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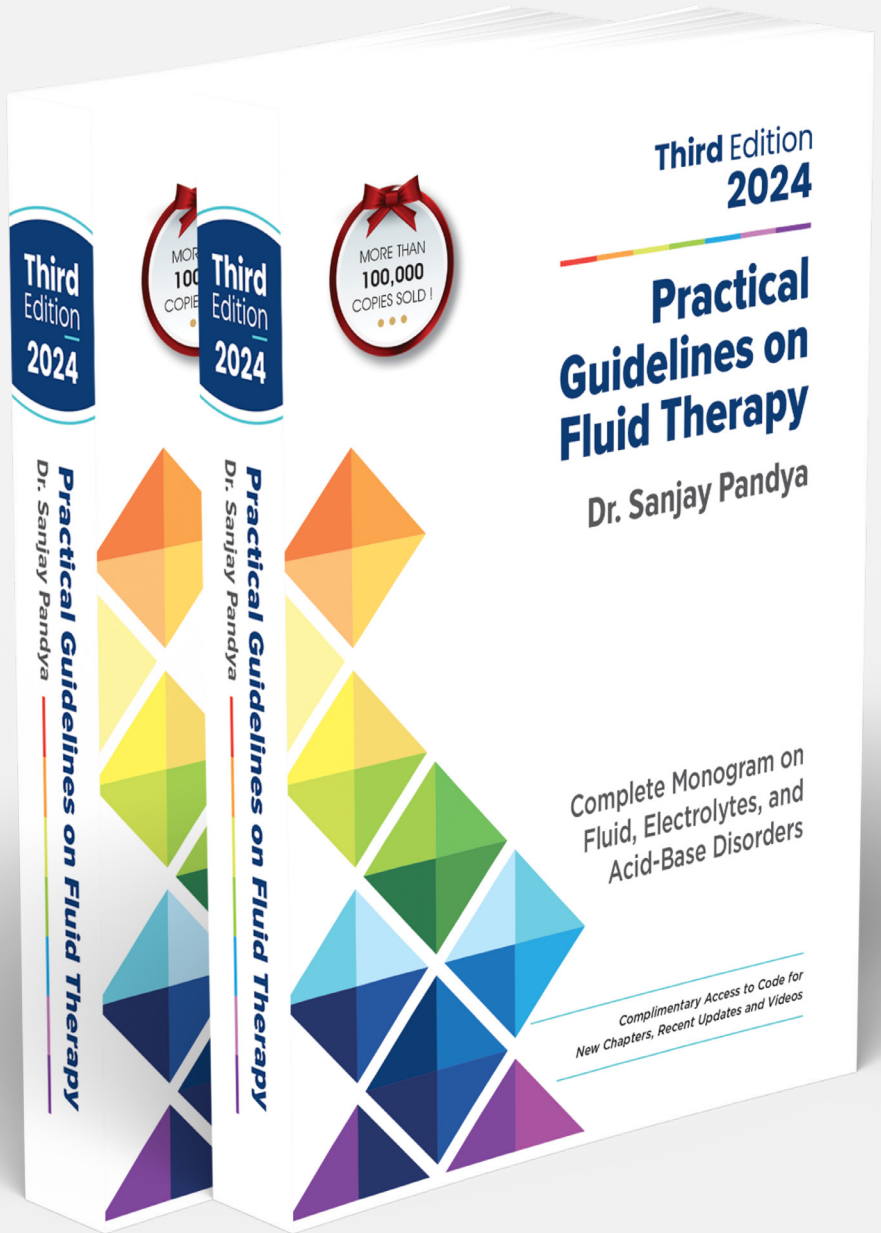
Chapter 57:

Parenteral Nutrition: Administration and Complications



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57 Parenteral Nutrition: Administration and Complications

ADMINISTRATION OF PARENTERAL NUTRITION

Parenteral nutrition (PN) is currently one of the most sophisticated forms of intravenous therapy. Appropriate use of parenteral nutrition provides life-saving treatment for patients who could not otherwise be nourished.

SELECTION OF MACRONUTRIENTS

Selecting an appropriate macronutrient mixture while administering parenteral nutrition in day-to-day practice is essential. Broad guidelines in the selection of the most suitable macronutrient solutions based on requirements for different patients are:

Indications of only dextrose containing crystalloids; avoid PN

In cases where patients are stable, not malnourished, and unable to consume oral intake for a brief period (less than a week), using PN support is unnecessary [1]. Instead, dextrose infusions (>100 gm/day in adults), electrolytes, and vitamins serve as the primary approach for short-term therapy in such individuals. Providing adequate dextrose (calculated as the daily energy requirement in kcal ÷ 3.4 = gm/day dextrose) fulfills calorie needs and helps conserve nitrogen [2].

Indications of amino acids plus dextrose-containing solutions, withhold lipid emulsion

Parenteral nutrition combining amino acids and dextrose may suffice to address nutritional needs over a short duration (less than one week) in patients who are stable and not malnourished, as long as their total caloric requirements remain relatively low. However, it is advisable to introduce lipid administration within ≤7 days of starting PN to prevent essential fatty acid deficiency [3]. Early lipid administration is also crucial for minimizing the risk of hyperglycemia resulting from high glucose intake.

Indications of PN with all three macronutrients (dextrose + amino acids + lipids)

PN solutions that incorporate all three macronutrients are widely utilized in clinical practice. The addition of lipid emulsion provides additional calories, reduces the osmolarity of the solution, and prevents essential fatty acid deficiency. PN solutions containing all three macronutrients are commonly recommended for patients:

- Those in need of PN support for prolonged period.
- Patients requiring peripheral parenteral nutrition (PPN) with significant calorie supplementation but unable to tolerate carbohydrates.
- Critically ill patients, and those with hyperglycemia, diabetes mellitus, and respiratory failure.

DELIVERING PARENTERAL NUTRITION

For proper supplementation of PN, it is essential to understand different fundamental aspects of delivering PN, as classified below:

- Routes of nutrient delivery:

  Peripheral parenteral nutrition vs. central parenteral nutrition.
- Systems of delivering PN:

  Multiple bottle system, multi-chamber-bag PN, or hospital compounded PN.
- Duration of delivering PN:

  Continuous infusion of PN vs. cyclic infusion of PN.

