Approach to Parenteral Nutrition Topic 9

Module 9.4

Monitoring and Complications of Parenteral Nutrition

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Learning Objectives

- To understand that maximum efficacy and safety of PN can only be achieved when it is carried out by a properly trained and expert Nutrition Team;
- To realise that monitoring, using data recorded in serial form is a vital tool for achieving optimal results;
- To understand how to implement monitoring protocols (standard operating protocols, SOPs) not only to optimise feeding methods and prescriptions but also to prevent complications or at least to detect them at an early stage, allowing timely action;
- To appreciate the technical, mechanical, clinical and infectious complications of PN and how monitoring helps in their management.

Contents

Key Messages

- The efficacy of PN is dependent on having an expert team to carry it out;
- Clinical and laboratory monitoring are essential tools for the team to achieve optimal results;
- Data should be recorded in an easily retrievable serial form in order to give a dynamic picture of the rate, direction and degree of any change, allowing anticipation of problems and early intervention;
- Proper monitoring by SOPs not only allows early detection of complications and timely intervention but also continuous adaptation of nutritional support to the needs of the patient;
- The appropriate monitoring protocol may vary according to the patient's underlying clinical condition;
- PN is potentially associated with technical (e.g. mechanical), clinical (e.g. thrombotic), metabolic (e.g. hyperglycaemia), and infectious complications, which are largely preventable;
- Adherence to strict SOPs and guidelines (e.g. in the insertion and care of central lines) and their conduct by trained staff reduces the risk of PN related complications and improves overall outcome.

1. Introduction

As with any other therapy, the use of parenteral nutrition (PN) is associated with potential relevant risks. Therefore, since the early years of PN therapy, much effort has been devoted to the identification of correct procedures to prescribe, prepare and deliver a PN bag. Considering the different expertise required to prevent PN-associated complications, it is now widely accepted that complication rates can be reduced by the employment of a trained and expert team of doctors, nurses, dietitians and pharmacists (1). A recent audit (2) performed in all secondary care hospitals in the North of England showed that PN was used for a median of 7 days with a 30-day mortality rate of 8%. Metabolic complications occurred in 34%, of which only 13% were avoidable. The catheter sepsis rate was 1.5 per 1000 PN days. More importantly, the audit suggested that nutrition team input improves patient assessment prior to starting PN and review once PN is established. Risk of refeeding syndrome was identified in 75%. Areas for improvement were identified and include documentation of treatment goal, review of PN constitution, ensuring patients are weighed regularly and documentation of line-tip position. This recent work strengthens the case for introducing nutrition teams in hospitals without this service.

The members of the Nutrition Team should regularly review their performance in terms of efficiency, complications avoided and, if possible, cost savings. In this light, benchmarking the team's performance with national and international standards is of paramount importance to constantly improve the quality of care. Also, the members of the Nutrition Team should regularly attend training courses to acquire specific abilities which have been proven to reduce complications (e.g., use of ultrasound scanning during positioning of central lines). There is now solid evidence that mechanical problems of line insertion are inversely proportional to the experience and expertise of the operator. Thrombotic and infectious complications can be reduced by following strict procedures and by thoroughly reviewing clinical cases in whom complications occurred and acting on the conclusions. Therefore, it is self-evident that monitoring and recording should be carried out according

to agreed standard operating procedures (SOPs) and data reviewed at least weekly in hospitalized cases.

2. Prescription

The most effective strategy to reduce PN-associated complications is the correct indication, as already discussed in the first module of this LLL course. In this light, it has been repeatedly shown that the presence of a multidisciplinary nutrition support team is critical in reducing inappropriate indications for PN. Boitano et al. showed that implementing process improvement strategies (i.e., revision of PN order form, education of clinicians, increased collaboration, initiation of PN rounds) led to reduced inappropriate use of PN and significant cost savings (3). Similarly, Martin et al. demonstrated that nutrition support teams and certified nutrition support clinicians can curtail preventable spending on inappropriate PN use (4).

3. Recording of Data

Merely doing tests, the results of which are stuck in the notes in a haphazard manner, cannot be classed as proper monitoring. Data should be recorded systematically in an easily retrievable and serial form either on charts near the patient's bed or in digital form on an accessible computer. It is important not only to know the results of current tests but also to be able to see, at a glance, any change from the previous tests giving a dynamic picture concerning rate, direction, and degree of change. This allows anticipation of trends and early warning upon which to base clinical decisions. Standardized systems of this sort also allow easy retrieval of data for audit and research purposes and provide an invaluable weapon when proving the team's cost-effectiveness to health service managers and grant giving bodies.

