training of patients/carers to recognize and manage complications ensuring that they have routine and emergency contact telephone numbers;
- maintain effective communication with all clinical teams, including referring teams and primary care;
- monitoring of patients for metabolic complications, nutritional status, quality of life;
- ongoing education of patients and clinical teams;
- contact with insurance companies or other health care institutions in respect of reimbursement arrangements for the therapy;
- bilateral contact with patient organizations.

The general effectiveness of a NST has not been conclusively demonstrated in hospital parenteral nutrition. There is evidence of a reduced incidence of mechanical complications in hospital, but less conclusive support for a reduction in catheter related sepsis and metabolic problems. However, high quality management appears likely to improve or maintain nutritional status, and to reduce morbidity and improve independence, with resultant improved quality of life, fewer complications, and cost-containment.

3. The nutritional requirements in patients on HPN?

Comments: The levels of specific nutrients provided for the adult receiving home parenteral nutrition should be based on a formal nutritional assessment. Nutritional requirements should include disease specific needs and factors to be considered include medical condition, nutritional status, activity level, and fluid restrictions and organ function. Absorption from the GI tract, usually improves with time due to intestinal adaptation.

The prescription is decided prior to the discharge of the patient and then reviewed shortly after discharge to make sure that it is still appropriate. The prescribed regimen should supply the complete nutrient range if required, and should be easily managed at home with regard to the number of nights of the week to be fed and the length of infusion time. Figures for requirements of macronutrients are generally prescribed on the basis of the actual weight of the patient and modified according to weight changes.

3.1. Requirements for nutrients

3.1.1. Fluid

It is important to assess the patient’s fluid status as part of their general assessment when considering parenteral nutrition and fluids. This will help determine the volume that should be provided to the patient on a daily basis. Disturbances of water and electrolytes have a more profound immediate effect on health than nutrients, and imbalances readily result in dehydration or fluid overload. The fluid and electrolyte composition of the HPN regimen should reflect fluid losses and the losses that might result from drug therapy. Table 1 provides estimates of fluid requirements according to different clinical conditions.

3.1.2. Electrolytes

3.1.2.1. The electrolyte composition of the HPN regimen should reflect fluid losses. The standard prescribing ranges for electrolytes assumes normal organ function, without abnormal losses. Additional sodium, potassium and magnesium may be required if serum...
levels are low. Table 2 illustrates the requirements for electrolytes in parenteral feeding.37 For patients on long-term home parenteral nutrition the recommendation is to supply sodium and potassium to meet the needs as governed by the clinical situation, stomal losses, renal function etc. The recommendation for calcium is to supply 10 mmol daily, with 25 mmol phosphate and 10 mmol magnesium for a standard parenteral program. Adjustments may be required depending on the clinical situation.

### 3.1.3. Energy

#### 3.1.3.1. The total calories should normally be 20–35 kcal/kg per day. Determining energy requirements should be on individual patient assessment. Predictive equations such as the Schofield Equation38 to estimate energy requirements in adults may be useful but care should be taken not to provide excess energy. The estimated quantity of total calories to be administered should normally fall in the range 20–35 kcal/kg per day, and rarely more than 40 kcal/kg per day.39 It should be taken into consideration that many HPN patients with benign intestinal failure do feed orally. Moreover intestinal absorption may improve with time. Therefore it is necessary to monitor the balance between oral intake, enteral absorption and intravenous supply, recognizing that the total sum of energy given may be more than required because of the ineffectiveness of non-absorbed nutrients taken enterally. The total expected to reach the circulation is the appropriate target figure to be considered at any time. Nutritional requirements of cancer patients are further considered in the ESPEN guidelines on PN oncology.40

#### 3.1.4. Energy sources

3.1.4.1. The non-protein energy provision should be 100–150 kcal for every gram of nitrogen in the HPN. The unstressed adult HPN patient will require 0.8–1.0 g amino acids/kg per day. Carbohydrates and lipids are used as the energy sources in parenteral nutrition. The non-protein energy provision should normally be in the range 100–150 kcal for every gram of nitrogen in the parenteral nutrition bag. The recommended ratio of glucose to lipid is approximately 70–85% from glucose and 15–30% from lipid in the long-term context of HPN. Contributions from oral intake should be considered and if possible, parenteral requirements provided over five/six nights (or days) rather than seven, to improve quality of life. Even in patients with high fluid losses needing daily water and electrolytes it may be possible to limit nutrient supplies to a smaller number of days per week with the potential advantage that the electrolyte infusion may be shorter in duration. Monitoring the patient’s weight will provide evidence of the need to alter fluid/energy prescription.