Table 57.1 Comparison of peripheral and central parenteral nutrition		
	PPN	**CPN**
Route of administration	Peripheral veins	Central venous access
Access site	Peripheral veins	Large peripheral veins or central veins
Location of catheter distal tips	Below the level of the axillary vein	Central circulation (usually SVC or uncommonly IVC)
Duration of therapy	less than 2 weeks	>7–14 days
Nutritional needs	Low	High
Daily caloric requirement	1000–1500	2000–3000
Daily volume need (mL)	2000–3000	1000–2000
PN osmolarity (mOsm/L)	Low (600–850)	High (>800–900)
Carbohydrate	30%	55%–60%
Fat emulsion	Major caloric source	Minor caloric source
Prerequisite	Good peripheral veins	Successful cannulation of large peripheral or central veins
Fluid permitted	No fluid restriction	Needs fluid restriction
Advantages	Easy insertion, lower risk of infection/complications	No limit to osmolality, pH, or volume of infusion
Disadvantages	Short life span, only for low osmolality infusion	Complex insertion, higher complication risk, and cost
Common complication	Thrombophlebitis of veins	Catheter sepsis

PICC: Peripherally inserted central catheter; CVCs: Central venous catheters; SVC: Superior vena cava; IVC: Inferior vena cava

A. Routes of nutrient delivery

The two routes used for nutrient delivery are peripheral parenteral nutrition, and central parenteral nutrition (CPN), which is compared in Table 57.1.

1. Peripheral parenteral nutrition

Peripheral parenteral nutrition is the frequently used method to deliver all the required nutrients through peripheral veins [4–6]. PPN aims to provide enough calories and nutrition for a short period (less than 2 weeks). PPN is generally intended when central PN is undesirable or unavailable.

Composition

The osmolarity of formulas for PPN should be less than 900 mOsm/L [7]. Formulas for PPN contain low concentrated dextrose (5–10%) and amino acids along with concentrated, calorie-dense lipids (usually 20% lipid emulsion), which can provide the patient's average basal energy and protein needs [8]. Lipid emulsion is an essential part of PPN. Lipid emulsion reduces the osmolarity of PPN because of its low osmolarity (260 mOsm/L) and therefore decreases the risk of thrombophlebitis of peripheral veins.

Prerequisite

For PPN, the peripheral vein should be readily accessible, and fluid restriction should not be an issue.

Indications [9]

- Requirements of PN for a short period

(less than a week). Postoperative patients requiring PN support are the most suitable candidates for PPN.

- Nutritional needs <1500–1800 kcals per day.
- Central venous catheter insertion is not possible, carries a high risk, or is contraindicated (e.g., patients with coagulopathy).
- Sepsis or bacteremia in patients with CPN to avoid central vein catheterization for a few days.

Contraindications

- In patients with high nutritional requirements (i.e., hypermetabolism, preexisting moderate to severe malnutrition, or high risk of protein depletion), PPN is not suitable, as it cannot provide enough nutrients.
- Patients who need fluid restriction (oliguric patients and edematous patients due to cardiac, hepatic, or renal failure).
- Critically ill patients who will not tolerate the high fluid volume of PPN required for providing their increased nutritional needs.
- If PPN does not allow complete nutritional requirements, PN should be administered centrally.
- If PN is required for a prolonged period (>2 weeks).

Advantages

- Easy and safe venous access.
- It avoids morbidity and risks of CPN and saves the cost of a central catheter.

Disadvantages

- Larger volume is required to provide even maintenance nutritional requirements.
- Difficulty in meeting high nutritional requirements (because the volume required to provide the same is prohibitively high in sick patients).
- The concentration of nutrients in peripheral parenteral nutrition is kept low to prevent thrombophlebitis of peripheral veins. So, a larger volume is required to meet the nutritional needs compared to central parenteral nutrition formulas.

Prevention of thrombophlebitis due to PPN

Various measures, which can prevent or reduce thrombophlebitis, are:

- Add heparin (1U/ml of total volume) and low-dose hydrocortisone to the PPN formulas [10, 11].
- Place a glycerine trinitrate transdermal patch on the skin overlying the tip of the IV catheter.
- Topical NSAID creams and gel may inhibit the local inflammatory response.
- Limiting the osmolarity of PPN to 600 mOsm/L.
- Chang peripheral lines every 72–96 hours.

2. Central parenteral nutrition

Central parenteral nutrition is the most effective method to deliver high concentration PN in a smaller volume into large diameter central veins (usually superior vena cava or uncommonly inferior vena cava) in patients who needs PN for >7–14 days. It is important to remember that the location of the distal tip determines central versus peripheral venous access and not the site of catheter insertion. When the distal end is located in the large-diameter central vein, administered hypertonic and acidic PN solutions mix quickly with surrounding turbulent blood flow and therefore avoid complications due to the local irritation of veins such as thrombophlebitis.

Goals and indications

The goal of CPN is to provide nutritional maintenance requirements and correct existing nutritional deficits. CPN is mandatory to provide long term PN support (weeks, months, or years) when volume and concentration of solution preclude peripheral administration (i.e., osmolarity exceeds 800–900 mOsm/L, pH <5 or pH >9, or fluid restriction is necessary), and to provide greater nutritional requirements to moderately to severely stressed patients [12].

Composition

As per patients' requirements, the composition of solutions for CPN varies. Most of the CPN solutions contain a higher concentration of dextrose (50–70%) and amino acids (8.5–10%), which makes these solutions hypertonic (osmolarity of CPN 1000–1900 mOsm/L as compared to plasma osmolarity 280 mOsm/L). These hypertonic CPN solutions are too irritant for a peripheral vein and should be infused only through central venous access. For safe and adequate delivery of CPN, it is essential to establish central vascular access with proper selection of the type of catheter and the site of insertion.

CPN permits the administration of a lower amount of fat emulsion than PPN because a higher concentration of dextrose and amino acids in CPN provides a significant amount of calories.

Selection of catheter for CPN

For CPN, a catheter made up of polyurethane and silicone is used routinely. Catheters made up of polyurethane are selected for short-term and medium-term use [12]. The advantage of polyurethane catheters is decreased catheter breakage but has a greater risk of thrombosis and catheter-related infection [13–15]. Silicon rubber catheter is preferred for long term or life-long PN therapy because of the reduced risk of thrombosis and infection, and is appropriate for using ethanol locks (to prevent bloodstream infections), but has decreased mechanical stability [14, 16]. Antimicrobial impregnated central venous catheters are superior in reducing central venous catheter-related bloodstream infection (CRBSI) [17].

Sites for insertion of a catheter for CPN

Short-term central access: Central venous access through a percutaneous non-tunneled catheter is commonly used and preferred for patients in the acute care setting for short duration therapies (<14 days) [12, 18]. In this method, the catheter is placed via the Seldinger technique into the internal jugular, subclavian, or femoral veins. For CPN, an upper body insertion site is preferred, and femoral vein catheterization is discouraged because of the higher risk of infection and thrombotic complications [19, 20].

