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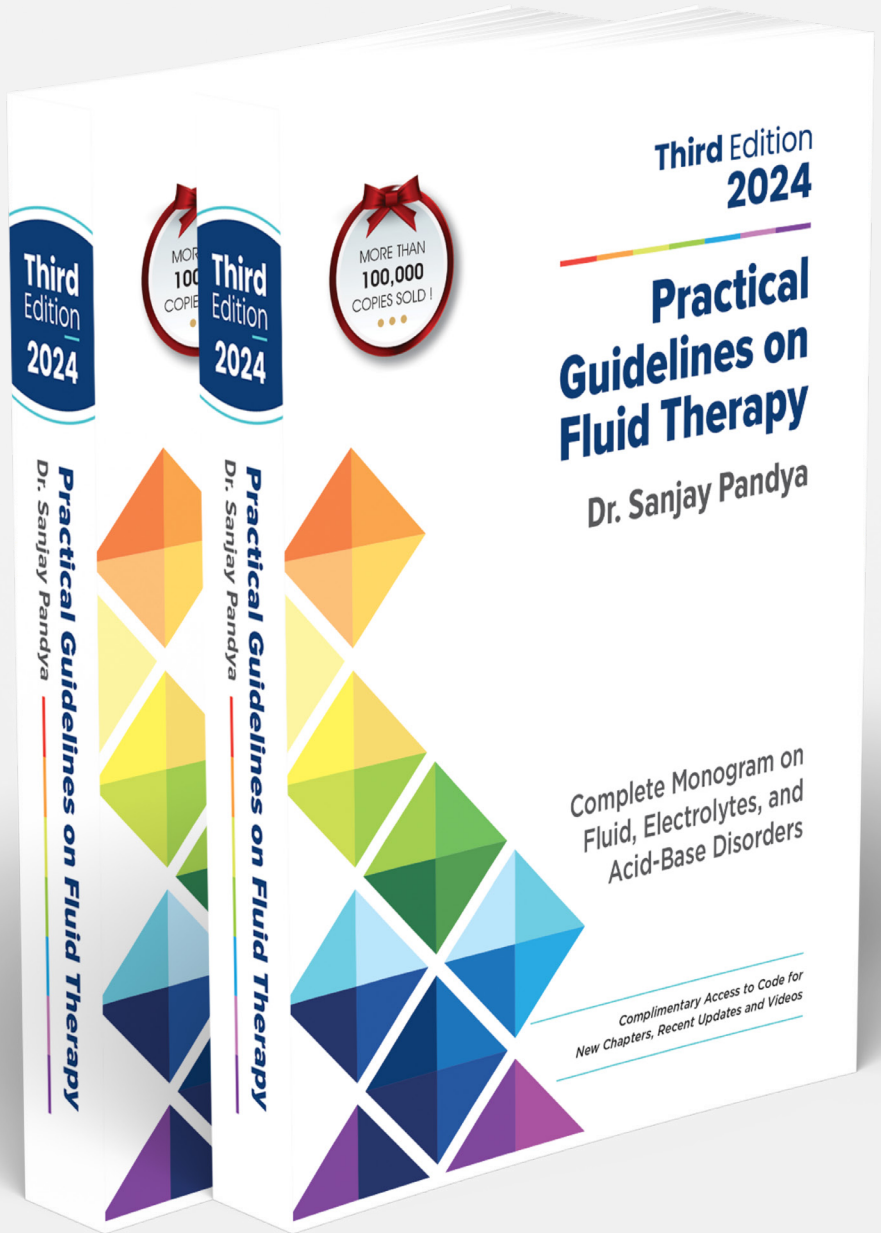
Chapter 55:

Parenteral Nutrition: Principles and Requirements



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55 Parenteral Nutrition: Principles and Requirements

Parenteral nutrition (PN) is currently one of the most sophisticated forms of intravenous therapy. Appropriate use of parenteral nutrition is lifesaving when there is no other option for nutrition.

DEFINITION

Parenteral nutrition is a method of intravenous administration of nutrients, vitamins, electrolytes, and medications

to patients who cannot take or tolerate enteral nutrition or have a non-functional gastrointestinal tract.

PN is an effective means of sustaining life and promoting recovery in critically ill patients incapable of ingesting, absorbing, or assimilating nutrients. Similarly, PN is a life-supporting therapy even for non-critically ill patients with pre-existing malnutrition and for non-stressed but hospitalized patients who cannot take oral intake for 5 to 7 or more days.

BASIC PRINCIPLES OF NUTRITION

- Avoid malnutrition as it is harmful [1].
- If the intestines are functioning properly, utilize them. When possible, it is recommended to use enteral nutrition instead of parenteral nutrition. However, ensuring the safe and sufficient delivery of nutrition is of higher priority than the route of delivery.
- Avoid overfeeding, as it can cause significant complications. Excess carbohydrates can cause hyperglycemia, hepatic steatosis, and increased CO_2 production; excess protein can cause azotemia and metabolic acidosis, and excess fat can cause hyperlipidemia [2, 3].
- While planning PN, more critical factors are the method of delivery, timing, and the type of formula rather than the specific amounts of nutrients provided.
- During acute stress, the body mobilizes endogenous amino acids and energy stores. It is not possible to make catabolic patients anabolic entirely. The goal of nutritional support is to prevent the wasting of protein and to provide essential and conditionally essential nutrients.

Importance of avoiding malnutrition

Malnutrition should be prevented due to its harmful consequences, including:

- Malnutrition leads to increased morbidity and mortality and should be avoided. In addition, it leads to increased susceptibility to infection, poor wound healing, pulmonary complications (weakness of respiratory muscles leading to the decreased ventilatory drive, reduction of vital capacity, and depressed lung defense due to reduces cough pressure and removal of secretions), electrolyte disturbances, and postoperative complications.
- Malnutrition leads to a prolonged recovery period and a longer duration of hospitalization.
- It can negatively impact the quality of life and is associated with higher morbidity and mortality.

Goals of parenteral nutrition

The role of PN is supportive. The principal goals of nutritional support are:

- To sustain or improve nutrition by administering all necessary nutrients such as proteins, carbohydrates, lipids, electrolytes, minerals, trace elements, and vitamins.
- To decrease the negative impacts of catabolism, it is essential to maximize protein synthesis, limit the breakdown of body protein, and slow down the rate of weight loss.
- To boost the immune function and to improve wound healing.
- Restoring glycogen storage increases the strength of cardiac and diaphragmatic muscles and improves cardiopulmonary function.
- To maintain or correct acid-base and electrolyte disturbances.

Table 55.1 Planning of parenteral nutritional support
1. Selection of patient: Determine if PN is truly indicated. PN is recommended only when potential benefits (improvement in prognosis and quality of life) exceed the risks.
2. Select and establish an appropriate route of administration on the basis of long-term vs. short-term requirements.
3. Calculations of nutritional requirements: Calculate the requirements of fluid, energy, glucose, lipids, proteins, minerals, and vitamins for individual patients (along with disease-specific modifications).
4. Prescribe parenteral nutrition: Convert nutritional requirements to prescription. Prepare or select an optimal formula to deliver nutrients.
5. Administration, monitoring, and avoiding complications of PN support.