4. Monitoring Clinical Indications

The importance attached to each aspect of monitoring and the frequency with which measurements are carried out will depend on the clinical situation. Patients who may require PN can be divided broadly into the following categories.

4.1. Acute and Critically Ill Patients

In acute and critically ill patients, (e.g. major trauma, burns, sepsis etc.), monitoring of organ function, vital signs and fluid needs take priority, while nutritional support is conducted in a cautious and conservative manner, striking a balance between trying to conserve lean mass as far as is possible under these circumstances and avoiding the ill effects of nutritional excess, (e.g. hyperglycaemia, salt and water excess, increased metabolic rate etc.), in a vain attempt to reverse catabolism completely. Some units have the technology to measure metabolic rate by indirect calorimetry and this is undoubtedly an advantage in prescribing an appropriate energy intake for unstable and critically ill patients, (e.g., burns). Prescription of nutritional goals based on the measurement of energy expenditure should be implemented worldwide. However, it is acknowledged that indirect calorimetry is not available in all units worldwide. Therefore, it is possible to conduct PN in most patients using predictive formulae, (e.g., 20 kcal/kg BW in the catabolic

phase, and 25-30 kcal/kg BW in the anabolic phase) as far as one recognizes the potential for error and variation in acute illness.

4.2. Post-Acute Patients

Patients in the post-acute phase, (e.g. >7-10 days after trauma or surgery with persistent GI dysfunction) deserve special consideration. These patients are often oedematous with persistent retention of salt and water which impairs recovery of GI function and of mobility, and also have hypoalbuminaemia due to dilution from administered crystalloids and redistribution from the inflammatory process. Initial management and monitoring will be dominated by the need to obtain a diuresis. In patients with short bowel, fistula, or other causes of excess fluid loss, subsequent management is dominated by the need to replace losses of fluid and electrolyte as well as the provision of adequate nutrition until the underlying condition has resolved and normal oral intake may be resumed. Daily weighing to monitor water balance, fluid balance charts, and regular measurement of serum biochemistry are important monitoring parameters. Paradoxically, initial clinical improvement is shown by weight loss as oedema resolves. Weight gain from restoration of lean mass awaits convalescence and mobility and is a slow process. It is only too easy to gain weight due to fluid retention or fat accumulation, neither of which is clinically desirable. One of the main problems of PN, as opposed to EN where intake is limited by GI tolerance, is that it is easy not only to administer excess salt and water, but also excess nutrients. Careful thought should be devoted to all details of PN prescriptions to ensure that they are appropriate to each patient.

4.3. Preoperative Malnutrition

Preoperative malnutrition - in cases not amenable to oral or enteral refeeding – exposes surgical patients at high risk of developing complications. The aim is to improve function, (e.g. muscle, immune, respiratory etc.), to enhance survival and rate of recovery from surgery. This can be obtained by 7-10 days' feeding. Some weight gain may occur through restoration of fluid deficit but further weight gain should be avoided as this signifies undesirable excess fluid retention which impairs outcome. Quite recently, the approach to surgical patients using the Enhanced Recovery After Surgery (ERAS) programme has become widely accepted. This programme is based on the assumption that patients should be metabolically primed before undergoing surgery (5). Therefore several procedures, including allowing clear fluid intake until a few hours before surgery, are now implemented in surgical units and the outcome has significantly improved (6).

4.4. Chronic Malnutrition

In patients with chronic malnutrition, (e.g. Crohn's and other GI diseases), deterioration of nutritional status occurs over time. Such patients often require prolonged PN or even permanent PN at home. Clearly, improved function and real tissue weight gain are desirable objectives. Monitoring may not need to be so frequent or so intense as in more acute conditions.

5. Monitoring Parameters

Parenteral nutrition is indicated in malnourished patients, or patients at risk of developing malnutrition, in whom the gastrointestinal tract is not functioning adequately or is not accessible (7). The goal of PN is to replenish malnourished patients nutritionally and to prevent/delay the development of malnutrition. Consequently, the efficacy of PN should be assessed by regularly monitoring of the patient's nutritional status using well-established parameters and indices (8, 9). Recently, ESPEN published an opinion paper on the proper monitoring of nutrition in the intensive care unit, which should inform the development of SOPs in the acute and chronic care facilities (10).