This approach has the advantage of easy insertion, lesser cost, and better patient comfort and mobility for the short-term need. However, when the patient needs central venous access for the long-term PN, avoid this modality due to a higher risk of infection.

Percutaneous inserted central catheter (PICC): A 50–60 cm long polyurethane catheter is inserted in a peripheral vein in the antecubital area of the arm (cephalic or basilic vein) and threaded into the subclavian vein in such a way that the catheter tip is placed in the lower portion of superior vena cava or right atrium.

The use of PICCs is preferred in adult patients for short-term and medium-term PN (usually more than 2 weeks or less than six months) [21–24].

The use of PICCs has grown substantially in recent years because they are convenient, carry a low risk of placement-related complications, and are long-lasting and cost-effective.

The use of PICCs has grown substantially in recent years because it is convenient, low risk of placement-related complications, long-lasting and cost-effective [18, 25]. However, PICCs are associated with a higher risk of catheter-related venous thrombosis [18, 24, 26–28]. The PICCs are also associated with a higher risk of catheter-related bloodstream infection [18, 22, 29, 30], but the supporting evidence is insufficient [24, 25, 31–33].

While using PICC, to reduce the risk of infection, use the sutureless device and secure the catheter (to prevent migration of catheter) by subcutaneously anchored stabilization device [24, 34].

Long-term central access: "Tunneled" catheters (such as Hickman, Broviac, Hohn, or Groshong) and implanted subcutaneous ports are more stable, acceptable, and safe for patients who need PN for medium or long-term use (e.g., >3 months-years) [12]. The tunneled device is preferred in patients who require daily or routine access for long term PN [23, 35]. Implanted ports are cosmetically more desirable, have lower rates of infection [36], and are preferred when the need for access is less frequent (e.g., medication like chemotherapy) but rarely used for PN due to the requirement of venous access regularly [35].

"Tunneled" catheters are usually placed in the subclavian or internal jugular vein, with the distal tip positioned in the lower portion of the superior vena cava. After exiting from great veins, the "Tunneled" catheter traverses for about 10 cm under the skin in the subcutaneous tunnel, with the external portion of the catheter lying on the anterior chest wall.

The femoral vein is not preferred and usually avoided for long-term central access for PN due to the high risk of infection at the exit site (at the groin) and an increased risk of venous thrombosis [12]. A subcutaneous tunnel is created, so the catheter exits from the skin several inches away from the venipuncture location.

The tunnel acts as a barrier and reduces the risk of infection substantially. The dacron cuff around the catheter is positioned in the subcutaneous tissue 2 to 3 centimeters from the exit site, stabilizing the catheter and acting as a mechanical barrier limiting bacterial entry and preventing ascending microbial infection [16].

Methods used to confirm the catheter tip position are chest radiography, fluoroscopy, point-of-care transthoracic echocardiography, or continuous electrocardiography [19, 37, 38]. In addition to accurately assessing the position of the tip of the catheter, a post-procedure chest X-ray also detects pneumothorax, malpositions, and kinking [39].

The central line must be handled with a strict aseptic technique for safe use, and the single-lumen catheter is preferred to prevent infection. Use a central line exclusively for administering PN and avoid its usage for administering of IV solutions or medications, blood sampling, and central venous pressure (CVP) monitoring.

B. Systems of delivering parenteral nutrition

Three different systems used for delivering parenteral nutrition are a "multiple bottle" system, commercially available multichamber bags parenteral nutrition (MCB-PN), and hospital compounded parenteral nutrition.

1. Multiple bottle system

In the past, separate bottles were used to infuse individual substrates (carbohydrates, lipids, and amino acids) for PN [40, 41]. The advantages of multiple

bottle systems are lower cost, flexibility, and ease of making adjustments in PN composition, particularly in critically ill patients with rapidly changing requirements [42].

Disadvantages of multiple bottle system are [40, 42]:

- Frequent manipulations during administering PN through multiple bottle systems carry a greater risk of nosocomial infections.
- Adjustment of different flow rates for different nutrients, adding different minerals and vitamins, and monitoring hyperglycemia, hypertriglyceridemia, and electrolyte disorders in each patient are cumbersome and are not without frequent mistakes.
- Simultaneous administration of various nutrients without maintaining proper proportion carries the risk of physicochemical incompatibilities.
- When costs of disposables and time spent by the nurse for administration of PN are considered, a multiple bottle system is costlier than commercially available multichambered PN formulations [43].

2. Multichamber-bag PN (MCBPN)

These products are standardized, easy-to-use nutrient mixtures, commercially available as two or three-chamber bags. Two-chamber bag systems ("2CB" or 2 in 1 formulation) contain dextrose and amino acids with or without electrolytes. Three-chamber bag systems (all-in-one admixture (AIO), "Three in One" system, 3 in 1 formulation) contain dextrose, amino acids, and lipid injectable emulsion (ILE), with/without electrolytes.

The advantages of three multichamber-bag PN products are:

- Convenience: The easy, convenient, and most preferred way for the single-line administration of PN. As all nutrients are available in a single container (referred to as premixed, "ready-to-use" commercial bags), it saves time and reduces the workload [44, 45].
- Less infection: Decrease bloodstream infection rates due to less handling during preparation and delivery (reduced connections and reduced need of changing bags) [46–49].
- Safer: Lesser chances of various calculations and compounding human errors and better stability and sterility as manufactured with high standards [44, 45, 50].
- Recommended standard practice: SCCM-ASPEN guidelines (2016) and other literature recommend using standardized commercially available PN formulations compared to compounded PN admixtures when the formulation meets the patient's metabolic needs [1, 51, 52].
- Lower cost: Cost-saving during preparation, handling, and delivery (requiring fewer bags and tubings and no extra pump for lipid emulsion) [40, 49, 53–55].
- Due to slow continuous infusion, better assimilation, and utilization of nutrients with lesser chances of metabolic complications.
- Storage is more convenient with long shelf life [44].

Disadvantages of Multichamber-bag PN are:

- Lack of flexibility: Changes in composition/proportion of contents are not possible.
- Inappropriate overuse due to easy commercial availability of different formulations with a wide choice.
- Absence of transparent color: Due to the presence of lipids, three in one

solution is opaque, which impairs visual inspection of the solution for particulate matter, precipitation, or fungal growth.

3. Hospital compounded PN admixture

This PN formulation containing various nutrients is designed to meet the nutritional needs of specific clinical conditions. Aseptic tailormade compounding of PN admixture in a hospital needs a sophisticated manufacturing system and skilled pharmacists, so its availability is problematic. The use of personalized hospital compounded PN is decreasing because of multiple limitations [56–59] and a greater risk of sepsis [60].