### 3.1.5. Carbohydrates

Glucose is the carbohydrate source of choice and in order to avoid acute and long-term complications, it is recommended that glucose should be administered at 3–6 g/kg per day.41

### 3.1.6. Lipids

3.1.6.1. For long-term HPN treatment (>6 months) the provision of intravenous lipid should not exceed 1 g/kg per day. Essential fatty acids should be supplied.

**The daily requirement for essential fatty acids is 7–10 g, which corresponds to 14–20 g LCT fat from soya oil and 30–40 g LCT fat from olive/soya oil.**

MCT/LCT and fish oil emulsions also appear safe and effective.

Almost all patients should be provided with lipid, particulary if there is no oral intake of fat. The available data indicates however that for long-term HPN patients (duration >6 months) the amount of soya-based fat provided should not exceed 1 g/kg per day.41 In a 5 year follow-up of 90 HPN patients44 the authors described chronic cholestasis and liver disease when 20% intravenous lipid was provided at higher doses than 1 g/kg per body weight per day. Prospective clinical studies with alternative fat emulsions in long-term use are still scarce and more data are needed. Lipid emulsion based on olive oil appears to be equally safe as those based on soya oil.45,46 Emulsions with MCT/LCT and with fish oil have also proven safe although data for long-term use in HPN patients is more limited.47,48

Essential fatty acid deficiency will develop in 2–6 months with a completely fat-free intravenous regimen. This can be normalized by providing 1.2–2.4 g soybean oil per kilogram body weight twice weekly. Patients who have existing serological essential fatty acid deficiency may require up to 2.4 g/kg twice weekly to correct it.49 Clinical experience indicates that essential fatty acid deficiency can be prevented with about 500–1000 ml of 20% soya-based lipid emulsions given on a weekly basis.42,43 If patients take some oral diet in the form of fat, essential fatty acid deficiency is rarely a specific problem.

### 3.1.7. Protein

Adequate energy substrate must be provided to optimize protein utilization. The unstressed adult patient with normal organ function will require 0.8–1.0 g/kg per day. However more will be required in the stressed or catabolic patient and may rise to 2.0 g/kg per day. For obese individuals with a BMI of 30–40 kg/m², use approximately 75% of the value estimated from body weight. For those with a BMI of >50 kg/m², use approximately 65% of the value estimated from body weight (Table 3).47

Generally, HPN patients are not catabolic or metabolically stressed. For patients in an anabolic phase the requirement should be individualized.

### 3.1.8. Micronutrients

Vitamins and trace elements act as co-factors and coenzymes involved in metabolism. There is always a need to add trace

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### Table 1

<table>
<thead>
<tr>
<th>Clinical condition</th>
<th>Baseline requirement</th>
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<tr>
<td>Maintenance requirements:</td>
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<tr>
<td>18–60 years</td>
<td>35 ml/kg body weight</td>
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<tr>
<td>&gt;60 years</td>
<td>30 ml/kg body weight</td>
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<tr>
<td>Replacement of ongoing fluid losses:</td>
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<tr>
<td>Fever</td>
<td>Add 2–2.5 ml/kg per day for each 1 °C rise in body temperature above 37 °C per 24-h period of pyrexia</td>
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<tr>
<td>Loss of body fluids</td>
<td>These individuals must be assessed on a daily basis</td>
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### Table 2

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Per kg/day (mmol)</th>
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<tbody>
<tr>
<td>Sodium</td>
<td>1–1.5</td>
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<tr>
<td>Potassium</td>
<td>1–1.5</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.1–0.2</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.1–0.15</td>
</tr>
<tr>
<td>Chloride</td>
<td>1–1.5</td>
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<tr>
<td>Phosphate</td>
<td>0.3–0.5</td>
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### Table 3

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<th>Protein g/kg per day</th>
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<tr>
<td>Maintenance</td>
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elements and vitamins for patients who need long-term parenteral nutrition, particularly in malabsorption states and if no oral diet is taken. The commercial preparations of trace element and vitamins for use in parenteral nutrition generally provide amounts in excess of basal requirements as they are intended also for patients who are either already nutritionally depleted or who have increased losses. Trace elements and vitamins are usually given as standard doses but care should be taken both to provide adequate intakes in patients fed intravenously for less than 7 days per week or with abnormal losses, and not to provide excess in patients with cholestasis or renal failure. The guidelines should therefore be considered as approximation of requirements and monitoring is recommended Table 4.53

4. Tunneled central catheters are used, as permanent access is required for long-term parenteral nutrition

Implanted ports are an acceptable alternative. PICC-lines are intended for shorter-term use and cannot be recommended for HPN patients.