- To accelerate recovery and improve the quality of life.

Planning parenteral nutrition

Planning of parenteral nutritional therapy is summarized in Table 55.1.

ENTERAL NUTRITION VS. PARENTERAL NUTRITION

Preference of EN over PN

Enteral nutrition (EN) is preferred when the gastrointestinal tract is functional and accessible. The potential benefits of enteral feeding are:

- Maintains mucosal integrity: Provides nutrients that are needed in the intestinal lumen to maintain the structural and functional integrity of the gastrointestinal (GI) tract. Enteral feeding prevents the atrophy of intestinal mucosa and maintains mucosal functions of the gut. Intact mucus membrane preserves the barrier functions of the bowel and prevents bacterial translocation, and therefore prevents the possible risk of sepsis.
- Unlike standard PN, EN provides gut-preferred fuels such as glutamate and short-chain fatty acids.
- More physiological as the liver is not bypassed. The complete volume of nutrient-rich venous blood from all parts of the gastrointestinal tract passes from the liver before it returns to the heart. So hepatic take-up, process, and storing of various nutrients from the venous blood and subsequent release on neural or hormonal command is maintained with EN.
- Prevents cholelithiasis by stimulating gall bladder motility.
- Fewer serious complications and avoids known and potential complications of PN.
- Less costly and easier to maintain than PN. Because of the potential advantages of EN, the provision of even "token" enteral supplementation is recommended to patients receiving total PN support whenever possible.

Contraindications EN

Major contraindications of enteral nutrition are:

- Gastrointestinal causes: Active severe gastrointestinal bleeding, small or large bowel obstruction, perforation, generalized peritonitis, severe paralytic ileus, high output external fistula, and intractable vomiting or diarrhea refractory to medical management.
- Cardiac causes: Active shock or

severe hemodynamic instability with poor end-organ perfusion and hypotensive patients on a high dose of inotropes/vasopressors. Avoid EN in patients who are hemodynamically unstable and not fully resuscitated [4, 5], but due to multiple benefits of EN [6, 7], initiate EN after adequately fluid resuscitation once the patient is stable and/or doses of vasopressors are declining [8, 9].

- Lack of access: Unobtainable safe access to the gastrointestinal tract.
- Complications of enteral feeding: Patients with enteral feeding complications (i.e., pulmonary aspiration, severe diarrhea, and intestinal ischemia or infarct precipitated by enteral feeding in patients with ischemic bowel syndrome) should not be fed by the enteral route.

Advantages of PN over EN

Potential advantages of parenteral nutrition over enteral nutrition are:

- Ensured desired volume delivery of nutrients without the concerns of gastrointestinal intolerance or compliance with transnasal feeding tubes.
- Improved metabolic, electrolyte, and micronutrient management.
- Better acid-base manipulation.
- Drug delivery capabilities (histamine H2 blockers, metoclopramide, insulin, heparin, etc.).

So, PN not only delivers nutrition but also regulates fluid, electrolyte, and acid-base homeostasis.

Factors considered while selecting parenteral nutritional support

The decision to use parenteral nutrition should take into account several important factors, including:

- Age and premorbid state (healthy or otherwise).
- Nutritional status, including endogenous fuel (fat) and protein (muscle) stores, weight loss, and serum albumin value.
- Duration of starvation and degree of the anticipated insult.
- Underlying disease, its severity, and concomitant medical therapy.
- Gastrointestinal function and the possibility of resuming normal intake soon.

INDICATIONS OF PARENTERAL NUTRITION

Parenteral nutrition is required in patients who cannot, should not, or will not eat enough to maintain adequate nutrition and are at risk of developing malnutrition. PN prevents the adverse effects of malnutrition and prevents or corrects specific nutrient deficiencies when the gastrointestinal tract cannot be used efficiently or safely for a prolonged period. Additionally, using PN can reduce total hospitalization costs due to faster recovery and reduced complications of the underlying condition.

However, PN is expensive and has the potential for serious complications. So benefits of PN should be weighed against the potential risks before initiating PN. Important indications of PN are summarized in Table 55.2 [10–12].

ADVANTAGES AND DISADVANTAGES OF PN

Major advantages and disadvantages of the parenteral nutrition are as follows:

Major advantages

- Lifesaving when the GI tract cannot be used.
- Ensured desired volume delivery of nutrients when:

Table 55.2 Indications of parenteral nutrition

A. General indications

1. Critical illness with inadequate oral or enteral nutrition for >5–7 days
2. In critically ill patients with severe malnutrition or high nutrition risk, initiate PN as soon as feasible if oral or enteral nutrition is not possible or inadequate

B. Anticipated or actual inadequate oral or enteral intake

1. Conditions that impair the absorption of nutrients
   a. GI fistula
   b. Short bowel syndrome
   c. Small bowel obstruction
   d. Effects of radiation or chemotherapy
2. Need for bowel rest
   a. Severe acute necrotizing pancreatitis
   b. Inflammatory bowel disease
   c. Mesenteric ischemia
   d. Peritonitis
   e. Perioperative (bowel resection, major gastrointestinal surgery)
3. Motility disorders
   a. Prolonged ileus
4. Inability to achieve or maintain enteral access
   a. Haemodynamic instability
   b. Massive gastrointestinal bleeding
   c. Unacceptable aspiration risk
   d. Hyperemesis gravidarum, eating disorders

C. Significant multiorgan system disease

- Significant renal, hepatic, and pulmonary diseases or critical illness (multi organ failure, severe head injury, burns, etc.), which prevents adequate oral or EN

  - GI intolerance prevents oral or EN.
  - Less than 2 to 3 feet of the small intestine.
- Easier correction of fluid and electrolyte disturbances.

Major disadvantages

- High cost.
- Catheter-associated infections and complications.
- Fluid overload and electrolyte abnormalities.
- More risk of metabolic problems like hyperglycemia, hypercholesterolemia, hepatic dysfunction, and refeeding syndrome.
- Leads to intestinal mucosal atrophy, causing damage to the gut barrier. Loss of this first line of defense predisposes patients on PN to risk bacteremia and infection.
- Daily PN is cumbersome.

CONTRAINDICATIONS OF PN

Contraindications of PN are broadly discussed in two groups:

General contraindications

- If enteral or oral nutrition meets the patient's nutritional requirements.
- Patients are well-nourished, stable,

non-catabolic, and within the short term (five to seven days), oral or enteral nutrition is likely to be initiated. For Most patients who require short-term support, the risks of PN outweigh the benefits.

- Severe liver failure, cardiac failure, cardiogenic shock, and blood dyscrasias.
- Cautious use in hemodynamic instability, volume overload, azotemia (BUN >100 mg/dL), severe hyperglycemia (glucose >300 mg/dL), or electrolyte disturbances (Na^+ >150 mEq/L, K^+ <3 mEq/L, Cl^- <85 mEq/L and phosphorus <2 mg/dL), where administration of PN carries high risk.
- Undue high risk in the insertion of catheter solely for PN.
- To prolong life in terminally ill patients with a poor expected outcome when there is little prospect of good quality of life.