5.1. Clinical Parameters

A daily clinical examination of the patient is important, looking for evidence of oedema, dehydration, sepsis and wound healing among other important signs. The catheter site should be inspected at regular intervals for signs of inflammation or infection (11). In some series once or twice weekly dressing by the nutrition nurse was associated with lower costs and no more infections than daily dressings. Charting of vital signs is crucial, (e.g. temperature, pulse rate, respiration, blood pressure etc.), supplemented, as appropriate, by other measurements (e.g. central venous pressure, cardiac output etc.).
A rise in temperature is, of course, the first indication of possible line sepsis, although this needs to be distinguished from other sources of sepsis. Blood cultures should be taken peripherally and through the line, and if fever persists the line should be locked. If this causes the fever to subside this incriminates the line which may be sterilized with antibiotics or removed and replaced. Records of all central catheters should be kept, including date inserted, date removed, reason for removal, and the result of tip culture (whether or not sepsis is present).
Fluid balance charts give invaluable information concerning fluid input and changes in urine or fistula output or in gastric aspirate. They have inherent inaccuracies however and do not measure insensible loss. This gives rise to cumulative errors in calculating water balance, which is much more accurately assessed by daily weighing, as practiced by nephrologists. If change in water balance can be obtained from weighing, then sodium balance can be inferred from changes in plasma sodium since this reflects the ratio of sodium to water in the extracellular space.

5.2. Anthropometric Indices

Weight As a reflection of real tissue gain or loss this is important in initial assessment and in the long-term monitoring of patients at prolonged risk of malnutrition or undergoing long periods of PN. In short periods of feeding, (i.e. < 3 weeks), or in acute and post acute patients, however, its main use is to monitor water balance as discussed above, since significant gain of lean mass is unlikely in these conditions. Weighing is also helpful for patients at home with large and variable GI fluid losses, (e.g. short bowel), allowing them to adjust their own salt and water balance intravenously or by subcutaneous crystalloid infusion (hypodermoclysis). In the elderly or disabled, this may need to be done by a carer.
Arm circumference**.** Using a tape measure around the upper arm mid-way between the acromion and the olecranon process. This reflects the combined mass of skin, fat, muscle

and bone. It is a useful surrogate for weight in patients whom it is difficult to weigh, and by adjusting for the triceps skinfold thickness, changes in muscle mass can be calculated. Triceps skinfold. Unfortunately this is very observer dependent with wide errors in unskilled hands. It is useful in research projects which involve one skilled observer but is much less helpful in normal clinical practice (12).

5.3. Nutrition Screening and Assessment Tools

As the name implies, these are of use in initial assessment and in long term monitoring of patients at risk. In the hospital setting, ESPEN recommends the use of the NRS 2002(13). The old so-called nutritional risk indices are outdated, containing as they do haematological parameters and serum albumin which are almost entirely a reflection of disease severity (14). They are therefore good as prognostic factors but not as nutritional indices. Also the total lymphocyte counts, complement and skin tests are not used anymore, because they have very low sensitivity (for a more detailed discussion of the available tools for assessing nutritional status please go to LLL Course 3 - Nutritional Assessment and Techniques). The relevance of nutrition screening has been repeatedly demonstrated. Kruizenga et al. demonstrated that screening and early standardized nutritional care improves the recognition of malnourished patients and provides the opportunity to start treatment at an early stage of hospitalization (15). More importantly, the additional costs of early nutritional care are low, especially in frail malnourished patients.

5.4. Function

In malnourished patients, nutritional support, by any means, results in rapid and measurable improvements in physical and mental function, generally within days, long before any change in tissue mass. Simple measurements to record these changes can be performed at the bedside.
As a research tool, involuntary muscle strength can be measured by direct stimulation of the adductor pollicis. In clinical practice, however, hand grip dynamometry, using one of the newer digital machines, gives a good reflection of changes in muscle strength. Respiratory muscle strength is reflected by simple Peak Flow measurements. Skin tests of immune function are not routinely used although serial white blood cell and lymphocyte counts give some reflection of immune function. Mental changes can be detected by an experienced observer and can be scored formally using the POMS or other validated scoring systems. These measures of function are the most sensitive indicators of change in nutritional status. Deterioration is detectable at only 5% weight loss in normal subjects, and is clinically significant with more than 10% weight loss in patients. As described above the first sign of response to refeeding is an improvement in function, which is probably the mechanism of benefit in perioperative feeding. However, it should be noted that functional measures may overestimate the actual prevalence of malnutrition. In a recent report, Bin et al. investigated patients with Crohn's disease in clinical remission and found that 26.7% of the patients were malnourished according to the arm circumference, 29.3% according to the muscle arm circumference, 18.7% according to the SGA, 6.7% according to the BMI, 37.3% according to the triceps skinfold and 73.3% according to the handgrip strength (16).