C. Duration and mode of delivering parenteral nutrition

Two methods used for administering PN include continuous infusion of PN and cyclic infusion of PN.

1. Continuous parenteral nutrition

Parenteral nutrition infuses over 24 hours continuously at a constant rate by a pump. Continuous PN is the most common regimen used for acute, critical, and hospitalized patients. Slow continuous infusion of PN by infusion pumps avoids volume overload and side effects secondary to rapid administration of carbohydrates and lipids (such as hyperglycemic and triglyceridemia), allows better utilization of nutrients, and provides nutritional requirements throughout the day. Drawbacks of this modality are poor mobility due to attachment to the pump and increased risk of fatty liver due to continuous high insulin levels.

2. Cyclic/intermittent parenteral nutrition

Cyclic/intermittent PN is the method in which PN is infused at a higher rate over 10 to 14 hours (typically at night when the patient is sleeping) and then stopped [61]. Cyclic PN improves the quality of life, decreases the incidence of hepatobiliary complications, and may limit or reverse PN-associated liver dysfunction [62–64]. In addition, this regimen allows for a 10 to 14 hour break each day from the pump, enabling the person to engage in normal daily activities. Cyclic PN should be attempted cautiously in the presence of glucose intolerance, edema, or fluid tolerance and is not suitable for critically ill patients [52]. However, cyclic PN is effective and safe for stable, chronically ill patients who require long-term nutrient support (e.g., home parenteral nutrition) [65].

DESIGNING PARENTERAL NUTRITION FORMULA

PN is a high-alert medication, and planning appropriate and safe prescriptions for the individual is complex. The parenteral nutrition formula can be designed by following steps:

Step 1: Calculate the daily nutritional requirements and convert them into a prescription.

Step 2: Choosing the appropriate commercially available formula for the infusion.

Step 1: Calculate the daily nutritional requirements and convert them into a prescription

The first step in preparing a PN prescription is to calculate the daily nutritional requirements. It is essential to conduct

a comprehensive evaluation of the patient and take into account all the factors that influence these requirements (refer to Table 57.2) to determine these requirements.

Sample calculation of the daily requirements of energy, protein dextrose, and lipids with consideration of fluid for a 60 kg patient, who is stable, euvolemic with good urine output and moderate stress is summarized below:

- Fluid requirement: Approximately 35 mL/kg.

  So, 35 (mL/kg) × 60 (kg) = 2100 ml/day.
- Caloric requirements: Approximately 25 kcal/kg.

  So, 25 (kcal/kg) × 60 (kg) = 1500 kcal/day.
- Protein requirements: For stable patients, 1 gm/kg body weight.

  So, 1 (gm/kg) × 60 (kg) = 60 gm/day.

  1 gm of protein provides 4 kcal, so 60 gm of protein will provide 60 × 4 = 240 kcal.
- Lipids requirements: 30% of total calories.

  So, 30% of 1500 (kcal/day) = 450 kcal.

  1 gm of fat provides 9 kcal, so to provide 450 kcal, 450/9 = 50 gm of fat will be required.
- Carbohydrate requirement:

  Total caloric requirements minus the sum of protein and fat calories.

  So, 1500 – (240 + 450 kcal) = 1500 – 690 = 810 kcal.

  1 gm of dextrose in solution provides 3.4 kcal. So to provide 810 kcal, 810/3.4 = 238 gm of dextrose will be required.

So, the total daily requirement of the patient is 2100 ml fluid volume, a total calorie requirement of 1500 kcal, 60 gm of amino acids, 50 gm of fat, and 238 gm of dextrose. In addition, electrolytes, trace elements, and vitamins should be added as per requirement.

Step 2: Choosing the appropriate commercially available formula for the infusion

According to the prescription, the PN solution is prepared either in a hospital pharmacy or a commercially available formula that best matches the prescribed nutrients is chosen for administration. Micronutrients are coadministered in the proper dose.

PN solution is prepared in hospital pharmacies only for a limited number of patients due to lack of facilities, higher risk of sepsis, and no advantage in clinical outcomes [1]. Due to these limitations, standardized commercially available PN products are widely used and preferred over tailormade hospital compounded PN solutions.

One or more commercially available readymade PN solutions that closely

Table 57.2 Factors determining PN requirements

• Weight of the patient
• Clinical status: stable or critical
• Medical or surgical conditions for which PN is indicated
• Nutritional status/malnutrition, volume status, urine volume
• Coexisting disorders (diabetes, hypertension, congestive heart failure, renal disorders, liver diseases, pulmonary diseases, sepsis, etc.)
• Electrolyte and acid base status

match the prescription are selected.

The volume of fluid permitted to the patient and the concentration of nutrients in the PN solution are inversely proportionate. Select a PN solution with a greater concentration of various nutrients if the patient needs fluid restriction (e.g., central PN). When the patient needs PN, and a larger fluid volume is permitted, a PN solution with a low concentration of nutrients (e.g., in peripheral PN) is selected.

Various commercially available PN products and their classification based on their composition and routes of administration (peripheral vs. central venous access) are summarized in Table 57.3 and Table 57.4. In addition, the classification of various lipid emulsion products based on their lipid source is summarized in Table 57.5. A summary of commercially available PN products in these tables can assist clinicians in selecting PN solutions quickly and accurately.

Table 57.3 Commercially available products for peripheral PN and their composition

Solution	Manufacturer	Volume (ml)	Calorie (kcal)	Osmolarity mOsm/L	Dextrose (gm)	Amino acids (gm)	Lipids (gm)
Amino acid containing solutions							
Aminosyn-PF 7%	Hospira	500	140	561	-	35	-
Aminoven 5%	Fresenius Kabi	500	100	490	-	25	0
Aminoven infant 10%	Fresenius Kabi	100	4	885	-	10	0
Amino acid and dextrose containing double chamber bag							
Aminomix peripheral	Fresenius Kabi	1000	390	770	63	35	-
Aminosyn II 4.25%/10%	Pfizer/Hospira	1000	483	894	100	42.5	-
Clinimix 4.25/10	Baxter	1000	510	930	100	42.5	-
Nutriflex peri	B Braun	1000	480	900	80	40	-
Lipid emulsions							
Intralipid 10%	Fresenius Kabi	500	550	260	-	-	50
Intralipid 20%	Fresenius Kabi	500	1000	260	-	-	100
Lipofundin MCT/ LCT 20%	B Braun	500	954	380	-	-	100
Clinolipid 20%	Baxter	500	1000	270	-	-	100
Lipoplus	B. Braun	500	955	410	-	-	100
SMOFlipid 20%	Fresenius Kabi	500	1000	270	-	-	100
Amino acid, dextrose and lipid containing triple chamber bag							
Kabiven peri	Fresenius Kabi	1440	1000	750	97	34	51
Nutriflex lipid peri	B Braun	1000	765	840	64	32	40
PeriOlimel N4	Baxter	1000	700	760	75	25.3	30
Smofkabivan peri	Fresenius Kabi	1448	1000	850	103	46	41