Disease-specific contraindications

- Excess use of carbohydrates results in the production of a large amount of carbon dioxide and therefore should be avoided in patients with compromised pulmonary function and with ventilator support during the weaning period.
- Use lipid administration with caution if the triglyceride level is consistently more than 350 mg/dL or in patients with severe sepsis, a moderate degree of jaundice, low platelet count (<50,000 to 60,000/mm), and ARDS or severe respiratory disease.
- Avoid the use of excess PN volume in patients with heart or kidney failure.
- In patients with hepatic encephalopathy and severe renal failure, modified amino acids are preferred over standard amino acids.

It is important to remember that parenteral nutrition must not be undertaken lightly. It is potentially harmful and dangerous if not administered with due precautions.

Timing of parenteral nutrition initiation

Even in critical patients, the decision to start PN is never an emergency. Before starting PN, if the patient is hemodynamically stable and there are no electrolyte or blood glucose abnormalities, the risks of adverse effects of PN are low. At times adequate initial therapy of critical illness may sufficiently improve clinical status to permit oral or EN, and the patient may not require PN. Early PN benefits severely malnourished, critically ill patients, patients with severe necrotizing acute pancreatitis, and high output fistula with large nutrient losses.

NUTRITIONAL REQUIREMENTS

Basic nutritional requirements include a balanced amount of fluid, macronutrients (carbohydrates, lipids, proteins), and micronutrients (electrolytes, minerals, trace elements, and vitamins).

A. Fluid requirements

The total fluid requirement in an adult patient can be calculated by adding abnormal losses to normal daily fluid requirements. In adult patients of average-sized, the fluid requirements are about 25–30 mL/kg/d. Correct volume deficit before initiating PN. Search and replace fluid additionally to replace abnormal fluid losses caused by diuretic therapy, diarrhea, vomiting, nasogastric tube drainage, wound output, perspiration, etc. Patients with fluid overload due to cardiac, pulmonary, hepatic, or renal failure need fluid restriction. The

volume of fluid delivered by the enteral route should be subtracted from the estimated total fluid requirement. Significant minerals are lost with enteric fluid loss, so an extra amount of these nutrients and fluid must be added to the parenteral solution.

B. Energy requirements

PN should provide adequate energy to patients. Four components of daily energy requirements/total energy expenditure (TEE) are resting energy expenditure-REE (normally two-thirds of TEE), activity energy expenditure (activity factor-AF, normally one-fourth to one-third of TEE), the thermal effect of food (Thermal factor-TF, normally 10% of TEE) and associated illness (disease factor-DF). Adult patients' appropriate total energy requirement is 20–30 kcal/kg/d [13].

Total energy expenditure can be estimated by any of three methods (Table 55.3):

- By using a simple calculation based on calories per kilogram of body weight.
- By using Harris-Benedict (HB) equation to calculate resting energy expenditure, plus additional calories for activity and illness or,
- By calculating energy expenditure with indirect calorimetry.

1. Simple body weight-based calculation

Energy requirements can be calculated roughly by multiplying actual body weight in kilogram by 25–30 kcal, which needs modifications considering physical activity and associated illness (Table 55.4). In obese patients, use ideal body weight

Table 55.3 Methods for estimating total energy expenditure (kcal)

1. Simple body weight based calculation: • REE (kcal/day) = 30 × weight in kg
2. Harris-Benedict equation: • REE (Man) = 66 + (13.7 × W) + (5.0 × H) - (6.7 × A) • REE (Women) = 655 + (9.6 × W) + (1.8 × H) - (4.7 × A)
3. Indirect calorimetry: • REE (Man) = (3.9 × VO2) + (1.1 × VCO2) - 61
A: Age in years; H: Height in cm; W: Weight in kg; REE: Resting energy expenditure

Table 55.4 Guidelines for adjustment in energy requirements

AF = Activity factor	DF = Disease factor	TF = Thermal factor
1.2 bed rest	1.10 on ventilator	1.1 38°C
1.3 out of bed	1.25 general surgery	1.2 39°C
1.4 active	1.3 sepsis	1.3 40°C
-	1.6 multiorgan failure	1.4 41°C
-	1.7 30–50% burns	-
-	1.8 50–70% burns	-
-	2.0 70–90% burns	-

for calculation. Severely malnourished critically ill patients are at high risk for refeeding syndrome, and therefore while initiating PN, administer hypocaloric PN (energy intake less than 20 kcal/kg/d) with adequate protein intake.

2. **Harris-Benedict equation**

   While calculating REE by the Harris-Benedict equation, undernourished patients use actual body weight, and obese persons use ideal body weight.

   To calculate TEE from REE, it is necessary to correct for physical activity (activity factor-AF), associated illness (disease factor-DF), and temperature (TF) as per Table 55.4.

   So, TEE = REE × AF × DF × TF

3. **Indirect calorimetry**

   Above both methods fails to provide accurate calculations of the actual energy used, especially for patients who are significantly underweight, overweight, or critically ill. Therefore, indirect calorimetry using the multi-component metabolic carts [14] is considered the gold standard method to evaluate energy expenditure in clinical practice. As this accurate and non-invasive technique helps in planning the prescription of nutrition and prevents both under and overfeeding in patients by spontaneously breathing and ventilation, its routine use to optimize nutrition care should be encouraged [15, 16].

   Calculation based on body weight and the HB equation is simple but often overestimates energy expenditure. Because of the complications of overfeeding, it is wiser to administer lesser calories rather than too many calories.

Providing energy requirements in parenteral nutrition

The approximate proportion of various macronutrients, including carbohydrates, lipids, and proteins, in the parenteral solution for energy supplementation is summarized in Table 55.5. Generally, the energy content of parenteral nutrition predominantly consists of carbohydrates and lipids (non-protein calories), as proteins are primarily directed towards anabolic processes rather than serving as an energy source. In clinical practice, a common approach is to provide approximately 60–70% of calories from glucose and 30–40% from lipids. This combination of fuel sources in critically ill patients significantly reduces carbon dioxide (CO_2) production, improving patient outcomes

In clinical practice, glucose and lipids are usually given roughly 60–70% glucose and 30–40% lipids.

This mixed fuel nutrient in stressed patients significantly reduces CO_2 production and, therefore, reduces the respiratory work of breathing.

Avoidance of overfeeding in parenteral nutrition

Overfeeding is associated with several significant complications that must be carefully managed to optimize patient outcomes. These complications include:

Table 55.5. Macronutrient composition in parenteral nutrition solutions

Macronutrient	% Contribution	Calories per gm
Carbohydrates	50–60%	1 gm dextrose = 3.4 kcal
Lipids	20–30%	1 gm lipid = 9 kcal
Proteins	15–20%	1 gm protein = 4 kcal

- Severe hyperglycemia: Overfeeding can lead to severe hyperglycemia, resulting in glycosuria, osmotic diuresis, and dehydration.
- Increased risk of infections: Hyperglycemia caused by overfeeding can elevate the risk of nosocomial infections.
- Increased oxygen consumption: Excessive calorie administration can lead to increased oxygen consumption and carbon dioxide production. This heightened metabolic rate may necessitate increased respiratory effort, potentially causing problems in patients with compromised lung function.
- Hepatic steatosis: Overfeeding and excess calorie intake can contribute to the accumulation of fat in the liver, leading to hepatic steatosis. This condition can result in long-term hepatic dysfunction [17].