5.5. Laboratory

This comprises biochemical, haematological, and microbiological data.
Biochemical measurements may be done daily in acute patients, approximately two or three times weekly in the post-acute setting and progressively less frequently in convalescent or long-term patients.
Plasma sodium concentration of itself is more a reflection of dilution or concentration due to changes in water balance and not of salt balance, but if water balance is known from weighing, then sodium balance can be inferred from changes in plasma sodium concentration. This is invaluable in patients with abnormal GI fluid losses, allowing accurate maintenance of salt and water balance for long periods.
Serum potassium is a good indicator of the adequacy of potassium intake and also gives warning of the development of the refeeding syndrome (see paragraph 6.1) as does the serum phosphate.
Chloride and acid base measurements are particularly useful in acute and immediately post-acute patients.
Calcium, Magnesium, Zinc and Selenium measurements are of particular value in patients with GI disease and are helpful in guiding replacement. Micronutrient screening is only available in a few laboratories but is helpful in long-term patients.
Blood glucose has become particularly important since the importance of control of glycaemia in determining outcome from critical illness has been demonstrated. Plasma proteins give less useful information concerning nutritional status than once thought. The acute phase protein C-reactive protein is however a most useful reflection of changes in the inflammatory state. As it rises with the onset of inflammation, the serum albumin falls as it is redistributed by capillary leakage. Hypoalbuminaemia is further exacerbated by dilution with crystalloid infusions. These are the dominant influences on the plasma proteins in the acute, post-acute, or perioperative patient. On the other hand in convalescent or long term feeding the restoration of serum albumin may occur faster with adequate nutrition, provided that there is not persistent inflammation or protein losing enteropathy. Liver disease of course may also contribute to hypoalbuminaemia.
Haematological screening should also be performed regularly. Anaemia may have nutritional causes or be secondary to blood loss but is more often the non-specific normochromic normocytic anaemia of inflammatory disease, improving spontaneously as the disease resolves. Regular microbiological cultures of swabs from relevant sites allow monitoring of colonizing organisms and may help to guide treatment. Blood cultures should always be performed if fever develops.

5.6. Practical Considerations

Although it is imperative to monitor the efficacy of PN in order to adapt it to the changing needs of the patient, at least in some clinical conditions, but particularly in the critical patient, it can be extremely difficult to obtain an objective marker of nutritional replenishment. Nitrogen balance is a sensitive tool to assess the efficacy of PN, but is difficult to measure accurately in clinical practice and is not normally used. Furthermore, it should be remembered that trauma and burn patients develop hypercatabolism, which cannot be reversed by feeding alone, although this does offset the starvation component of disease and therefore helps to slow the loss of lean mass. The aim of management is to reduce the severity of the catabolic stimulus by modern techniques, such as

control/prevention of infection, nursing in a warm environment, better analgesia/anaesthesia, improved surgical technique, etc. These measures in combination with nutritional support have lessened the loss of lean mass in such patients and contributed to better outcome. In stable conditions, the monitoring of PN efficacy is much easier and allows regular review of the nutritional and metabolic needs of patients receiving PN. By correctly identifying the patient's needs, the efficacy of PN is greatly improved and the risk of developing complications significantly reduced.

6. Complications of PN

Parenteral nutrition may be associated with the development of complications, which can be metabolic, technical or infectious. For this reason, PN should be used for the shortest period possible, and oral or enteral feeding should be initiated as soon as is clinically feasible. Indeed, the gastrointestinal route remains the most physiologically appropriate and cost-effective way of providing nutritional support. As emphasized above, the complication rate from PN is significantly reduced in those hospitals where a multidisciplinary specialized Nutrition Support Team has been created. This team includes doctors, pharmacists, nurses, and dietitians. The combined expertise of these personnel is critical in correctly assessing the needs of the patients, preparing and safely administering the PN bag, and monitoring for the early signs and symptoms of complications.