Table 57.4 Commercially available products for Central PN and their composition							
Solution	**Manufacturer**	**Volume (ml)**	**Calorie (kcal)**	**Osmolarity mOsm/L**	**Dextrose (gm)**	**Amino acids (gm)**	**Lipids (gm)**
Amino acid containing solutions							
Aminoven 10%	Fresenius Kabi	1000	400	999	-	100	-
Aminosyn 10%	Hospira	1000	400	938	-	100	-
FreAmine 10%	B Braun	1000	388	950	-	97	-
Travasol 10%	Baxter	1000	400	999	-	100	-
Amino acid and dextrose containing double chamber bag							
Aminomix Novum	Fresenius Kabi	1000	1000	1779	200	50	-
Aminosyn II 4.25%/20%	Pfizer	1000	850	1295	200	42.5	-
Clinimix 8/10	Baxter	1000	663	1308	100	80	-
Nutriflex plus	B Braun	1000	792	1400	150	48	-
Amino acid, dextrose and lipid containing triple chamber bag							
Kabiven	Fresenius Kabi	1026	872	1060	100	34	40
Nutriflex lipid plus	B Braun	1250	1265	1540	150	48	50
Olimel N9/ Triomel N9	Baxter	1000	1070	1170	110	56.9	40
Smofkabivan	Fresenius Kabi	986	1100	1500	125	50	38

Table 57.5 Commercially available lipid emulsion products and their composition							
Lipid source	**Product**	**Manufacturer**	**Soybean oil**	**MCT oil**	**Olive oil**	**Fish oil**	**ω-6: ω-3 Ratio**
Soybean oil-based	Intralipid Ivelip Lipofundin N Liposyn III	Fresenius Kabi Baxter B Braun Hospira	100%	-	-	-	7:1
SO/MCT-based	Lipofundin MCT/LCT	B Braun	50%	50%	-	-	7:1
	Structolipid	Fresenius Kabi	64%	36%	-	-	7:1
Olive oil-based	ClinOleic Clinolipid	Baxter Baxter	20%	-	80%	-	9:1
Fish oil containing emulsions	Lipoplus (Lipidem)	B Braun	40%	50%	-	10%	3:1
	SMOFlipid	Fresenius Kabi	30%	30%	25%	15%	2.5:1
	Omegaven	Fresenius Kabi	-	-	-	100%	1:8

INITIATION OF PN

- It is essential to evaluate the patient's nutritional status by careful history, physical examination, and laboratory studies before initiation of PN.
- PN may be initiated in hemodynamically stable patients who can tolerate the fluid volume. Correct electrolyte abnormalities and hyperglycemia before the initiation of PN.
- PN should be initiated slowly (no more than 50% of the calculated requirements on the first day) to avoid adverse effects like hyperglycemia and electrolyte disturbances [66]. PN is increased gradually over 4 to 7 days to achieve the nutrition goal.
- PN may precipitate refeeding syndrome in severely malnourished patients due to rapid fall in potassium, magnesium, and phosphorus levels. So slow initiation and close monitoring of the patient's electrolytes is necessary to avoid adverse effects on cardiac and respiratory function.

Care of PN mixture

- Store reconstituted PN bags in a refrigerator until 30 min before using.
- Always examine the PN solution before administration to exclude particulate matter, cloudiness, or an oily layer in the bag.
- Follow strict aseptic techniques while connecting and administering PN.
- To administer dextrose/amino acids PN formulations, use an infusion set with an in-built air vent and a 0.22-micron filter [52]. For administering lipids containing PN formulations, use a 1.2 micron - larger sized filter to avoid clogging of the filter.
- Do not use a three-way stopcock as it increases the risk of infection.
- Do not insert a needle for air venting in a PN bag.
- Do not add any medication to the PN bag.
- Do not allow the PN solution to hang for more than 24 hours.
- Do not use the PN line to draw blood for the test, administer medications, or measure central venous pressure.

MONITORING OF PN

Every patient receiving PN should be monitored carefully for the prevention or early detection of complications and to judge the effectiveness of therapy. Meticulous monitoring is aimed at monitoring, detecting, or assess:

- Metabolic status, including hyperglycemia and hypoglycemia.
- Risk of refeeding syndrome or clues of overfeeding.
- Micronutrient deficiency and toxicity.
- Fluid and electrolytes status.
- Catheter-related complications, including sepsis.
- Hepatic and other long-term complications.

A clinical data and laboratory study used routinely for monitoring patients receiving PN is summarized in Table 57.6:

- Always obtain a chest X-ray to check catheter placement after insertion.
- Record vital signs at least every 4 hours. Temperature elevation is one of the earliest signs of catheter-related sepsis.
- Patients should be weighed daily at the same time each morning after voiding on the same scale. Weight gain may indicate fluid overload.
- Perform site care and dressing change at least three times weekly or whenever the dressing becomes wet.

Table 57.6 Monitoring the patient on parenteral nutrition			
Clinical data monitoring			
History: Focused on patient's sense of well-being, strength to perform routine activities, fever, and medical history for signs of fluid overload or glucose and electrolyte imbalance.			
Vital signs: Monitor temperature, pulse, blood pressure, and respiratory rate.			
Fluid balance: Strict input/output chart, daily weight, and signs of fluid overload or dehydration.			
Local care: Inspecting and dressing vascular access site (to rule out infection).			
Delivery system: Inspection of solution for contamination and watch for the proper functioning of infusion pump, catheter function, and timely changing of tubing and bags.			
Monitoring of laboratory data during PN			
Parameter	**Baseline and initial period**	**Stable period**	**Long term**
Blood glucose	6 hourly	1–2 times/ week	Monthly
BUN, creatinine, electrolytes, HCO_3, PO_4, Ca^{2+}, Mg^{2+}	Daily	Weekly	Monthly
CBC, liver function test (LFT), triglycerides, PT	Weekly	Weekly	Monthly
Micronutrient tests, as indicated			