Multi-lumen catheters are not recommended in order to minimize the risk of infection. The routes most commonly used are the subclavian vein or internal jugular vein.

Comments: HPN requires a well functioning central venous line. When considering which is the best type of central venous device a number of issues must be taken into consideration; these include the number of weekly infusions, for how long the therapy is going to continue (temporarily or lifelong), the diagnosis of the underlying disease (benign or not), any previous history in relation to the number of weekly infusions, for how long the therapy is going to continue (temporarily or lifelong), the diagnosis of the underlying disease (benign or not), any previous history in relation to cholestasis or renal failure. The guidelines should therefore be considered as approximation of requirements and monitoring is recommended Table 4.53

4.1. PICC-lines – an option for HPN?

For short-term treatment, mostly for in-patients, a peripherally inserted central catheter (PICC) can be used for intravenous nutrition. PICC-lines have limitations; insertion may be difficult since many patients with a need of parenteral therapy will have damaged peripheral veins and short bowel patients may need infusion of a high volume of parenteral nutrition with a high osmolality thus exceeding the capacity of the line. For in-patients lower rates of infections have been reported with PICC-lines and the cost is definitely lower, compared to conventional central lines or ports.58,59 Based on the available evidence, PICC cannot be recommended for HPN.

4.2. Choice of central vein

There are no data on the best choice of vein for catheters for long-term use. Studies in the intensive care setting have shown that subclavian puncture is associated with a lower frequency of catheter related infections compared to jugular insertion.60 A further advantage of subclavian cannulation relevant to HPN is that the exit site of the tunneled catheter can be placed more readily visible and available to the patient, thus facilitating the necessary self-management of parenteral nutrition and line care. In patients with thrombosis of the superior vena cava catheterization of the femoral vein will be needed, but the risk of mechanical complications and thrombosis are about 10 times the rate for subclavian access.60

4.3. Insertion

Catheter insertion and complications therefore are not specific to HPN. Further details can be found in the ESPEN guidelines on central venous catheters. Central lines of any type can be used for patients with active cancer, but tunneled catheters are recommended. For intermittent therapy an implanted port may provide a better choice.
5. How should teaching of patients (benign disease) for HPN be carried out?

There should be a formal teaching program for the patient and/or carer. The teaching program should include catheter care, pump use, and preventing, recognizing and managing complications. Experienced nurses are usually best placed to take responsibility for the teaching program.

Comments: HPN is a complex therapy and selecting patients suitable for this treatment option is a demanding task. It is important to evaluate the patient's cognitive and physical abilities before starting a HPN training program.

The home environment, medical suitability, rehabilitation potential, social and economic factors and reimbursement sources should be assessed by the extended nutrition team (including for example social workers and other designated health care professionals) before starting training for HPN.

Screening tools for testing the abilities of the patient are available in selected centers, but no validation of these have been published.

5.1. What should be included in the teaching program?

5.1.1. The use of specific brochures or videotapes for teaching, and affiliation with national support organizations, are associated with better outcomes

Different methods of training can usefully be employed when training patients for HPN, including written handouts, manuals and videotapes. Training can involve multiple patients, team members and relatives. It is of key importance however that only designated members of staff perform the training and that the procedures used are always consistent. A progress chart is useful to confirm proficient practice for each individual skill (see below). Additional helpful literature is available.

5.2. Where to teach patients?

5.2.1. Training is usually carried out in an in-patient setting, but training at home can be considered in patients who are clinically stable, have an appropriate indication for PN, are able to be evaluated in the home and are thought capable of future safe administration of the therapy

Training for HPN is usually carried out in an in-patient setting prior to discharge. No time limits for training should be set for allowing patients to make progress at their individual pace.

The patient/carer must be able to: recognize vascular access device complications, recognize signs and symptoms of fluid imbalance; perform testing of the urine for glucose and recognize signs and symptoms of hyperglycemia or hypoglycemia.

5.3. Monitoring of learned skills and quality of life for HPN patients?

Patients should be affiliated to a specific specialist team, and if possible to a national supportive organization since studies show that the outcomes are then improved, in terms of fewer complications and better quality of life.

Detailed written and oral instructions on the management of the central line should be given since this will reduce the incidence of catheter related infections. Patients will nonetheless need continual support from a well trained team. Patients affiliated to a specialist team and to a national organization have better outcomes. Patients who receive more detailed written and oral information on the aseptic management of catheters have a lower incidence of line sepsis.