6.1. Metabolic Complications

The inappropriate assessment of the caloric needs of the patients may increase the risk of developing the refeeding syndrome, a serious and potentially fatal complication of artificial nutrition. Although more frequent during enteral rather than parenteral nutrition (17), the refeeding syndrome occurs in severely malnourished patients whose energy metabolism is mainly based on the utilization of fatty acids or ketone bodies (18). When these patients are suddenly given a high energy intake, especially from glucose, the attendant increase in insulin secretion promotes the entry into the cells of potassium and phosphate, thereby reducing their extracellular concentrations. In particular, the reduction in phosphate may cause serious derangement of cardiac function. To prevent the refeeding syndrome, severely malnourished patients should initially receive only 20 to 30% of their energy requirements, building up to full intake over several days. This should be combined with a high intake of phosphate and potassium, with frequent monitoring of blood levels. A bolus injection of 100 mg of thiamine should also be given and a high level of provision continued. Recently, early diagnostic markers for refeeding syndrome have been proposed. Elnenaei et al. showed that the "refeeding index", a marker based on IGF-1 and leptin levels, is a sensitive and specific predictor of the refeeding syndrome in hospitalised patients before starting PN (19).

Hyperglycaemia may occur in patients receiving PN, and if marked and persistent may induce an osmotic diuresis and dehydration (20, 21). Strict glycaemic control has been shown to improve mortality in ICU patients, further emphasizing the need for the prevention of hyperglycaemia. More recently, Pasquel et al showed that hyperglycaemia during PN without tight blood glucose control is associated with increased risk of hospital complications and mortality (22). To prevent this complication, it is important that PN provides only the amount of glucose that each patient can utilize (< 5 mg/kg BW in the critically ill patient). Also, frequent monitoring of glycaemia and glycosuria during the first

days of PN is important in the assessment and treatment of hyperglycaemia, particularly in diabetic patients.
Hypoglycaemia may occur during withdrawal from PN, particularly if the infusion rate is not reduced gradually during the last few hours of PN infusion before it is stopped (21).
Hypertriglyceridaemia may develop in patients receiving lipid-containing PN, and may lead to the occurrence of pancreatitis (23). Also, it should be remembered that some clinical conditions, including liver cirrhosis, are associated with a reduced clearance of exogenous triglycerides. Monitoring of triglyceridaemia weekly may be useful in helping to prevent the development of this complication.
Hepato-biliary complications of PN, which range from liver steatosis to cholestatic liver disease, which may progress to liver cirrhosis and liver failure, are observed mainly in patients receiving long-term PN (for a more detailed discussion of these complications, please go to Topic 19 - Home Parenteral Nutrition). The pathogenesis is multifactorial, but the decrease in the enterohepatic cycle of bile acids, associated with bacterial overgrowth, appears to play a critical role. To prevent this complication, the cyclic (non-continuous) delivery of PN and the limitation of energy intake (particularly from carbohydrates) may be useful, as well as regular monitoring of hepatic function. More importantly, promotion of some oral intake/enteral nutrition, to stimulate biliary secretion and avoid stasis, is critical in reducing the risk of developing hepato-biliary complications (24).
PN-induced bone disease occurs in approximately 30% of patients receiving long-term PN (for a more detailed discussion of these complications, please go to Topic 19 - Home Parenteral Nutrition). In these patients, bone density should be measured regularly (25).
The inadequate delivery of micronutrients and vitamins may cause subclinical and clinical deficits of these nutrients, resulting in neurological and/or muscular symptoms and signs (26), delayed wound healing and other clinical problems. Among the above-mentioned metabolic complications, some should be considered clinically important relevant and deserving of prompt intervention (see **Table 1**).

Table 1
Definition of clinically relevant metabolic complications

Complication	**Evidence**
Hyperglycaemia	>10 mmol/L (even this limit may be too high)
Hypoglycaemia	<3 mmol/L
Ketoacidosis	Arterial pH≤7.30 + >2 dipstick for urinary or serum ketones
Hyperosmolar hyperglycaemic non-ketosis	Severe hyperglycaemia + serum osmolarity >305 mOsm/L + absence of urinary ketones, serum osmolarity raised >295 mOsm/L
Na, K, Cl, Ca, Mg, P disorders	Serum values outside the reference ranges
Hypertriglyceridaemia	>150% of upper reference limit measured >8 hrs after lipid emulsion (check milky plasma)
Hyperazotaemia	Blood urea >twice of upper limit of reference (may also reflect excessive nitrogen intake)
Hyperchloraemic acidosis	Serum Cl >115mmol/L + arterial pH≤7.30

Hepatic dysfunction	AST, ALT, alkaline phosphatase, bilirubin >twice the upper limit of reference
Fluid overload	Heart failure, oedema or weight gain >0.45 Kg/day for 3 or more consecutive days
Coagulopathy	Prothrombin time and/or partial thromboplastin time >150% of upper limit of reference