- Patients receiving PN should be monitored carefully to detect early signs of complications such as fluid overload, electrolyte imbalances, nutritional problems, or allergic reactions.
- Monitor serum glucose levels every 6 hours initially, then once a day. Watch for the symptoms of hyperglycemia, such as thirst and polyuria. Maintain blood glucose <180 mg/dL [1, 67].
- Monitor renal function, electrolyte levels, liver function, phosphate, calcium, and magnesium daily in the first week of initiating PN. Once the patient is stable, these tests are performed once or twice a week and less frequently in the long term.
- Monitoring response to nutritional therapy. There is no single criterion that can reliably indicate the effectiveness of PN. Improvement in clinical status and visceral protein concentrations (e.g., albumin, prealbumin, and transferrin) are most commonly used to monitor nutritional status. When interpreting visceral protein values, it is essential always to consider the patient's fluid status, organ function, and presence of infection. If nutritional recovery is inappropriate, a nitrogen balance study may guide changes in amino acid intake. Similarly, if traditional methods of calculating calorie requirements are unsatisfactory, indirect calorimetry is indicated.
- If the patient receiving PN develops fever, chills, or hypotension, its most common cause is a catheter-related bloodstream infection. Therefore, for diagnosis of CRBSI, blood cultures should be drawn immediately before initiating antibiotic therapy.

TERMINATION OF PN

- PN is the temporary method of nutritional supplementation. The ultimate goal is slow and smooth transit from PN to oral/enteral food intake once the gastrointestinal function returns.
- During the transition period, discontinue PN when the patient can tolerate

60–70% of the total nutritional requirements orally or enterally.

- If the patient cannot tolerate oral or enteral supplementation and intake is less than 60% of nutritional requirements, restart PN in 2–3 days.
- Plan a gradual transition from PN to oral or enteral nutrition to avoid overfeeding during the phase of reduction of PN and worsening of nutritional status when PN is discontinued.
- If there is a need for abrupt discontinuation of PN, administer 10% dextrose for a few hours to prevent hypoglycemia.
- After discontinuing PN, monitor blood glucose closely for several hours to detect hypoglycemia.
- During the transition period, closely and carefully monitor clinical status, hydration status, weight, and laboratory tests.

COMPLICATIONS OF PARENTERAL NUTRITION

The primary complications of parenteral nutrition include mechanical, metabolic, and infectious complications. However, most complications are reduced with careful management and supervision by an experienced nutritional support team. Commonly encountered complications are summarized in Table 57.7.

MECHANICAL COMPLICATIONS

Potential mechanical complications related to central venous catheter placement are malposition of the catheter, pneumothorax, hemothorax, arterial injury, thoracic duct injury, nerve injury, air embolism, cardiac arrhythmia, and cardiac perforation with tamponade.

Table 57.7 Complications of PN

	Mechanical	Metabolic/GI	Infectious
First 48 hours	Malposition, Haemothorax Pneumothorax Chylothorax Air embolism, Cardiac arrhythmia Injury to the subclavian/carotid artery	Fluid overload Hyperglycemia Hypophosphatemia Hypokalemia Hypomagnesemia Refeeding syndrome	-
First two weeks	Catheter displacement Catheter thrombosis Catheter occlusion Air embolism	Hyperglycemic coma Acid base imbalance Electrolyte imbalance	Catheter induced sepsis Exit site infection
Three months induced onwards infection	Fracture or tear of the catheter Catheter thrombosis Air embolism Blood loss	Essential fatty Acid deficiency Vitamin or trace element Deficiency PN metabolic Bone diseases PN liver diseases	Tunnel infection Catheter Sepsis Exit site

Ultrasound-guided central venous catheter insertion by trained and experienced personnel can reduce mechanical complications significantly [68].

Post subclavian and jugular CVC insertion, chest X-ray in the upright or semi-upright position is helpful to exclude malposition of the catheter, pneumothorax, or hemothorax and confirm the correct tip position (in the inferior third of superior vena cava or at the junction of the superior vena cava and the right atrium, parallel to the vessel wall). Avoid excessive advancement of a catheter because the tip of the CVC in the cardiac chamber carries the risk of cardiac arrhythmia. It is also important to avoid the inadequate length of insertion because the infusion of high osmolarity PN solutions with a catheter tip at a higher level can cause direct damage to the vein (thrombophlebitis) [69].

The osmolarity of PN solutions is three to eight times the normal serum osmolality. PN with high osmolarity in the long term can cause injury to endothelium and vein wall inflammation with resultant upper extremity deep venous thrombosis.

Most patients are asymptomatic, but swelling of the neck or arm with erythema, tenderness, and warmth is the common presentation in a few patients [70].

Catheter-related thrombosis is treated primarily with anticoagulation, and thrombolytic therapy is offered in selected patients having a high risk of thrombosis [71]. Removal of the catheter is recommended in catheter-related thrombosis if the catheter is non-functional or not needed, anticoagulation is contraindicated, inadequate improvement in symptoms with anticoagulation, or the thrombosis is limb or life-threatening [70, 71].

CATHETER-RELATED BLOODSTREAM INFECTION

In patients receiving CPN, catheter-related bloodstream infection (CRBSI) is the most common and serious complication that increases hospital stay and cost and is associated with significantly high morbidity and mortality.

In most cases, it is preventable with proper aseptic techniques and is often related to non-adherence to aseptic techniques, suboptimal catheter care, and inadequate patient education.

The upper body insertion site (internal jugular or subclavian vein) is preferred over the femoral site to reduce the risk of infection [19].

CRBSI is usually caused by the migration of skin organisms at the catheter exit site for short-term catheters and direct contamination of the catheter or catheter hub in long-term CVC [72].

The risk of line infection can be minimized by:

- Strict asepsis when handling (connecting/disconnecting) the line.
- Single-lumen central venous catheters should be dedicated solely to the infusion of parenteral nutrition.
- Use of a dedicated lumen on a multiple lumen CVC or a PICC line for administration of PN.
- Use of antibiotic-coated or antibiotic-impregnated catheters.

Fever in a patient with no other identifiable infection source raises suspicion of catheter-related infection. Staphylococcus and candida are the most frequent pathogens. Whenever catheter-related sepsis is suspected, the following steps should be considered:

- Evaluate the catheter insertion site and culture any drainage.

- Obtain blood cultures: For diagnosis of CRBSI, blood cultures should be drawn from each lumen of the catheter and two sets of blood cultures from peripheral veins via separate venipuncture sites before initiating antibiotic therapy [73]. Catheter tip cultures cannot be used as a substitute for blood cultures to confirm catheter-related bloodstream infection [74, 75].
- Begin empiric antibiotic therapy:

  In uncomplicated patients, it is unnecessary to remove the CVC. Instead, treat CRBSI immediately by administering broad-spectrum antibiotics through the lumen to salvage the catheter.