6. How to monitor HPN treatment

Biochemistry (electrolytes, kidney function, liver function, glucose, hemoglobin, iron, albumin and C-reactive protein), and anthropometry should be measured at all visits; measurement of trace elements and vitamins are recommended at intervals of 6 months. Bone mineral density assessment by DEXA scanning is recommended at yearly intervals. Monitoring should usually take place at the supervising hospital by the nutrition support team. Monitoring can also be carried out by a home care agency with experience in HPN and may involve both the hospital and the general practitioner. Intervals between monitoring visits vary, but will typically be 3 months. The clinically unstable patient will need more attention.

The patient with malignant disease usually will be monitored for outcome parameters in the home. Specific non-nutritional issues including pain relief, psychosocial problems should also be addressed.

Comments: The purpose of monitoring is to secure and improve the quality of life of patients managed in the home with parenteral nutrition. Although well trained, patients must cope with the initial phase of potential complications, including infections, mechanical problems with the catheter, venous thrombosis, and metabolic disturbances. Psychological monitoring is also important given the necessarily complex and everyday nature of HPN and its potential adverse effects on the mood of the patient.

Assignment of responsibility for monitoring is probably very important in optimizing its quality. In general responsibility will be assigned to a specific person in the hospital specialist team.

Patients on HPN who have active malignant disease can be expected to have problems (e.g. pain relief, psycho-social problems), which differ significantly from those seen in benign disorders. In monitoring, it is important that the nutrition support team works closely with the palliative unit and/or the oncologists.

Evidence-based literature on monitoring in HPN is scarce. The observational study by Wengler et al. 2006 confirmed that bodyweight or anthropometry is measured at every visit in all centers. At every visit 88% of the centers evaluate the state of hydration, and 74% formally ask patients about oral intake. The mood of the HPN patient is specifically in 86% centers at every monitoring visit.

The following are recommended for laboratory monitoring: Hematology, tests for liver-function, creatinine and electrolytes, calcium, magnesium, phosphate and albumin should be measured about every 3 months in the stable patient. Measurement of trace elements, vitamins A, E, D, B12 and folic acid should be done at 12 month intervals. Measurement of bone mineral density by DEXA scanning is also recommended yearly.
Evidence-based guidelines for monitoring are not available, and prospective studies of the impact of different monitoring regimens on outcomes (including quality of life) of HPN are warranted.

7. Liver disease in HPN

HPN-associated liver disease is related to the composition of the HPN and to the underlying disease or coexisting liver disease. The fat/glucose energy ratio should not exceed 40:60 and lipids should comprise no more than 1 g/kg per day. All forms of over-feeding should be avoided. Glucose administration in excess of 7 mg/kg per min, and continuous HPN are also considered risk factors.

7.1. Prevention of chronic cholestasis is of utmost importance. Infections, in particular line sepsis must be promptly controlled to help prevent deterioration of any liver abnormalities.

Comments: Abnormalities of liver function tests occur in both children and adults on HPN, at a frequency of between 15 and 85%. More severe liver disease is also reported. In a retrospective cohort study of 90 HPN patients, the reported occurrence of liver disease was high. About 65% developed chronic cholestasis and 42% had liver disease with a bilirubin level >60 µmol/l, factor V < 50%, portal hypertension, encephalopathy, ascites, gastrointestinal bleeding, and histologically proven extensive fibrosis or cirrhosis was high. About 65% developed chronic cholestasis and 42% developed severe liver disease after a mean period of 6 and 17 months, respectively. Liver disease accounted for the death of 7% of the patients (22% of the deaths). Fortunately in other HPN populations the incidence of severe liver disease has proved significantly lower and serious liver complications and death related to end stage liver disease less frequent. Impaired liver excretory function may lead to an accumulation of manganese and copper, which is of special interest and concern in patients on HPN given that standard trace element preparations may contain too much of several metals for long-term intravenous administration. Plasma or whole blood concentrations of these elements should be monitored and their intake reduced if necessary.

Mild increase of alkaline phosphatase often indicates cholestasis and is then frequently associated with modest increases in transaminase levels. This is reported in about 50% of HPN patients, and not uncommonly together with a small increase in conjugated bilirubin. Although a working diagnosis of intrahepatic cholestasis with no obstructed or dilated bile ducts will be made, this should be confirmed by liver imaging. Liver abnormalities in HPN patients may progress to severe histological changes with portal fibrosis and/or cirrhosis, which may, in the long-term (months to years) result in liver failure and death.