C. Carbohydrates

Dextrose is the least expensive and most commonly used - a primary source of calories in parenteral nutrition.

1. Caloric value, preparations, and requirements

Each gm of hydrated dextrose monohydrate used to prepare parenteral nutrition supplies 3.4 kcal (The caloric contribution of dietary carbohydrate is 4 kcal/gm). Commercially made formulas are available in a concentration ranging from 5% to 70% (Table 55.6). Most central parenteral nutrition (CPN) formulations use dextrose in concentrations ranging from 50–70%, which is then diluted to 15–30% when mixed with other macronutrients. Usually, 50–70% of the total energy requirement is provided in the form of dextrose. Dextrose requirements are about 4–5 mg/kg/min in stable patients and less than 4 mg/kg/min in critically ill, trauma, and sepsis patients and should not exceed 5 mg/kg/min [13, 18]. The minimal requirement of carbohydrates for PN is about 2 gm/kg/d of glucose [19].

Start with no more than 150 to 200 gm of dextrose on the first day of PN. In patients with diabetes or patients at risk for refeeding syndrome, start with a lower dose (100 to 150 gm) of dextrose.

2. Functions and advantages

- Low cost: Dextrose is the least expensive macronutrient and hence, most commonly used.
- Supplies calories: Parenteral carbohydrate in the form of dextrose in PN is the primary source of calories. Many tissues, such as erythrocytes, white blood cells, and renal medulla, rely primarily on glucose as an energy source and cannot easily use alternative fuels. Brain tissues, red blood cells, immune cells, and renal medulla preferentially use glucose as fuel [19]. So, it is safer to provide a minimum of 100–150 gm (about 2 gm/kg body weight) of dextrose per day to meet these demands [18].

Table 55.6 Characteristics of dextrose solutions

Solution concentration	5%	10%	20%	25%	50%	70%
Dextrose content (gm/L)	50	100	200	250	500	700
Supply of calories (kcal/L)	170	340	680	850	1,700	2,380
Osmolarity (mOsm/L)	253	505	1,010	1,330	2,525	3,535

- Nitrogen-sparing effect: Adequate carbohydrate supplementation has an important nitrogen-sparing effect, especially in patients with metabolic stress. When calories are provided as glucose, it stimulates insulin secretion, reduces muscle protein breakdown, and reduces the release of glucose from the liver. Thus, dextrose prevents protein catabolism by inhibiting the release of amino acid precursors from skeletal muscle for gluconeogenesis. In addition, glucose oxidation is also stimulated, thus sparing the oxidation of amino acids.

3. Disadvantages

- Low-calorie supply: Dextrose is a poor source of calories (3.4 kcal/gm of dextrose vs. 9.0 kcal/gm of fat). So to meet the total calorie requirements, the patient either needs a larger fluid volume (if we use diluted dextrose solution) or a highly concentrated dextrose solution (which can cause thrombophlebitis).
- Hyperglycemia: The development of hyperglycemia is the most common drawback of dextrose in PN. The risk and severity of hyperglycemia are greater with IV dextrose than with the same amount of oral or enteral administration because IV dextrose bypasses the entero-insular axis. Hyperglycemia due to a larger amount of dextrose limits the increment in the dose of dextrose in PN.
- Increased CO_2 production (high respiratory quotient): Carbohydrates produce more carbon dioxide compared to lipids, which increases the work of respiratory muscles to eliminate carbon dioxide. Therefore, carbohydrate is not preferred as an only source of calorie in respiratory compromised patients and patients weaning from ventilator support.
- Thrombophlebitis: Concentrated dextrose solution (above 10%) has high osmolarity as compared to plasma osmolarity (280 mOsm/L), so it can cause thrombophlebitis, requiring a central line for administration.

4. Administration of dextrose infusion and monitoring

The infusion rate of dextrose should not exceed the body's glucose oxidative capacity. The maximum rate of dextrose oxidation is approximately 4–5 mg/kg/min (5.8–7.2 gm/kg/day). Providing an excess amount of dextrose increases the risk of complications such as hyperglycemia, fatty liver, respiratory problems due to excess CO_2 production, and increased infectious-related mortality. Therefore, in patients at high risk of developing hyperglycemia (pre-existing diabetes, sepsis, obesity, steroid therapy, etc.), initiate carbohydrate infusion at a low rate (i.e., 1–2 gm/kg body weight/day). Monitor dextrose infusion closely and maintain blood sugar levels between 140–180 mg/dL [20]. Administer regular insulin only if necessary. Insulin therapy is usually initiated in diabetic patients when blood sugar is more than 140 mg/dL and in non-diabetic patients when blood sugar is more than 180 mg/dL [21].

To control hyperglycemia, insulin can be administered using different regimens, but the continuous infusion of insulin and adding insulin to the nutrition bag are common and efficient methods [21–23].

5. Example of calculation of carbohydrate/dextrose requirements

Example: For a 60 kg male with 25 kcal/kg/d energy requirements, how much 50% dextrose solution is needed (considering 60% of daily total energy requirement in the form of carbohydrates) in a day?

Calculation:

- Total caloric requirements will be 60×25=1500 kcal/day, and carbohydrate requirement will be 900 (60% of 1500) kcal/day as dextrose.
- Divide caloric requirements from carbohydrates by 3.4 (there is 3.4 kcal/gm of dextrose) to determine the gm of dextrose required. 900 divided by 3.4 = 264.7 gm of dextrose/day.
- D50% has 50 gm of dextrose per 100 ml. So to provide 264.7 gm of dextrose/day required volume of D50 will be about 529 ml/day (22 ml per hour).

D. Protein

Protein supplementation is an essential component of parenteral nutrition. The primary source of protein supplementation in parenteral nutrition is free amino acids. Amino acids given in PN are not provided as an energy substrate. But the rationale for its supplementation is that they are essential for synthesizing protein, replacing nitrogen losses, and preventing further skeletal muscle breakdown.

1. Calorie value and preparations

When an amino acid is oxidized for energy, it provides 4 calories per gm. 6.25 gm of protein contains 1 gm of nitrogen. The standard amino acid solution contains approximately 40–50% essential amino acids (N=9) and the rest 50–60% nonessential amino acids (N=10) plus semi-essential (N=4) amino acids. Crystalline amino acid solutions used in PN are of high biological quality. Standard commercially made crystalline amino acid formulations are available in 3 to 15% concentrations. 10% solution of amino acids contains 100 gm of protein per liter.

2. Requirements

Approximately 15 to 20% of total energy requirements should come from protein. Protein and energy requirements are closely related. To minimize protein catabolism, a sufficient amount of non-protein calories, such as carbohydrates and fats, must be administered simultaneously. A calorie to nitrogen ratio of 100–150:1 will be satisfactory for normal patients. The protein requirement for an average stable adult is about 0.8–1.5 gm/kg/day. When patients receive protein without adequate calories, the requirement for protein increases because, in addition to its use for protein synthesis, the protein supplied is also utilized for energy production. Amino acid administration is essential to prevent protein-energy malnutrition (PEM). PEM may lead to immunosuppression and infection in critically ill patients.