  It is unnecessary to remove the CVC in uncomplicated patients and treat CRBSI immediately by administering broad-spectrum antibiotics through lumen for catheter salvage.
- Remove catheter: Indications of catheter removal are [76]:
  - Tunnel and pocket infections.
  - Clinical deterioration, septic shock, or presence of severe complications such as endocarditis, septic thrombosis, or abscess formations.
  - Repeated positive blood culture besides antibiotic therapy.
  - Although guidewire exchange has a lower risk of technical complications, it is not recommended as an alternative approach to removal.

METABOLIC COMPLICATIONS

The most common problems caused by PN are hyperglycemia, fluid overload, electrolyte imbalances, refeeding syndrome, and hepatobiliary complications. Therefore, proper monitoring and adjustments in the composition and rate of PN are essential to reduce the metabolic complications caused by PN.

A. Hyperglycemia

Hyperglycemia occurs in more than half of patients receiving PN [77, 78] and is associated with increased hospital complications and mortality [77, 79].

The risk factors for hyperglycemia are excess and rapid administration of dextrose, obesity (BMI>25 kg/m2), preexisting diabetes mellitus or liver impairment, hyperglycemia before starting PN, surgical indications of PN, corticosteroid use, presence of infection, and critical illness [78, 80, 81]. Hyperglycemia in a previously normoglycemic patient should also raise suspicion of infection.

Hyperglycemia is the greatest danger from PN during the first 24 hours. It may lead to osmotic diuresis and glycosuria, leading to excessive excretion of free water by the kidney, thus causing hyperosmolar nonketotic dehydration, coma, and even death. Therefore, it is best treated by prevention.

As blood glucose values above 180 mg/dL are associated with a higher incidence of complications [77], the current recommendation is to keep glucose concentration 140–180 mg/dL [82–85].

Various insulin regimens used to control hyperglycemia in patients receiving PN are [86]:

- **Continuous intravenous insulin infusion:** Ideal for unstable and critically ill patients receiving PN requiring maximal flexibility in dose modifications.
- **Insulin added to PN:** Directly adding insulin to the parenteral nutrition bag is a convenient and physiologically favorable method to treat

hyperglycemia, particularly in general wards where separate IV insulin administration may not be feasible. However, this method is inappropriate in unstable patients and increases the risk of infectious complications.

- **Insulin added to PN and supplemental subcutaneous insulin using a sliding scale:** This regimen is widely used for non-critically ill T2DM patients and provides better glycemic control after PN interruption [87].
- **Subcutaneous insulin injection:** This regimen is useful in stable patients on PN before discontinuation of IV insulin for transitioning from IV to subcutaneous insulin administration.

Measures to prevent hyperglycemia during PN administration

- Do not overfeed the patient (starting dose less than 20–25 kcal/kg/d).
- Restrict dextrose in PN to 100–150 gm/day initially and administer it slowly (2–3 mg/kg/minute).
- Increase the portion of lipid administration if needed (to supply calories and to limit the required dextrose).
- Consider other sources of IV dextrose such as peritoneal dialysis solution, antibiotic drips, etc.
- Monitor blood glucose closely (every 4–6 hours) and increase insulin doses accordingly.

B. Hypoglycemia

Although the incidence of hypoglycemia is low among hospitalized patients receiving PN, it needs careful attention because of its detrimental consequences [88, 89].

PN associated hypoglycemia may be a consequence of:

- Overtreatment of hyperglycemia with the use of insulin via PN, IV infusion, or subcutaneous injection. The risk of hypoglycemia is higher when insulin is administered by drip.
- "Rebound hypoglycemia" after abrupt discontinuation of PN formulations (e.g., cyclic infusion of parenteral nutrition) [65].

Patients prone to develop hypoglycemia are advanced age, poor nutritional status, previous history of diabetes, renal failure, liver disease, ICU patients, patients on long-term PN, insulin administered by drip, and inadequate monitoring [88].

Measures to prevent hypoglycemia are:

- Slow tapering: Before discontinuing of the PN, tapper down infusion at half the rate for 1–2 h to reduce the risk of rebound hypoglycemia.
- If PN infusion needs to be discontinued abruptly, administer dextrose-containing fluid for about 1 or 2 hours to avoid the risk of hypoglycemia.
- When insulin is added to the PN solution, the risk of hypoglycemia is low on abrupt discontinuation of PN.
- As aggressive treatment of hyperglycemia to achieve tight blood glucose control carries the risk of hypoglycemia, a target blood glucose in the range of 140–180 mg/dL is recommended to reduce the incidence of hypoglycemia [82].
- Close monitoring of blood glucose and meticulous adjustment of insulin dosage (avoid higher insulin to dextrose ratio in PN).

C. Refeeding syndrome

This is a potentially serious but often neglected condition that can occur due to shifts of fluid, electrolytes, metabolic, and vitamin disturbances during re-initiation of nutritional therapy in patients with malnutrition or prolonged fasting. It can

cause significant morbidity and even mortality.

Common high-risk factors for refeeding syndrome are [90, 91]:

- Severe malnutrition, BMI less than 18.5 kg/m2, recent weight loss (>10% within the last 3–6 months), poor or no nutritional intake for more than 5 days.
- Alcoholism abuse, anorexia nervosa, depression, bariatric surgery, bowel resections, malabsorption, insulin, chemotherapy, antacids, or diuretics.
- Low baseline levels of phosphate, potassium, or magnesium.

Pathophysiology: Refeeding syndrome is related to the shift from the catabolic to the anabolic metabolic pathways, which occurs with the reintroduction of glucose (refeeding) after a prolonged phase of starvation [92].

During the starvation (catabolic) period, the body adapts to less carbohydrates; fat becomes the primary source of energy requirements, and levels of blood glucose and insulin decline.

Prolonged fasting leads to severe depletion of intracellular phosphate, potassium, and magnesium and deficiencies of various vitamins, including thiamine.

The initiation of carbohydrate-containing nutrition leads to a rise in blood glucose levels, which in turn causes a rapid increase in insulin secretion.

Endogenous insulin surge causes massive shifts of phosphorus, potassium, and magnesium intracellularly, leading to severe hypophosphatemia, hypokalemia, hypomagnesemia, and potentially lethal complications. Hypophosphatemia is the hallmark of the syndrome.

Thiamine requirements increase significantly during the nutritional replenishment, so in the state of thiamine deficiency, re-initiation of feeding can cause metabolic acidosis and neurologic abnormalities (i.e., confusion, Wernicke's encephalopathy or dry beriberi) or cardiovascular complications (i.e., peripheral edema, congestive heart failure, or wet beriberi). In addition, thiamine is an essential coenzyme in carbohydrate metabolism. Therefore, glucose is converted to lactate instead of adenosine triphosphate (ATP) via the Krebs cycle, causing lactic metabolic acidosis when thiamine is lacking.