Underlying disease: Resection of the ileum, short bowel syndrome with less than 150 cm of remnant bowel and colon exclusion are positively related to the development of chronic cholestasis during HPN. In such patients, chronic cholestasis is associated with significantly increased risk of severe liver disease.

Nutrition regimen: Intravenous lipid (20% soya emulsions – rich in n-6 PUFAs-) chronically given at more than 1 g/kg per day has been found to be clearly associated with both chronic cholestasis and severe liver disease in patients on HPN. This outcome proved linked to intravenous lipid intake and patients were not overfed. The risk of suffering severe liver disease after 2 years of HPN was 50% in patients having more than 1 g/kg per day of soya lipids daily compared to a probability of only 20% in those on less than 1 g/kg per day.

Supplementation with taurine in parenteral nutrition has been reported to ameliorate PN-associated cholestasis through promoted bile flow and to prevent lithocholic acid-induced cholestasis in guinea pigs. Taurine may increase the level of hydrophilic tauro-conjugated bile acids and may further prevent cell membrane changes caused by oxidative stress. Some investigators have proposed the routine inclusion of taurine in parenteral nutrition mixtures for pediatric patients. No reliable studies are available.

The prevalence of gallstones in patients with HPN is significantly increased. Case series predict probabilities of developing gall stones during HPN of 6.2, 21.2 and 38.7% at 6, 12, and 24 months, respectively.

8. Prevention and treatment of metabolic bone disease

8.1. Aluminum contamination of HPN should be less than 25 µg/l

The amount of sodium should be no more than required, to avoid sodium induced hypercalciuria. The calcium, magnesium and phosphate content of the HPN should maintain normal serum concentrations and 24-h urinary excretion.

The recommended ratio is 1 mmol of calcium to 1 mmol of phosphate.

The amount of amino acids prescribed should not be greater than losses, in order to limit hypercalciuria.

8.2. The recommended intravenous dose of vitamin D is 200 IU/day

Consider vitamin D withdrawal in patients with low bone mineral density (BMD), low serum parathyroid hormone, and 1,25-dihydroxyvitamin D concentrations associated with normal 25-hydroxvitamin D.

8.3. Reducing infusion rates may decrease hypercalciuria

Bisphosphonates (such as clodronate 1500 mg iv or pamidronate 20 mg iv every 3 months), may maintain BMD in patients with osteopenia. Regular physical exercise, sunlight exposure, stopping smoking, and limiting alcohol consumption are also helpful. The patient should reach and maintain normal weight. Underlying disease related factors must be strictly controlled, by treating inflammation and minimizing the dosage of bone damaging drugs.

Comments: Metabolic bone disease is common in patients on HPN. Using dual-energy-X-ray absorptiometry (DEXA) an ESPEN multicenter cross-sectional survey of 165 HPN patients evaluated the prevalence of metabolic bone disease. In 84% the bone mineral density (BMD) T-score of the femoral neck or spine was lower than −1 (the number of standard deviations below the mean BMD of young subjects). According to the WHO criteria 41% of patients had osteoporosis, with a T-score below −2.5. The incidence of metabolic bone disease in the HPN population remains unknown, but follow-up studies on relatively large patient groups indicate that long-term HPN is not necessarily associated with a decrease of BMD, and in some cases an increase in bone density occurs. Histomorphometric studies have shown both osteomalacia and osteoporosis, and indicated that most patients had features of hyperkinetic bone turnover at their first assessment that evolved later to features of low rates of bone formation.

8.4. Pathogenesis

The pathogenic factors for MBD in HPN patients comprise the underlying disease, the HPN treatment itself, and general and life-
style factors including age, menopause, alcohol and tobacco abuse. Underlying disease related factors include the malabsorption of calcium and vitamin D, chronic inflammation, and medication particularly the long-term use of corticosteroids.

HPN related factors include toxicity from aluminum contamination of the PN formula. Increased sensitivity to vitamin D suppressing PTH secretion, and hypercalciuria induced by the intravenous infusion of nutrients have also been proposed as potential causes. HPN related MBD might also be caused by deficiency or toxic effect of other micronutrients known to interfere with bone metabolism. This is potentially the case for vitamin K, vitamin C, and copper, fluoride, boron and silicon deficiency, and for vitamin A, cadmium, strontium and vanadium toxicity. However, no consistent data have yet been provided linking abnormal levels to MBD in patients on HPN.