Protein requirement is higher (1.5–2.5 gm/kg/day) in massive burns, severe trauma, hypoproteinemia, protein-losing enteropathy or nephropathy, or in patients receiving dialysis treatment. In critically ill patients with sepsis, a large amount of nitrogen loss results from abnormal metabolism. General guidelines for protein requirement in hospitalized patients are summarized in Table 55.7 [13].

Table 55.7 Recommended daily protein intake

Clinical condition	Protein requirements (gm/kg ideal body wt/day)
Stable	0.8–1.5
Critically ill, trauma, sepsis	1.2–2.5
Acute kidney injury (undialysed)	0.8–2.0
Renal replacement therapy	Additional 0.2 gm/kg/d, up to 2.5 gm/kg/d
Burns	1.5–2.0
Hepatic failure	1.2–2.0
Traumatic brain injury	1.5–2.5

For critically ill patients, optimal protein intake is approximately 1.5 gm/kg/day. This amount of protein intake can decrease the degree of nitrogen loss in catabolic patients, mostly by enhancing visceral protein synthesis and, to a lesser extent, by diminishing peripheral protein catabolism. Delivering an additional amount of protein does not further reverse this trend and does not yield a positive nitrogen balance. On the contrary, if excess protein (>1.7 gm/kg/day) is provided, it results in excess ureagenesis rather than contributing to protein anabolism.

3. Functions and advantages

- Protein synthesis: The main function of protein is the growth and maintenance of cells and tissues in a steady stage.
- Reduces the rate of protein catabolism: In critically ill patients, protein catabolism exceeds protein synthesis and leads to net protein loss. Administration of an adequate amount of protein along with calories decreases body protein loss but does not prevent the loss completely.
- Calorie supplementation: 1 gm of protein provides 4 kcal energy. Patients receiving inadequate calories from carbohydrates and lipids will utilize protein for energy production. Thus, excess protein is needed for nitrogen balance when energy intake is low.

4. Contraindications and adverse effects

- Hepatic insufficiency: In patients with hepatic insufficiency, infusion of standard amino acids may cause metabolic alkalosis, increased levels of ammonia, stupor, or coma.
- Renal failure: A patient with impaired renal function may develop a marked rise in BUN.
- Metabolic or respiratory alkalosis may be exacerbated by the excess acetate ions present in amino acid solutions.
- Rapid administration may cause nausea, vomiting, headache, chills, or fever.
- Administration of excess protein or insufficient calorie supplementation results in the production of an increased amount of urea. Renal loss of excess nitrogen leads to water loss and may cause hypertonic dehydration (especially in young children) unless extra water is provided.

5. Monitoring

In stable patients receiving an amino acid infusion, the adequacy of protein support can be assessed by analyzing nitrogen balance.

Nitrogen Balance =
Nitrogen Intake - Nitrogen Loss

Nitrogen Intake =
Protein Intake[gm] / 6.25

Nitrogen Loss = 24-Hour UUN + 4

Where 24-hour UUN represents the gm of nitrogen excreted in the urine over 24 hours, and the addition of + 4 accounts for 4 gm of nitrogen lost each day as insensible losses via the skin and gastrointestinal tract.

Positive nitrogen balance suggests anabolism or nitrogen retention. Nitrogen loss greater than nitrogen intake (negative nitrogen balance) suggests net nitrogen loss. If the blood urea nitrogen (BUN) level exceeds 100 mg/dL or a patient with hepatic encephalopathy shows clinical worsening with a rising ammonia level while infusing amino acids, the dose of standard amino acids needs to be reduced or discontinued [24].

6. Example of calculation of protein/amino acid solution requirements

Example: For a 60 kg male with 1.0 gm per kg per day protein requirements, considering basic requirements and adding stress factors, how much amino acid solution is needed for PN in a day?

- Total daily protein requirements will be 60 kg × 1.0 gm/kg = 60 gm per day.
- 100 ml solution of 5% and 10% of amino acid preparation provides 5 gm and 10 gm of amino acid, respectively. So, to provide 60 gm of amino acid/day required volume of 5% and 10% of amino acid preparations will be 1200 and 600 ml/day, respectively.

E. Lipids

Lipid injectable emulsions (ILEs, formerly known as Intravenous Fat Emulsion) are an essential component of PN formulations that have two main functions: to provide an energy-dense source of calories that help in reducing the dextrose load needed to meet energy goals and supply essential fatty acids (EFAs) such as linoleic and linolenic acids which prevent or correct essential fatty acid deficiency.

1. Contents of lipid emulsion

Different lipid emulsions contain varying amounts and proportions of omega-3, omega-6, and omega-9 fatty acids. Lipid emulsions containing soybean oil are the mainstay and the first-generation lipids for parenteral nutrition and have been used extensively with fair success for decades [25, 26]. This formulation for PN also contains three other components: egg yolk phospholipids as an emulsifying agent to mix two immiscible liquid phases, fine droplets of oil suspended in water; glycerin to make the formulation isotonicity with plasma; and sodium hydroxide, which adjusts the final pH around 8.0 [27, 28].

First-generation soybean oil containing lipid emulsions are composed mainly of omega-6 FA-rich linoleic acid with low content (about 10%) of omega-3 FA containing α-linolenic acid (ALA), and therefore has a high (7:1) omega-6/omega-3 FAs ratio. The high content of omega-6 FA in soybean-based lipid emulsions has pro-inflammatory and immunosuppressive harmful effects and therefore is associated with adverse outcomes in critically ill patients [25, 29, 30].

Alternative lipid emulsions, such as generation 2 (combining soybean oil with medium-chain triglycerides), generation 3 (using olive oil), and generation 4 (using fish oil) lipid emulsions, have been developed to decrease the harmful effects of the omega-6-rich linoleic acid content and to lower the ratio of omega-6 to omega-3 fatty acids as summarized in Table 55.8 [26, 31–33].

2. Caloric values, preparations, and requirements

Lipid is the richest source of calories; 1 gm of lipid provides 9 kcal (vs. dextrose provides 3.4 kcal/gm and protein provides 4.0 kcal/gm). The lipid emulsions are available as 10% (1.1 kcal/ml), 20% (2.0 kcal/ml), and 30% (3.0 kcal/ml) solution and have low osmolarity (260 mOsm/L). The use of 30% lipid emulsion is approved for preparing a total nutrient admixture or "3 in 1" delivery system in a pharmacy admixture program. Still, it is not recommended for direct intravenous administration.

