

Fluid and Electrolyte Management in Parenteral Nutrition

Jodi Kingley, MS, RD, CNSD



Abstract

An understanding of basic fluid and electrolyte physiology can aid clinicians in administering parenteral nutrition (PN). Disturbances in electrolytes, fluid, and acid-base balance require changes in therapy. Therefore, close monitoring of these parameters is essential during the administration of PN.

Introduction

Parenteral nutrition (PN) is a complex therapy containing more than 40 components, including dextrose, amino acids, fat emulsions, water, electrolytes, trace elements, and vitamins. To order PN appropriately, clinicians must have a good understanding of body composition, fluid balance, electrolyte assessment, and acid-base balance.

Body Fluid Compartments

Total body water (TBW) comprises approximately 60% of body weight in men and 50% in women. There are two primary compartments of water in the body. Intracellular fluid volume (ICFV) contains two thirds of TBW, and extracellular fluid volume (ECFV) contains the remaining one third (1). The ECFV contains interstitial fluid and plasma. Interstitial fluid surrounds cells and comprises three quarters of the ECFV volume. Plasma makes up the remaining one quarter of ECFV.

Plasma proteins maintain plasma volume primarily through oncotic pressure (1). In response to changes in solute concentrations, water passes throughout these compartments to maintain osmotic equilibrium (1).

Water Balance

Maintaining an appropriate water balance is crucial for optimal metabolic function. Thirst, antidiuretic hormone (ADH), and aldosterone regulate water balance. During periods of acute illness, ADH and aldosterone production are often increased. Hypotension, stress, decreased intravascular volume, pain, surgery, and increased plasma osmolality all increase ADH output, favoring water retention. Aldosterone production increases when kidney perfusion decreases, causing sodium and water retention (1). An aging individual, generally defined as older than 65 years, has a diminished ability to adjust to hemodynamic changes compared with a younger person. Therefore, in a hospitalized, acutely ill elderly patient, extra care must be taken with total fluid provision, fluid balance, and monitoring of serum chemistry values (2).

Assessing Fluid Requirements

An average adult requires approximately 2,000 to 2,500 mL/d of water (3). Oral fluids provide 1,100 to 1,400 mL; solid foods provide 800 to 1,000 mL;

and oxidation of protein, carbohydrate, and fats yields approximately 300 mL water. Fluid output consists of losses from urine (1,200 to 1,500 mL) and stool (~100 to 200 mL) (4). Other output is termed insensible because it cannot be measured, but it has been estimated that the average adult loses 450 mL of fluid per day (5).

During illness, there are multiple other sources of input and output, including intravenous (IV) fluids, medications, and drips. IV medications and drips should be subtracted from estimated fluid requirements before calculating the PN formulation. Variables for output include nasogastric suctioning losses/vomiting, diarrhea, fistula drainage (4), and sequestration of fluids resulting from injury, infection, peritonitis, and burns (6). Such losses must be replaced to prevent fluid deficits. When accounting for significant losses from the gastrointestinal tract, it is important to have a general understanding of the amounts of electrolytes lost that require replacement (Table 1) (4). The PN solution can be adjusted to provide for these ongoing electrolyte losses.

Insensible losses occur primarily with fever; fluid needs increase 12.5% with each degree increase in body temperature greater than 37°C (4) or approximately 60 to 80 mL daily for each degree over normal (98.6°F) (2).

(Continued on page 16)

Table 1. Electrolyte Composition of Body Fluids (6)

Type of Secretion	Volume (mL/24 h) (range)	Sodium (mEq/L) (range)	Potassium (mEq/L) (range)	Chloride (mEq/L) (range)	Bicarbonate (mEq/L) (range)	Tonicity
Saliva	1,000	30 to 80	20	70	30	Hypotonic
Sweat	200 to 1,000	20 to 70	5 to 10	40 to 60	0	Hypotonic
Stomach	1,000 to 2,000	60 to 80	15	100	0	Hypotonic
Small bowel	2,000 to 5,000	140	20	100	25 to 50	Isotonic
Colon	200 to 1,500	60	30	40	0	Hypotonic
Bile	1,000	140	5 to 10	100	40	Isotonic
Pancreas	1,000	140	5 to 10	60 to 90	40 to 110	Isotonic

Increased insensible losses occur from hyperventilation, low humidity, and increased ambient room temperature (4). Fluid requirements vary with age, sex, body weight, disease state, and degree of insensible loss.

Table 2 lists several methods to determine fluid requirements. Methods 1 and 3 should be used carefully because they can result in insufficient fluid provision for those with low body weights and excess fluid provision in obese patients. Conversely, method 4 (the Adequate Intake) is based on healthy individuals (5) and, therefore, may not be applicable during acute illness. The literature suggests a minimum of 1,500 mL/d of fluids for most elderly persons (7). Fluid restrictions may be required for those with cardiac, liver, and renal disease.