Clinical features: Symptoms generally appear within the first 2–5 days of initiating nutritional therapy, and it's highly variable, ranging from mild to severe and life-threatening, depending on the severity of malnutrition and comorbidities [92]. The clinical symptoms of the refeeding syndrome are nonspecific and chiefly due to underlying hypophosphatemia, hypokalemia, hypomagnesemia, sodium retention, and thiamine deficiency:

- Cardiovascular: Fluid overload, congestive heart failure, arrhythmias, bradycardia/tachycardia, and hypotension.
- Respiratory: Respiratory failure, pulmonary edema, hypoventilation, and failure to wean from the ventilator.
- Neurological: Paraesthesia, ataxia, delirium, Wernicke's encephalopathy.
- Musculoskeletal: Weakness, fatigue, myalgias, and rhabdomyolysis.
- Miscellaneous: Abdominal pain, constipation, vomiting, anemia, metabolic acidosis.

Measures for the prevention and treatment [91–95]

- Search and recognize high-risk patients for refeeding syndrome.
- Order baseline laboratory tests to assess potassium, magnesium, and phosphorus status before initiating nutrition support.

- Prophylactic administration of adequate electrolytes (even if blood levels are in the low-normal range), vitamin (thiamine, water, and fat-soluble), and micronutrient (Zn, Fe, Se) in "standard" maintenance doses, concurrently with the nutrition support. An approximate daily dose of electrolytes supplementation suggested is 1–1.5 mEq/kg potassium, 0.2–0.4 mEq/kg magnesium, and 0.3–0.6 mmol/kg phosphate. If values of electrolytes are severely low, it is recommended to delay the initiation of nutrition support until the electrolyte imbalances are corrected.
- The recommended dose of thiamine is 100 mg per day, to be administered before initiating dextrose-containing IV fluids and to be given for a period of 5–7 days or longer.
- Start refeeding gradually and cautiously in a stepwise manner to avoid excessive nutritional replenishment and limit the resultant risk of refeeding syndrome. First, start caloric supplementation in low dose (no more than 50% of energy requirements [NICE guidelines] or 100–150 gm of dextrose or 10–20 kcal/kg for the first 24 hours [ASPEN guidelines 2020]) and increase the dose slowly (advance by 33% of a goal every 1 to 2 days).
- Careful administration of sodium and fluids to avoid fluid overload.
- Close clinical and laboratory indices monitoring. Measure vital signs every 4 hours on the first day and maintain daily weight and intake output chart. Monitor serum potassium, magnesium, and phosphorus every 12 hours for the first three days.
- If overt symptoms and abnormal electrolyte values, curtail nutritional supplementation. In patients with refeeding hypophosphatemia, reduce energy intake temporarily or restrict it for 48 hours and gradually increase subsequently. Reduce fluid intake if edema or congestive heart failure and replace electrolytes aggressively according to the serum electrolyte levels.

D. Hepatic abnormalities

In patients receiving parenteral nutrition, liver diseases are common, and their prevalence ranges from 4.3% to 65% [96, 97]. Three major and most frequently encountered hepatobiliary complications are steatosis (accumulation of fat in the liver due to overfeeding), cholestasis (impaired or blocked secretion of bile), and gallbladder sludge/stones (due to gallbladder inactivity and stasis) [98, 99]. The broad spectrum of hepatic manifestations of PN-associated liver disease ranges from a benign and temporary rise in liver function tests to steatosis to fibrosis and, eventually, progress to portal hypertension and end-stage liver failure in a few [100]. Elevated serum conjugated bilirubin >2 mg/dL is the primary marker of PN-associated liver disease, which generally occurs early in therapy (within 2 weeks of initiation of PN). Therefore, when a patient receiving PN develops hepatic complications, it is essential to exclude other causes of liver disease.

Three terms used to describe the spectrum of liver disorders in patients receiving PN are PNAC (Parenteral nutrition-associated cholestasis), PNALD (Parenteral nutrition-associated liver disease), and IFALD (Intestinal failure-associated liver disease) [101]. Parenteral nutrition-associated liver disease is the general term used to describe the different hepatic and serum abnormalities associated with liver injury in adult and pediatric patients receiving long-term PN [102]. As long-term administration of PN

can cause cholestasis, the term Parenteral nutrition-associated cholestasis (PNAC) is frequently used in the pediatric literature [103].

The term "Intestinal failure-associated liver disease" (IFALD) is now preferred to "PNALD" or "PNAC" for describing liver disease associated with PN in both pediatric and adult patients, as it more accurately reflects the multifactorial nature of the problem and its relation to intestinal failure [104, 105]. However, both terms, PNALD and IFALD, are used interchangeably in clinical practice to describe hepatic dysfunction secondary to intestinal failure in patients who are on PN.

Major risk factors for the development of PNALD are [98, 99]:

- Excessive energy intake or overfeeding.
- Glucose overload or excessive carbohydrate administration.
- Excess administration of lipid >1 gm/kg/d.
- Administration of soybean oil-based lipid emulsion.
- Continuous infusion of PN.
- Lack of enteral stimulation.
- Carnitine and choline deficiency.

Interventions recommended to prevent or treat hepatic complications are:

- Avoiding excessive calorie administration: Avoid administration of >25 to 30 kcal/kg calories to reduce the risk of steatosis or fat deposition in the liver.
- Avoiding excessive carbohydrate administration: Avoid administration of >5 mg/kg/min/d carbohydrate to prevent PNALD/IFALD [96].
- Appropriate carbohydrates to lipids ratio: PN solution should contain about 70–85% carbohydrates and 15–30% lipids to provide nonprotein energy [106].
- Restrict the dose of soybean-based lipid emulsions (<1 gm/kg body weight/d) to treat children with PNALD [21, 107].
- Change the composition of lipid emulsions: Supplementation (partial or complete) of omega-3-fatty acids enriched fish oil to soybean-based lipid emulsions (with the reduced n6/n3 ratio) is recommended to prevent and treat PNALD [103, 108–110].
- Prefer cyclic PN instead of continuous PN: Cyclic PN (9 for 12 to 16 hours) allows time for the mobilization of fats during the non-administration period of PN [105]. Therefore, a switch to cyclic PN infusion helps stabilize or improve impaired liver function [64, 65, 111].
- Early oral or enteral nutrition: Even small amounts of oral or enteral nutrition (EN) stimulates enterohepatic circulation of bile acids and reduce the risk for PNALD.

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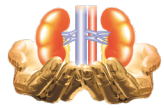
KidneyEducation 

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