In PN, lipids should be infused to provide about 25–40% of non-protein calories [34]. ILE requirements are 1 gm/kg/d in stable patients and less than 1 gm/kg/d in critically ill, trauma, and sepsis patients (ASPEN 2019) [13]. Lipid emulsions should be started usually

Table 55.8 Classification, composition, and benefits of lipid injectable emulsions

Generation of ILEs	Composition of ILEs	The ratio of ω-6:ω-3 FAs	Rationale and benefits	Selected ILEs products
First	100% soy oil	7:1	Used to supply EFA and energy	Intralipid, nutrilipid
Second	50% soy oil, 50% MCT	7:1	MCT is added to reduce the soy content and the amount of ω-6 FA	Lipofundin MCT/ LCT
Third	20% soy oil, 80% olive oil	9:1/NA	Reduce the soy content. Less prone to inflammatory processes and immune suppression	ClinOleic/ clinolipid
Fourth	30% soy oil, 30% MCT, 25% olive oil, 15% fish oil	2.5:1	Reduce the soy content, ω-6 to ω-3 FA ratio, infectious complications, and hospital stay. Preferred in critically ill and surgical patients	SMOFlipid

EFA: Essential fatty acid; FA: Fatty acid; ω-3, Omega 3; ω-6, Omega 6; ILE: Lipid injectable emulsion; LCT: Long chain triglycerides; MCT: Medium-chain triglyceride; MUFA: Monounsaturated fatty acid; Soy: Soybean

at a dose of 0.7 gm/kg/day, the upper recommended dose is 1 gm/kg/day, and it should not exceed 1.5 gm/kg/day (ESPEN 2019) [18]. In obese patients, underfeeding help in the mobilization of the endogenous fat store and, as a result, improves insulin sensitivity and glycemic control [35].

3. Functions and advantages

- Dense calorie supplementation: IV lipid emulsion is a concentrated calorie source (9 kcal/gm), so it is the other major calorie-rich fuel that provides energy effectively. Providing more energy in a given volume (compared to IV dextrose fluids) is an essential advantage of lipid emulsion in critically ill, volume overloaded patients.
- Avoids hyperglycemia: Lipid emulsion provides a portion of the total calorie requirement, thereby allowing a lower rate of dextrose infusion and reducing the potential adverse effects of infusing excess glucose for calories.
- Protein sparing effect: IV lipid emulsion is more effective than IV dextrose in providing energy. In PN, adequate supplementation of calories by curtailing protein oxidation prevents protein catabolism and exerts a protein-sparing effect.
- Less CO_2 production (lower respiratory quotient): Compared to carbohydrates, lipids produce less CO_2 and, therefore, are preferred in respiratory compromised patients. Lipids' respiratory quotient (RQ) is the least (RQ of lipids 0.7 vs. 0.8 for proteins and 1.0 for carbohydrates). The respiratory quotient is the ratio of CO_2 production to O_2 consumption.
- So, IV lipid emulsion has the advantages of better glucose tolerance, less hyperinsulinemia, less fatty infiltration of the liver, and less production of CO_2. Because of these benefits, lipid emulsion is widely utilized in patients with hyperglycemia, diabetes, liver disease, and respiratory failure.
- Prevention of essential fatty acid deficiency: Lipid emulsion assists in wound healing, the production of red blood cells (RBC), and prostaglandin synthesis. PN administration without

Table 55.9 Advantages of lipid emulsion in PN solutions
• Large amount of calories in a small volume. • Improve glucose tolerance and reduce insulin levels. • Reduces the risk of refeeding syndrome. • Lower osmolarity. Reduces the risk of thrombophlebitis. Safe for PPN. • Supply of essential fatty acid. • Less CO_2 production than glucose oxidation, which is beneficial in respiratory compromised patients weaning from ventilator support.

lipid supplementation for more than 2 weeks should be avoided because it can lead to essential fatty acid deficiency, causing dry, scaly skin rash, hair loss, thrombocytopenia, anemia, poor wound healing, and increased susceptibility to infection. To prevent essential fatty acid deficiency, supplement about 2% to 4% of total caloric intake as linoleic acid and 0.25% to 0.5% as alpha-linolenic acid beyond 2 weeks of administering PN.

- Reduced risk of thrombophlebitis due to lower osmolality: Hypertonic solutions are irritant to veins, thus increasing the risk of thrombophlebitis. Unlike the hypertonic dextrose solutions, the osmolarity of lipid emulsion is low (260 mOsm/L), almost the same as that of plasma. So the addition of lipid emulsion reduces the osmolarity and, therefore, reduces the risk of thrombophlebitis due to PN. Besides, lipid emulsion exerts a protective effect on vascular endothelium. For the same reason, lipid emulsion is an important component of solutions for peripheral parenteral nutrition (PPN).

The advantages of including lipid emulsion in PN are summarized in Table 55.9.

4. Adverse effects and disadvantages

The adverse effects of lipid administration are:

- Increased triglyceride levels: Infusion of lipid emulsion causes an increase in plasma triglycerides, cholesterol, phospholipids, and concentration of lipoproteins. When lipid emulsion is infused rapidly and/or in high doses, the rate of infusion of triglyceride exceeds the rate of hydrolysis of triglyceride by endothelial enzyme lipoprotein lipase and, therefore, can cause hypertriglyceridemia [36].
- Sepsis: Lipid emulsion carries a risk of infection when administered separately over a prolonged time.
- Fat embolism: Lipid is less stable when infused with amino acids and glucose as a combined "three-in-one solution". Destabilized particles of fat coalesce into larger droplets and subsequently form fat emboli. For the same reason, a three-in-one solution has a shorter storage life, and improperly mixed or delayed in the use of solution carries the risk of fat embolism.
- Less frequent complications: Immediate or early adverse reactions include dyspnea, cyanosis, nausea or vomiting, headache, allergic reactions, chest and back pain, or thrombocytopenia. Delayed complications with prolonged administration include hepatic dysfunction, fat overload syndrome, pancreatitis, and delayed gastric emptying.

Most adverse effects are instead due to hypertriglyceridemia than due

to lipids per se. Hypertriglyceridemia occurs due to the infusion of lipids at a rate faster than lipid clearance. Thus, if lipids are infused at proper infusion rates and serum triglycerides are monitored regularly, most adverse effects of lipids are avoided.

5. Indications

Lipid administration is indicated in all patients needing a home or prolonged PN. Lipid administration is also indicated in patients who need PPN, high caloric supplementation but fail to tolerate carbohydrates, critically ill patients, and patients with hyperglycemia, diabetes mellitus, and respiratory failure.

6. Contraindications

Avoid lipid emulsion in patients with severe hypertriglyceridemia (reduce dose if serum triglycerides >400 mg/dL and do not use if serum triglycerides >1000 mg/dL), in patients who are at risk of developing fat embolism, hypersensitivity to lipid emulsion, severe metabolic acidosis, in patients with acute shock, anemia, severe coagulopathy, and evidence of intravascular coagulation [34]. In addition, lipid emulsions should be used cautiously in obese patients because of the greater risk of hyperglycemia and hypertriglyceridemia.

7. Administration and monitoring

IV lipid emulsion used to prevent essential fatty acid deficiency is given 3 to 4 days a week; while used as a calorie source, it is provided daily. The lipid can be administered IV either separately by piggyback infusion with the 2-in-1 system (containing dextrose and amino acids) or as 3 in 1 admixture (all-in-one infusion) of dextrose, protein, and lipids in a single bag. Lipid emulsions may also provide rich media for the growth of bacteria and fungi. Therefore, scrupulous handwashing before handling lipids is mandatory to reduce the risk of touch contamination. As exposure of the lipids to light causes the formation of potentially toxic peroxides, avoid it by wrapping it in aluminum foil or carbon paper.