The risk of complications depends not only on the competence of the nutritional team but also on the patient's clinical condition. The more severely ill the patient, the greater the risk of complications. Furthermore, the patient's clinical condition influences the type of complication, (e.g. the refeeding syndrome is more likely in a severely malnourished patient). As a consequence, the monitoring schedule should be tailored to the patient's condition. As a general rule, during the early phase (3-5 days), step-wise increments of macronutrients should be introduced slowly until estimated and/or tolerated nutrient requirements are achieved. Blood glucose, urea, sodium, potassium, magnesium, phosphorus, and ionized calcium, should be obtained daily, at least initially (21). In critically ill patients, arterial blood gases should also be monitored daily. Thereafter in hospitalised patients, the full set of laboratory parameters should be obtained 2-3 times weekly. For home PN, the intervals between measurements can be considerably extended.

6.2. Technical Complications

Catheter or cannula insertion is associated with a risk of technical complications, which are different for central and peripheral PN.

Technical Complications of Peripheral PN. Cannulae and midline catheters are used to infuse peripheral PN. To prevent mechanical complications (catheter kinking), site selection should identify a vein where the need for excessive flexion is avoided (27). The most common complication of peripheral PN is however phlebitis (3 to 31%). In some cases, the consequences of phlebitis can be very serious, including local suppuration, local tissue necrosis, bacteraemia and sepsis. In this respect, the insertion site should be monitored daily to check for early signs of phlebitis. Therapies not appropriate for peripheral devices include parenteral nutrition fluids with more than 10% dextrose and/or 5% protein, solutions and/or medications with a pH less than 5 or greater than 9, and solutions and/or medications with osmolarity greater than 500mosm/L. Peripheral cannulae should be daily changed, since the risk of phlebitis increases when they are left in place >72 hrs. Midline catheters have been associated with lower rates of phlebitis than short peripheral catheters. Paediatric silastic catheters have also been used in adults for peripheral PN and can be left in place for several days without increased risk. A diminution of the endothelial reaction to infused fluids and trauma can be achieved by adding heparin (1000 IU/L) and/or hydrocortisone (5-10 mg/L) to the regimen, reducing the rate of thrombosis to 8%.

Technical Complications of Central PN. Central venous catheters (CVC) and peripherally inserted central catheters (PICC) are used to infuse central PN. The insertion of a central catheter is associated with early and late complications. The former are mainly technical complications and include: failure of insertion, local haematoma or abscess, misplacement and migration, catheter embolism, arrhythmias, haemothorax, pneumothorax, central venous thrombosis and/or thromboembolism. The risk of developing technical complications during catheter insertion is reduced if the catheter is placed by qualified and

well-trained personnel. Also, the use of ultrasound/Doppler scanning of the venous anatomy significantly reduces the risk of complications **(Fig. 1).**

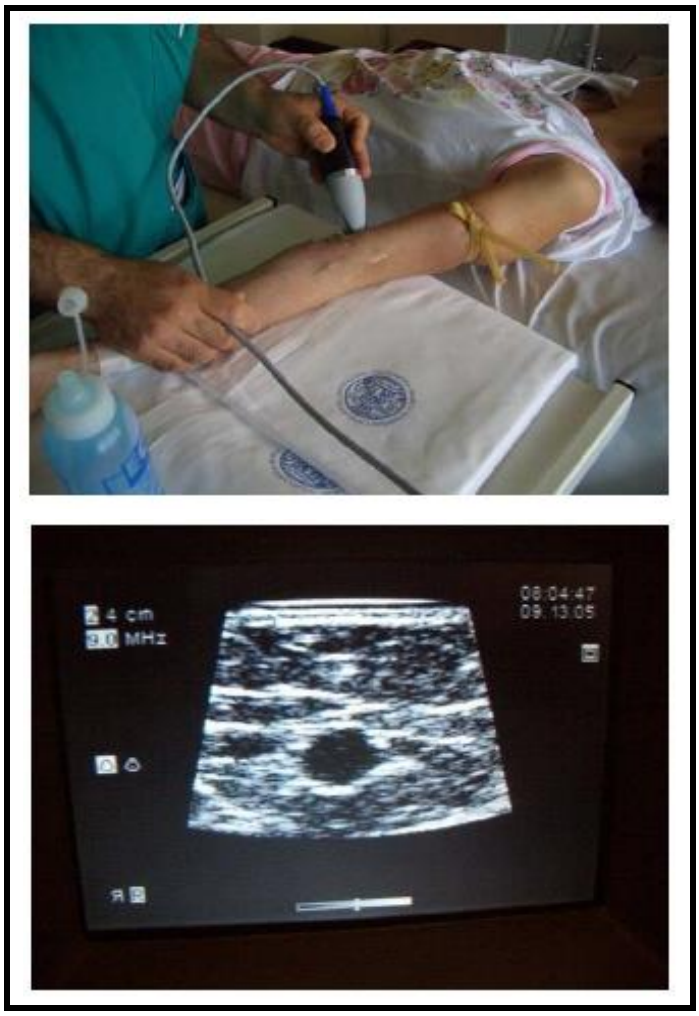

Fig.1. Ultrasound scanning of the venous anatomy before midline insertion (courtesy of Dr. Pittiruti)