8.5. Prevention and treatment

Few controlled studies exist to guide strategies to prevent and treat the MBD associated with long-term HPN. Patients should be advised to engage in regular physical exercise and to ensure sunlight exposure, to stop smoking and to limit alcohol consumption. Normal weight should be reached and maintained. Oral or enteral feeding should be advocated unless contraindicated or prevented by the underlying intestinal disease. Disease related conditions should be strictly controlled, treating inflammation and minimizing the dosage of any bone damaging medication. Oral calcium and magnesium supplementation should be prescribed whenever possible.

Prevention of MBD related to HPN factors is based on the optimization of the parenteral solution. Aluminum contamination should be less than 25 µg/L. The amounts of calcium, magnesium and phosphate provided should aim to maintain normal serum concentrations and 24-h urinary excretion. Particular attention should be paid to the calcium/phosphate ratio in the solution, even though the optimal ratio of 1 mmol of Ca to 1 mmol of P cannot always be achieved because of problems of stability in solution. Amino acids and sodium should not be added in amounts greater than losses because of the risk of induced hypercalciuria.

The recommended intravenous vitamin D for adults is 200 IU/day. Normal vitamin D nutritional status is represented by normal serum concentrations of 25-hydroxivitamin D (and of 1,25-dihydroxyvitamin D). However, excess of vitamin D should be avoided because it may result in net bone resorption and thus in bone demineralization. In patients with low BMD, low serum PTH and 1,25-dihydroxyvitamin D concentrations associated with normal 25-hydroxyvitamin D, vitamin D withdrawal may be considered. Finally, in some patients, slowing the infusion rate may reduce hypercalciuria.

Medical therapy may be useful for the prevention and treatment of MBD in HPN patients, but to date only a single randomized controlled study of bisphosphonate treatment has been carried out in patients on HPN. Intravenous clodronate decreased the urinary excretion of markers of bone resorption, and BMD at the lumbar spine was maintained in patients on HPN after 12 months, but no significant increase in BMD was observed. Anecdotal reports suggest that IV pamidronate is also useful.

8.6. Diagnosis and monitoring

Diagnosis of MBD relies on bone densitometry. The gold standard is currently dual-energy-X-ray absorptiometry (DEXA). Bone densitometry measures BMD, independently of the presence of osteomalacia or osteoporosis. When a specific diagnosis is needed, bone histology becomes necessary, a barrier being the invasive character of this diagnostic tool. Exploration of factors related to life-style and the underlying disease must also be performed before classifying the MBD as HPN-associated or HPN related, the latter being a diagnosis of exclusion.

In monitoring, repeated DEXA measurements are generally recommended at yearly intervals. Biochemical assessment of MBD requires the measurement of serum concentrations and 24-h urinary excretion of minerals, serum concentrations (and/or urinary excretion) of biochemical markers of bone turnover, serum PTH, 25-hydroxivitamin D and 1,25-dihydroxyvitamin D concentrations. Measurement of serum aluminum concentrations should also be considered in patients with pathological BMD.

9. Quality of life in HPN

HPN will have an impact on quality of life (QoL) either positively or negatively depending on the patient and underlying disease. Patients with a chronic disease will have had time to cope with the condition and can usually accept the need for HPN. In contrast, those with previously good health who have to adjust to HPN and the impact of sudden illness will encounter a loss of quality of life. HPN treatment aims to rehabilitate the patient and restore quality of life.

Generic tools for measuring quality of life may be used to study quality of life in HPN patients, but these instruments are not considered optimal since they will not distinguish between the effects of underlying disease and HPN. Specific tools for HPN patients are being developed for monitoring of the individual patient.

Comments: For patients with underlying benign diseases, the duration of HPN is less than 1 year in about 50% of the cases. The goal of HPN is not only to save life in providing adequate nutrients but also to improve QoL and to allow socio-professional rehabilitation.

There are methods to measure QoL, but in the particular case of patients on HPN, it is still more difficult to distinguish the impact of the illness from that of HPN. Nevertheless, HPN, a demanding and often difficult treatment, introduces a series of complications and restrictions to life activities which affect survival and QoL. The variable prevalence of HPN in different countries (or even areas within the same country) is dependent on multiple factors which in part reflect the perception of its influence on QoL. Continuing medical and technical progress affect the indications and outcomes over time and this adds to the difficulty in making assessments and comparisons.