Intravenous Fluids

A basic understanding of IV solutions and what they provide can assist when evaluating sodium, electrolyte, and fluid provision in nutrition support regimens. IV fluids provide maintenance

or repletion of fluid and electrolytes, especially sodium chloride and potassium (Table 3). Some contain dextrose as a protein-sparing source. IV fluids are also used to provide IV antibiotics, which are mixed in dextrose or normal saline (9).

Electrolytes

Plasma electrolyte abnormalities are common in acutely ill patients. The nutrition support clinician should understand the factors that cause irregular electrolyte levels because PN is often the primary fluid source for those receiving the therapy. PN frequently is used to help correct such deficits or excesses, unless the patient is unstable. Separate IV administration of electrolytes is more practical for frequent changes in volume and electrolyte requirements (10).

Sodium

Evaluating abnormal sodium concentrations is not always straightforward. Plasma sodium concentration is the primary measurement used to determine the volumes of the ICF and ECF, not the actual amount of total body sodium (11). Sodium is the main cation in the ECFV. If the total amount of sodium in the ECFV is elevated, the size of the ECFV also increases, which may lead to a state of volume overload. Insufficient sodium in the ECFV compartment results in volume depletion (1).

Hyponatremia

Hyponatremia is defined as a serum sodium concentration of less than 135 mEq/L. The mortality of patients with hyponatremia is approximately double that of patients with normal plasma sodium concentrations (11). It is also the most common electrolyte disorder seen in hospitalized patients (4).

Hyponatremia is associated with low, normal, or high tonicity. Tonicity is the combined effort of solutes such as sodium and glucose that causes water movement from one body compartment to another (1). When evaluating hyponatremia, the first step is to calculate the serum tonicity or request a plasma osmolality. Calculated tonicity and plasma osmolality are viewed as

interchangeable because the only difference between the two is blood urea nitrogen, which is the smallest contributor to plasma osmolality (Table 4). If plasma osmolality is normal (275 to 295 mOsm/kg), the hyponatremia is usually due to hyperlipidemia or hyperproteinemia; this is rarely seen with modern laboratory assays. If plasma osmolality is high (>295 mOsm), the hyponatremia is likely due to hyperglycemia or intravenous infusions of glucose or mannitol (4). The pseudo-hyponatremia value should be corrected: for every 100-mg/dL increase in glucose, plasma sodium decreases 1.3 to 2 mEq/L (13).

If hypertonic and isotonic hyponatremia are ruled out, hypotonic hyponatremia is present. This is the most common cause of hyponatremia and requires assessment of the ECFV. Hypotonic hyponatremia results from an excess of water in relation to existing sodium stores and usually is due to decreased renal water excretion. Complications of hypotonic hyponatremia are more severe when the decrease in serum sodium concentration is large or rapid (occurring over hours). Most patients with serum sodium concentrations greater than 125 mEq/L are asymptomatic. If clinical symptoms occur, they include headache, nausea, vomiting, muscle cramps, lethargy, disorientation, depressed reflexes, seizure, or coma (14).

Sodium stores can be decreased, normal, or increased with hypotonic hyponatremia. The associated conditions are usually termed hypovolemic, isovolemic, and hypervolemic hyponatremia (4,8).

Hypovolemic hyponatremia occurs with renal and/or extrarenal sodium losses. Renal losses occur from diuretics, renal tubular acidosis, osmotic diuresis, mineralocorticoid deficiency, and salt-losing nephritis. Extrarenal losses occur with vomiting, diarrhea, fistula drainage, burns, and third spacing of fluids (15). In an acutely ill patient, plasma volume may decrease due to a gradual loss of plasma into the inflamed tissue or the bowel or due to increased capillary permeability, also called "third spacing." The leakage moves

Table 2. Estimating Water Requirements

Method 1 (1)

30 to 40 mL/kg

Method 2 (4)

1. 100 mL/kg for first 10 kg body weight
2. 50 mL/kg for second 10 kg body weight
3. For age <50 y: 20 mL/kg for each additional kg body weight
4. For age >50 y: 15 mL/kg for each additional kg body weight

Method 3 (4)

16 to 30 y, active: 40 mL/kg
20 to 55 y: 35 mL/kg
55 to 75 y: 30 mL/kg
>75 y: 25 mL/kg

Method 4 (5)

1. Adult females >19 y: 2,700 mL (includes 540 mL or 20% from solid food consumption)
2. Adult males >19 y: 3,700 mL (includes 740 mL or 20% from solid food consumption)

Table 3. Standard Intravenous Solutions (1,8)