Since most complications are associated with rapid IV lipid infusion (greater than 1.0 kcal/kg/hr or 0.11 gm/kg/hr), the rate should not exceed 0.7 kcal/kg/hr. Usually, lipid emulsions should be administered slowly over 12 hours. However, avoid a prolonged infusion of lipids and discard bottles and tubing hung alone after 12 hours. PN solution bag may hang for a maximum of 24 hours and discard any remaining solution and tubing after 24 hours [37].

In patients with lipid infusion, triglyceride levels should be monitored at least weekly. Lipid infusion should be reduced or discontinued if the triglyceride level exceeds 400 mg/dL to decrease the risk of pancreatitis or decreased diffusion capacity in patients with severe chronic obstructive lung disease.

8. Selection of lipid emulsions (ILE)

The most commonly used soybean based first-generation lipid emulsions are usually recommended for short-term use (<2 weeks) in stable critical patients with normal LFTs [33].

Newer lipid emulsions for PN are developed which has a lower content of harmful omega-6 FA and contains omega-3 FA in a higher amount [31]. In contrast to omega-6 FA, omega-3 FA-enriched newer lipid emulsions (i.e., fish oil containing ILE) has beneficial anti-inflammatory and immunomodulatory effects, which reduces the risk of infection and sepsis and shorten ICU and hospital stay and therefore preferred in high-risk patients requiring PN such as sepsis, critically ill and surgical patients [33, 38–40]. Lipid emulsion preparation containing a

mixture of soybean oil, medium-chain triglycerides (MCTs), olive oil and fish oils, such as SMOF lipid is available commercially [41].

9. Example of calculation of lipids/lipid emulsion requirements

Example: For a 60 kg male with 25 kcal/kg/d energy requirements, how much lipid emulsion is needed (considering 30% of total energy requirement in the form of lipid) in a day?

- Total caloric requirements will be 60 × 25 = 1500 kcal/day, and lipid requirement will be 450 (30% of 1500) kcal/day.
- 10% and 20% of lipid emulsions provide 1.1 kcal/cc and 2.0 kcal/cc, respectively. So, to provide 600 kcal/day required volume of 10% and 20% of lipid emulsion will be about 409 ml (450 ÷ 1.1) and 225 ml (450 ÷ 2.0) respectively.

F. Diseases-specific amino acids

Modified specialized solutions with adjusted amino acid contents are available for the specific disease state.

1. For hepatic encephalopathy

Specific "hepatic formula" for parenteral nutrition is a modified amino acid solution rich in branched-chain amino acids (BCAAs) (valine, leucine, and isoleucine) and has a low content of aromatic amino acids (AAA) (phenylalanine, tryptophan, and tyrosine), and sulfur-containing amino acids like methionine [42].

Potential mechanisms by which branched-chain amino acids benefits are:

- Compared with non-branched chain amino acids (Non-BCAAs), which are metabolized by the liver, BCAAs are uniquely oxidized chiefly in skeletal muscle and adipose tissues (and not in the liver). BCAAs enhances detoxification and removal of ammonia in skeletal muscles, reduces plasma ammonia concentration, and may reduce hepatic encephalopathy [43].
- In hepatic insufficiency due to liver cirrhosis, high aromatic amino acids (AAA) and low BCAAs/AAA ratio play an important role in developing hepatic encephalopathy [44]. BCAAs and aromatic amino acids are transported into the brain via the same carrier [45]. So, BCAAs compete with aromatic amino acids, potentially decreasing the passage of aromatic amino acids across the blood-brain barrier, reducing the release of neurotransmitters, notably serotonin, and thereby having beneficial effects on brain function [46, 47].

A high concentration of BCAAs (35–45%) in "hepatic formula" corrects the amino acid imbalance and is recommended in selected patients of liver cirrhosis with hepatic encephalopathy grades III–IV refractory to standard management [42].

BCAAs-enriched formulations show highly significant improvement in mental recovery [48, 49], but no evidence suggests improvement in the patient's outcome [4, 49].

Because of increased cost and controversial efficiency, BCAAs should not be used as the first-line treatment for hepatic encephalopathy [4].

In patients with liver diseases, use standard amino acid (and reduce the cost of therapy) in the absence of encephalopathy, grades I or II hepatic encephalopathies, once the encephalopathy resolves, and for preoperative nutrition after liver transplantation [50].

2. For acute kidney injury (AKI)

Supplementation of protein leads to accumulation of end products such as urea

with worsening of uremia. Therefore, protein restriction was previously practiced to reduce uremic symptoms and avoid or delay initiating dialysis therapy. But as per current recommendations, protein restriction should be avoided in patients with renal insufficiency [4, 51].

Recommended doses of protein in non-dialysis AKI patients are 0.8–1.0 gm/kg/day in non-catabolic AKI [51], and in AKI patients on renal replacement therapy (RRT) are 1.0–1.5 gm/kg/d as per KDIGO guidelines (2012) [51], or additional protein 0.2 gm/kg/day, up to 2.5 gm/kg/day as per ASPEN guidelines (2016) [4].

The role of specially designed amino acid-containing solutions ("nephro-solutions") is controversial but may benefit patients who do not require dialysis [52].

G. Immunomodulators

Immunonutrients are specific nutrients that have the potential to modify inflammatory or immune responses with beneficial effects on mucosal barrier function, cellular defense, and local or systemic inflammation [53]. The use of immune-modulating nutrients such as glutamine, arginine, and omega-3 fatty acids are common. However, a recent Cochrane Database Systematic Review (2019) found the effect of these immunonutrition supplements on the duration of ventilator days, ICU length of stay, or oxygenation in patients with acute respiratory distress syndrome to be uncertain [54].

1. Glutamine

Glutamine is the body's most abundant amino acid, which is primarily synthesized by skeletal muscles. glutamine is the primary energy source for rapidly dividing cells such as intestinal epithelial cells, vascular epithelial cells, and proliferating immune cells. Glutamine is vital for maintaining the gut barrier function and is considered a "fuel for the immune system," which exerts antioxidant and cytoprotective effects, helps defend the body against pathogens, and decreases infectious complications [55].

Studies in septic and critically ill patients have shown that administering glutamine does not improve outcomes such as mortality, organ failure, infectious complications, or length of stay [56–58]. Some studies have even shown harmful effects [58–60], leading to the recommendation against administering glutamine in septic critically ill patients [61]. In recent guidelines, parenteral glutamine is not recommended in critically ill, unstable, and complex ICU patients and with multiorgan failure, especially with liver and renal failure (Canadian guidelines 2015, ASPEN guidelines 2016, ESPEN guideline 2019) [4, 18, 62].

As clinical benefits of parenteral glutamine are documented in various studies [63–67], IV glutamine may be used in selected patients on PN who are stable, together with adequate parenteral energy and protein after excluding hemodynamic instability, hepatic or renal failure [68].

Parenteral glutamine supplementation is preferred over enteral for patients in the intensive care unit [69]. When IV glutamine supplementation is indicated in PN, the recommended dose of glutamine is 0.2–0.4 gm/kg/day (0.3–0.6 gm/kg/day of alanyl-glutamine dipeptide) [70].