The current literature on QoL in HPN is quite difficult to interpret because of the limited number of studies, the wide variety of instruments that were used and the lack of patient participation in most of the studies. There is an urgent need for a specific tool to assess QoL in HPN patients. At present, and taking into account the several published studies, the following factors are considered to alter negatively the QoL of patients on HPN:

- Age older than 55 years.
- Certain underlying diseases (including mesenteric vascular disease, pancreatic disease, malabsorption, systemic sclerosis).
- The presence of a stoma.
- Use of narcotics.

Amongst physical problems, fatigue and diarrhea have the most impact on daily life. Fatigue may be due to sleeping disturbances. This may, in part, be due to highvolume infusions of cyclic HPN causing frequent...
nocturia, or to noisy feeding pumps. When interviewed about the effects of HPN, patients identified 125 different problems relating to treatment. Nearly 60% of these were of a psychosocial nature, such as negative mood and feelings, lack of freedom, social limitations, being dependent, problems relating to holidays and inability to work. Over 60% of patients had depressive disorders of which 17% were severe, yet only one-third of patients with an indication of severe depression were taking antidepressant drugs. Other causes of concern were: (a) problems with care providers; (b) connecting the HPN infusion to the bag; (c) problems related to the pump; and (d) financial limitations.

The number of infusions administered per week may vary with intestinal adaptation capacities. In the European survey the number of bags used per week was as follows: 7 (67%), 6 (9%), 5 (12%), 4 (8%) and 3 or less (4%). It was observed that the number of infusions per week, but not their duration, worsened the QoL of HPN patients. A prospective approach to evaluate measures taken, their impact on complications, and on the definition of good practice in defined patients and situation is obviously needed but often lacking.

Sleep disturbances may be related to the use of noisy feeding pumps. The use of pumps is very variable from one to another country throughout Europe. This is due partly to different legislation, local resources and willingness of the patient. The newer small portable pumps available today allow HPN patients to overcome some of the very disturbing and QoL influencing aspects of the treatment. This includes noise and obligations to stay at home for their PN treatment, excluding HPN patients from outside social activities. Even if QoL is very much dependent on such innovations, their high cost may exclude HPN patients from their use because of a lack of reimbursement.

10. Catheter related complications

All of these issues are addressed in detail in the ESPEN guidelines on central venous catheters. This section will therefore address only those aspects particular to HPN.

Infection:

Comments: Efforts should be made to ensure that the longevity of lines is as high as possible in HPN since the risk of cumulative complications and loss of vascular access have directly life-threatening consequences in dependent patients.

In a study to investigate the difference in bacteriology between colonized catheters and blood stream infection in 354 HPN patients 249 catheter tips of a total of 600 catheters were cultured. Sixty tips were culture positive. There were significant differences between the microbiology of those who were judged to have catheter related sepsis and those who only had a colonized catheter. The presence of fungi indicated true catheter infection, in contrast to the finding of Gram positive cultures, which more often indicated colonization. In fungal infections it is always necessary to remove the line, but in bacterial line infection in HPN the line generally can be saved in about 30% of cases. Prolongation of HPN line longevity has been attempted by the prophylactic use of line lock with antibiotics, urokinase to lyse thrombi and alcohol to dissolve debris, but no controlled studies of these procedures are available. Daily antimicrobial chemotherapeutic treatment with taurine was used as a catheter lock in seven HPN patients. The pre-treatment infection rate of 10.8 line infections per 1000 catheter days dropped to 0.8; more studies are warranted.

Thrombosis of the vein associated with the central line is common in PN in general and has been reported on ultrasound imaging in 30–50% of patients, but in the HPN population this complication is more rarely diagnosed, with 0.05 episodes per catheter year, with a positive correlation to line infection. Removal of the line is not always required and a decision about this must be based on the clinical setting, symptoms, catheter function and the possibility of obtaining an alternative intravenous route. If associated with bacteremia however, removal of the catheter is usually required. Anticoagulant therapy with heparin and then warfarin will be introduced, and systemic thrombolysis and thrombectomy may be considered, but no randomized studies comparing thrombolytic agents to heparin treatment or placebo are available in HPN patients. Patients considered at particular risk of thrombosis can be offered prophylactic warfarin treatment.

The use of a heparin lock (50 units in 5 ml saline) to prevent catheter related thrombosis has been recommended in HPN, but analysis of 110,896 HPN days by the ESPEN HAN Group showed significant disadvantages of heparin flushes, with more infections, removals and occlusions. Adverse effects of long-term heparin are common and include thrombocytopenia, bone disease and loss of hair, as well as concerns about formation of precipitates with lipid components of the feed, all of which go to support the use of plain saline flushed. No objective data have yet shown benefit from heparin flushes in long-term HPN patients.