Late mechanical complications of central catheter insertion include blockage of the catheter; urokinase, sodium hydroxide, hydrochloric acid or 70% ethanol lock may then be used to unblock the lumen. Catheters can occasionally fracture in their intraluminal part and embolize. Some evidence of central vein thrombosis is common (up to 50%) when assessed by ultrasound imaging, but major thromboses causing clinical manifestations are uncommon. In severe cases, however, it can be a dangerous complication, leading to a high rate of morbidity and mortality. The risks of thrombosis can be reduced by appropriate selection of the insertion site, proper catheter tip location, i.e. at the junction of the right atrium and superior vena cava, and meticulous insertion. Also, Vegting et al. showed that thromboprophylaxis significantly decreases catheter-related thrombosis and occlusion in children on PN without creating new complications (28). The use of modern less rigid catheters and the avoidance of feeds with high glucose concentration have also contributed to a reduction in thrombosis. As far as PICC are considered, PN is a risk factor for upper extremity venous thrombosis, but prophylaxis with low molecular weight heparin,

unfractionated heparin or the use of warfarin seem unable to prevent the development of venous thrombosis in some patients with these cannulae (29).

6.3. Infectious Complications

Infection remains the most serious complication of PN, and particularly of central PN. Catheter-related blood-stream infection (CRBSI) is the preferred term to define septic complications of intravascular catheters. From a practical point of view, some convenient definitions to be used when referring to these complications include:

- local infection

- Catheter colonization, when growth of a microbial pathogen is found in a specimen without general or local signs of infection;
- Exit site infection, tunnel infection, and pocket infection of a totally implanted device;

- invasive infection

- CRBSI, which is the most dangerous complication and may occur at any time when a central venous catheter is in place.

Pathogenesis. A catheter can be colonized on its outer surface, in its lumen or both. The most common causes of endoluminal colonization are:

- colonization of the catheter hub (by far the most common);
- broken or leaking line due to poor connections;
- contaminated nutritional admixture (during preparation, infusion, connection, additives added in the ward: rare with adequate pharmacy support);
- use of the central venous catheter for other purposes by inexpert users (e.g., blood sampling). With strict aseptic protocols, the use of the line by experts, (e.g. experienced nutrition nurses), for blood sampling or drug administration has a relatively low risk. Multi-use lines in ICUs, however, should probably be replaced at least weekly as they have a high contamination rate after a few days.

The most common causes of extraluminal contamination are:

- migration of microorganisms along the catheter from the cutaneous exit site;
- direct contamination during catheter insertion ("third day surgical fever");
- haematogenous seeding, especially in critical care settings, (e.g. organisms from abdominal sepsis colonizing the line from the blood stream).

The clinical picture of CRBSI has local and/or general manifestations, whose potential presence should be regularly monitored. The local signs include: redness, pain, swelling, or drainage of serous or purulent fluid at the exit site. Tunnel suppuration presents as a painful, inflammatory string along the subcutaneous tunnel. The general signs may be non-specific, and they cover a wide spectrum from subfebrile status up to signs of septic shock and organ failure. Fever is often accompanied by chills (rigors), and symptoms often appear 1-3 hours after starting a new infusion. Non-specific signs such as nausea, vomiting, lethargy, mental and vision disturbances have also been reported. A catheter-related bloodstream infection rate well below one episode per 1,000 catheter days is feasible for hospital PN and can be achieved without the use of antimicrobial agents (30). A maximum rate of 0.1-0.5 infectious episodes/year of central venous catheter use for home PN appears generally acceptable as they may be inevitable even under optimal conditions. The priority is early recognition and action.