2. Omega 3 fatty acids

Omega-3 fatty acids have anti-inflammatory and immunomodulatory effects and have been shown to improve clinical outcomes in surgical, trauma, cancer, and critically ill patients, as well as during long-term parenteral nutrition due to their inflammation-resolving effects [29, 30, 71].

Administration of injectable lipid emulsion containing omega-3 fatty acids provides significant benefits such as the reduction in risk of infection, sepsis, and length of stay in both ICU as well as hospital, and therefore is preferred over standard lipid emulsions (without omega-3 fatty acids) in hospitalized adult patients requiring PN [30, 40, 71].

Omega-3 fatty acids are abundant in fish oil. Newly designed **SMOFlipid** solution is a **S**oybean oil (30%), **M**edium-chain triglycerides (30%), **O**live oil (25%), and **F**ish oil (15%) containing **lipid** emulsion, which is used to provide omega-3 fatty acids enriched PN [26]. The higher cost of omega-3 fatty acids enriched lipid emulsions is a concern. But improved clinical outcomes (reduced infectious complications and shorter hospital and ICU stays) offset the overall costs [72, 73].

3. Arginine

Arginine is a nutrient that boosts the immune system and is considered a nonessential amino acid under normal circumstances. However, during times of catabolism, it becomes a conditionally essential nutrient. Arginine plays an essential role in protein synthesis, nitric oxide generation, and immunomodulation, thereby playing a major role in cellular defense and wound healing. In addition, arginine supplementation reduces the rate of infectious complications and the duration of hospitalization postoperatively [74].

Intravenous or enteral arginine supplementation as a standalone treatment is not recommended for critically ill patients or those with severe sepsis [4, 75, 76]. For patients requiring enteral nutrition therapy, an immune-modulating formula containing both arginine and fish oils should be used in the perioperative or postoperative period, including in malnourished patients undergoing major cancer surgery and in severe trauma cases in the SICU [4, 76].

H. Micronutrients

Electrolytes, trace elements, and vitamins come under micronutrients. Requirements of micronutrients for PN in the normal adult are summarized in Table 55.10. The minerals and vitamins required in parenteral nutrition are much lesser than in enteral nutrition because of better bioavailability with direct intravenous infusion. These value needs to be modified considering the clinical situations.

I. Electrolytes

As electrolytes are essential to perform critical metabolic activities, it is a must in all PN formulas. As sodium influences intravascular volume status, it is restricted in patients at risk of volume overload (e.g., cardiac, liver, and renal failure) and given liberally when volume expansion is desired (those with GI losses). Potassium requirement increases in patients with increased renal loss of potassium, in those who receive amphotericin B therapy, and in severely malnourished patients while initiating PN.

After meeting phosphate requirements, sodium and potassium cations are usually added to parenteral nutrition solutions in the form of chloride or acetate salts. The choice of the salt form has an impact on acid-base balance. The liver metabolizes acetate into bicarbonate, which acts as an alkaline buffer. Therefore, acetate is a preferred salt in patients with metabolic acidosis. Loss of a large amount of chloride (such as nasogastric aspiration) can cause metabolic alkalosis. Sodium and potassium are provided in such patients, preferably as chloride salt for PN.

Table 55.10 Recommended daily parenteral requirements of micronutrients			
Nutrient	**Requirements**	**Nutrient**	**Requirements**
Electrolytes		**Fat soluble vitamin**	
Sodium	1.0–2.0 mEq/kg	Vitamin A	990 mcg (3300 IU)
Potassium	1.0–2.0 mEq/kg	Vitamin D	5.0 mcg (200 IU)
Magnesium	8.0–20 mEq	Vitamin E	10 mg (10 IU)
Phosphate	20–40 mmol	Vitamin K	150 mcg
Calcium	10–15 mEq	-	-
Trace minerals		**Water soluble vitamins**	
Chromium	≤10 mcg	Thiamine (B1)	6.0 mg
Copper	0.3–0.5 mg	Riboflavin (B2)	3.6 mg
Manganese	55 mcg	Niacin (B3)	40 mg
Selenium	60–100 mcg	Pantothenic acid (B5)	15 mg
Zinc	3.0–5.0 mg	Pyridoxine (B6)	6.0 mg
-	-	Folic acid (B9)	600 mcg
-	-	Cobalamin B12	5.0 mcg
-	-	Ascorbic acid (Vit C)	200 mg
-	-	Biotin	60 mcg

The use of sodium bicarbonate in PN is incompatible as it forms insoluble coprecipitates, mainly with calcium and magnesium. Thus, bicarbonate salts should never be infused through a common intravenous line with PN.

J. Trace elements

Trace elements, in small amounts, are crucial for efficient substrate utilization and other supporting functions and therefore are an essential component of PN. A deficiency of trace elements develops quickly in stressed patients or patients with increased GI losses.

On the other hand, stable patients do not develop evidence of deficiency, even though trace elements are not supplemented for about two months. Commercial preparations are available as injections in various combinations, providing required trace elements.

Most trace element PN formulations contain zinc, copper, chromium, manganese, and selenium but do not have iron and iodine [13]. Selenium supplementation is recommended for patients receiving long-term PN because of the risk of muscle weakness and fatal cardiomyopathy caused by selenium deficiency.

The daily requirement of iodine is 70–150 mcg and 1 mg of elemental iron, but most PN formulations do not contain these trace elements. In most patients receiving PN, iron is not supplemented because of adequate body storage. Note that iron is not generally part of commercially available standard additives and not added to PN solutions because it can cause lipid emulsions to destabilize and therefore is incompatible with lipid-containing PN formulas like "3 in 1" solutions. In addition, iron is not given routinely to patients who are critically ill because free iron may promote bacterial growth and increase susceptibility to infection [77].

The requirements for many trace elements in PN are lower than for oral or enteral nutrition. This is because the gut absorbs only a portion of the supplemented nutrient, sometimes less than 10% (e.g., chromium).

However, it is important to remember that some trace elements' parenteral requirements are higher than actual body requirements. These increased requirements result from increased urinary losses, as they are delivered via systemic rather than portal circulation (and therefore not captured by the liver).

K. Vitamins

Vitamins are essential for normal metabolism and are an important part of PN. Requirements of trace elements for PN are generally lower than in EN, but the reverse is true for vitamins.

Parenteral requirements of vitamins are higher than those required through oral or enteral administration due to the following reasons.

- Vitamins supplemented orally are generally absorbed much more than most trace elements.
- Vitamins get degraded during preparations and storage. For example, vitamin A, riboflavin, and vitamin K are degraded by light, and thiamine is degraded by sulfite ions used as a preservative for amino acid solutions.
- Vitamins are lost partially due to adherence to tubing and delivery bags.

The recommended dose for water-soluble vitamins is four to five times the usual and minimum daily requirements for fat-soluble vitamins. Commercially available aqueous multivitamin preparations will provide normal daily requirements for most vitamins except for vitamin K.

Commercially available aqueous multivitamin preparations will provide normal daily requirements. Vitamin K is beneficial to most patients on PN and is administered as multivitamin preparation or added separately to lipid emulsions, but it may be detrimental to patients receiving oral anticoagulants [78, 79]. It is important to remember that vitamins and trace elements are added to PN shortly before use because of the concern about stability.

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