11. Intestinal transplantation

11.1. The indication for intestinal transplantation is irreversible, benign, chronic intestinal failure associated with life-threatening complications of HPN

Present data do not support direct referral for intestinal transplantation of patients with high risk of death due to underlying disease, chronic dehydration or significantly impaired quality of life. In all patients an individual case-by-case decision is required.

Comments: Intestinal transplantation is a relatively new therapeutic option for irreversible chronic intestinal failure associated with life-threatening complications due to long-term home parenteral nutrition (HPN). By 2003 more than 50 centers worldwide had performed this procedure in a total of fewer than 1000 patients.

HPN is still considered the primary treatment for intestinal failure since it is relatively safe and maintains the life of the patient. The U.S.A. Center for Medicare and Medicaid Services has approved payment for intestinal transplantation when life-threatening complications related to HPN occur. The American Society of Transplantation position paper on pediatric transplantation also considers patients with high risk of death or with very poor quality of life related to the underlying intestinal failure condition as candidates for an intestinal transplant.

11.2. The timing of patient referral is key to obtaining best graft and patient survival

Early referral is recommended to minimize mortality from HPN related complications whilst on the waiting list.

Epidemiological data on HPN cannot help us to judge when intestinal transplantation is indicated but suggest that patient referral currently often comes too late, which may increase mortality rates on the waiting list or following the transplantation procedure. Thus selecting patients for transplantation is a major challenge. It is easier when there is clearly a high risk of death on HPN, but it remains difficult to judge when to refer the clinically stable patient. The differential risks of death on HPN and
from transplantation must be balanced against the potential increase in quality of life from successful transplantation compared to relatively poor clinical status while on HPN.

A multicenter survey in Europe evaluated the prevalence of candidacy for intestinal transplantation on the basis of the Medicare and of the American Society of Transplantation indication criteria. Forty-one HPN centers from nine countries enrolled 688 adults (>18 years old) and 166 children. Overall candidacy was 15.7% in adults; the reasons given were HPN failure (62.1%), high risk gastrointestinal disease (25.9%) and a high morbidity associated with intestinal failure (12.0%).

Regardless of these evaluations performed by the European centers very few patients were referred for evaluation.

The main contraindications for intestinal transplantation are advanced cardiopulmonary disease and non-resectable malignancy (local or metastatic). Patients with active infection should be put on hold as candidates for transplantation.

The following transplant procedures are performed: (a) isolated small bowel transplant, including the jejunum and ileum. (b) Multivisceral transplant, including stomach, pancreas, duodenum, jejunum and ileum (and sometimes other organs such as the kidney when clinically indicated), (c) Combined liver-intestine transplant, including both the jejunum and ileum. (d) Liver-multivisceral transplant, thus including the liver with the multivisceral graft.

The indication for isolated small bowel transplantation is irreversible intestinal failure with no possibility of bowel rehabilitation, with normal liver function, associated with one or more of the other HPN related, life threatening complications.

A recent European 3 year follow-up of candidates for intestinal transplantation confirmed the appropriateness of following American Medicare and Medicaid Services criteria for referral of patients for intestinal transplantation, which are as follows.

- Impeding or overt liver failure with elevated serum bilirubin and/or liver enzymes; splenomegaly; thrombocytopenia; gastro-esophageal varices; coagulopathy; gastric bleeding; hepatic fibrosis; or cirrhosis.
- Thrombosis of two or more of the six major central venous channels: the subclavian, jugular or femoral veins.
- Frequent central line sepsis; two or more episodes of systemic sepsis secondary to line infections per year; one episode of line-related fungemia; septic shock.
- Acute respiratory distress syndrome.
- Frequent severe dehydration.

The presence of HPN-associated liver failure and of CVC-associated multiple deep vein thrombosis or of frequent and severe line sepsis were reported to be associated with a 5.7 and a 2.8 fold increased risk of death respectively.

All potential candidates for intestinal transplantation will be subject to a multidisciplinary assessment evaluating the gastrointestinal tract, their nutritional status and their hepatic, renal, cardiopulmonary, hematological and immunological function – as well as investigation for infectious disease. Also, a psychosocial assessment is mandatory.

The highest survival rates are observed among younger individuals, those at home rather than in hospital, and in patients managed in experienced transplant centers. There has been steady improvement in patient and graft survival.

Conflict of interest

Conflict of interest on file at ESPEN (espenjournals@espen.org).

References