Prevention. The most important preventive measures are as follows (31) and are outlined in **Table 2**:

- a high level of training of staff responsible for the insertion and maintenance of catheters;
- the strict avoidance of any handling of the catheter or line by inexpert staff, be they doctors or nurses;
- quality assurance and continuing education;
- correct choice of site of insertion (lower extremity insertion sites are associated with a higher risk for infection than are upper extremity sites);
- type of catheter material (polyurethane catheters have been associated with fewer infectious complications than polyvinyl chloride or polyethylene);
- hand hygiene and aseptic technique;
- skin antisepsis (preparation of insertion site with 2% aqueous chlorhexidine gluconate lowered bloodstream infections rates compared with 10% povidone-iodine or 70% alcohol);
- catheter site dressing regimens (transparent, semipermeable polyurethane dressings have become a popular means of dressing catheter insertion sites, allowing for continuous inspection of the exit site).

Table 2
Outline of a central venous catheter care protocol

Type of handling	**Preventive measures**	**Optional extra measures***
Catheter insertion	Avoid femoral vein insertion sites Introduce maximal sterile barrier precautions: wash hands with antiseptic soap or solution; wear a surgical mask, sterile gloves, cap, and use sterile instruments; use a sterile sheet to cover the patient; disinfect skin at insertion site with 2% chlorhexidine in alcohol solution	Eradicate *S. aureus* nasal carriage by topical mupirocin for 2 weeks, followed by a once-weekly maintenance dose of the same agent
Inspection of exit site	Visual inspection and palpation with sterile or clean gloves at every PN infusion Look for signs of infection, such as swelling, pain, redness and pus Swab and culture when infection is suspected When clinical suspicion of infection is high start prophylactic antibiotics that are effective against *S. aureus*	Have a low threshold for removing non-tunnelled central venous catheters (not evidence based)
Change dressings	Change dressings at every use and promptly replace loosened or soiled dressings Before applying a new dressing, clean skin with antiseptic solution, preferably a 2% chlorhexidine in alcohol solution	Application of a topical antimicrobial agent to the exit site, such as mupirocin (shown in patients on haemodialysis)

	Use non-occlusive or semipermeable dressings Note that a fully ingrown, cuffed, tunnelled central venous catheter may not need a dressing	
Opening and closing the CVC	Wash hands with an antiseptic soap or sterile solution Wear sterile gloves, surgical mask, sterile gown Place a sterile sheet under the central venous catheter Soak the catheter hub in an antiseptic solution (such as 2% chlorhexidine in alcohol) for at least 5 min Minimize exposure of the opened catheter hub to air	Lock the central venous catheter using an antimicrobial solution A membrane-closed or needleless connector device may be used, but the effect on the incidence of catheter-related bloodstream infection is unknown
Catheter replacement over a guidewire	Use sterile barrier precautions similar to those applied when inserting a new central venous catheter	Intravenous vancomycin 1 g after replacement (not evidence based)

* Extra preventive measures should be taken when the incidence of catheter-related infection remains persistently above the benchmark rate. Adherence to the catheter care protocol and training of staff should be ascertained.

Administration sets used for PN should be changed every 24 hours or immediately upon suspicion of contamination or when the integrity of the product or system has been compromised. PN administration sets should be changed using aseptic technique and observing universal precautions.

The use of antimicrobial/antiseptic impregnated catheters and cuffs has yielded conflicting results but may be used in patients at high risk of infectious complications (e.g., critically ill patients).

No benefit has been demonstrated from the use of systemic antibiotic prophylaxis, whereas the use of antibiotic/antiseptic (i.e., mupirocin) ointments at the exit site has been proved effective in patients on haemodialysis (32). To prevent CRBSI, antibiotic lock prophylaxis has been attempted by flushing and filling the lumen of the catheter with an antibiotic solution and leaving the solution to dwell in the lumen of the catheter. Clinical studies have demonstrated the usefulness of such prophylaxis in neutropenic patients with long-term catheters. It is important to note that catheter replacement at scheduled time intervals as a method to reduce CRBSI has not lowered rates.

7. Summary

The cost effectiveness and outcome of PN is dependent on its being conducted by a trained team working to agreed protocols including a proper monitoring programme, with measurements being carried out in a systematic manner appropriate to the clinical problem involved. Data should be recorded in an easily retrievable serial form to allow a dynamic picture of the patient's progress. Such a programme helps to guide PN prescriptions and to prevent complications or give early warning of their onset, allowing timely intervention.

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Useful Links

Center for Disease Control and Prevention, Atlanta, GA, USA (www.cdc.gov)
European Society of Clinical Nutrition and Metabolism (www.espen.org)
National Institute of Clinical Evidence (www.nice.org.uk)
Royal College of Nursing (www.rcn.org.uk)