Solution	Glucose (g/L)	mOsm/L	Sodium (mEq/L)	Chloride (mEq/L)	Indications	Cautions
<i>Hydrating</i>						
D5W	50	252 Isotonic (becomes hypotonic when metabolized)	0	0	Provides free water	Contains glucose; can impair control of diabetes
0.45% NaCl	0	154 Hypotonic	77	77	Provides free water and sodium; used to treat hypertonic ECFV-depleted states	Can cause serious hyponatremia
D51/2 NS	50	336 Hypertonic (becomes hypotonic when metabolized)	77	77	Provides free water, sodium, and dextrose; used for maintenance hydration and repletion of volume deficits	As above
<i>Replacement</i>						
0.9% NaCl	0	308 Isotonic	154	154	Provides ECFV replacement	Can cause ECFV overload in patients with congestive heart failure or renal failure
D5 in 0.9 NS	50	560 Hypertonic (becomes isotonic when metabolized)	154	154	Provides ECFV replacement plus calories	As above
Ringer Lactate (also contains 28 mEq/L lactate, 4 mEq/L potassium, 3 mEq/L calcium)	0	272 Isotonic	130	109	Provides ECFV replacement; similar to electrolyte content of plasma; used mostly for perioperative fluid	Can cause ECFV overload in patients with congestive heart failure or renal failure
3% NaCl	0	1,026 Hypertonic	513	513	Treats severe, symptomatic hyponatremia	Can cause ECFV overload, iatrogenic hypernatremia

ECFV=extracellular fluid volume

proteins, electrolytes, and water from the intravascular compartment to the interstitial space. This allows immune mediators to reach the site of injury or infection (16). Because plasma volume is reduced, ADH is secreted, which acts on the kidney to increase water reabsorption. Urine volume usually decreases as a result. The adrenal glands

respond to the decreased perfusion by releasing aldosterone, which causes sodium retention in the distal kidney tubules. Urine sodium concentrations are less than 20 mEq/L. Replacing losses with hypotonic fluids or the consumption of low-solute fluids such as water or tea worsens the hyponatremia (17). Physical symptoms of hypovolemia

include tachycardia, decreased blood pressure, decreased skin turgor, and sudden weight loss. Because there is more sodium loss relative to water loss, treatment is volume expansion, usually with normal saline (4,11,15).

Isovolemic hyponatremia represents an essentially normal ECFV that occurs

(Continued on next page)

with the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), water intoxication, and glucocorticoid use. There is a small gain in free water that cannot be detected clinically. Urine sodium values usually are greater than 20 mEq/L. Treatment is fluid restriction (4). The IV fluid should be normal saline (14,15).

Hypervolemic hyponatremia means an increased ECFV that results from excess body sodium and water and occurs with cardiac, renal, or hepatic failure. Urine sodium values usually are less than 20 mEq/L with congestive heart failure and cirrhosis and greater than 20 mEq/L with acute or chronic renal failure. Treatment involves sodium and fluid restriction, although symptomatic patients should receive judicious quantities of hypertonic saline (14,15). IV administration should be in normal saline (14). Diuretics may also be used (14,15).

Hypernatremia

Hypernatremia is defined as serum sodium greater than 145 mEq/L (11). It is always a hypertonic state, which causes water to move from the ICF to the ECF (15). There are three types of hypernatremia. Evaluation depends upon the ECFV level. Hypovolemic hypernatremia is the most common and occurs with the loss of hypotonic body fluids such as urine, diarrhea, sweat, and furosemide diuresis. Water loss exceeds sodium loss. Treatment is with hypotonic saline (¼ or ½ NS). Isovolemic hypernatremia results from a net loss of free water, such as with diabetes insipidus or insensible losses from the lungs and skin. This is treated with water replacement (D5W via IV fluids or orally ingested water). Clinicians should use an equation to estimate the amount of water required for repletion (Table 4) (12). Hypervolemic hypernatremia occurs with excess sodium chloride or bicarbonate solution administration. Total body sodium gain exceeds total body water gain. Treatment involves diuretics and water replacement or adjustment of IV fluids to decrease sodium provision. Hypernatremia should be corrected gradually to avoid rapid brain cell swelling, which causes severe neurologic dysfunction (15).

Table 4. General Calculations

1. Plasma Osmolality and Tonicity (11):

$$\text{Plasma osmolality} = (2 \times [\text{Na}]) + \frac{[\text{glucose}]}{18} + \frac{[\text{BUN}]}{2.8}$$

where serum glucose and urea are measured in mg/dL

hypo-osmolar = <275 mOsm/L

isosmolar = 275 to 295 mOsm/L

hyperosmolar = >295 mOsm/L

$$\text{Plasma tonicity} = (2 \times [\text{Na}]) + \frac{[\text{glucose}]}{18}$$

hypotonic = <270 mOsm/L

isotonic = 270 to 285 mOsm/L

hypertonic = >285 mOsm/L

2. Total Body Water (TBW) Estimation (12):

$$\begin{aligned} \text{TBW} &= 0.6 \times \text{wt (kg) males; } 0.5 \times \text{wt for males } \geq 80 \text{ years of age} \\ &= 0.5 \times \text{wt (kg) for females; } 0.4 \times \text{wt for females } \geq 80 \text{ years of age} \\ &\text{subtract 10\% for obese, 20\% for very obese} \end{aligned}$$

3. TBW Deficit Estimation (12):

$$\text{Water deficit (L)} = [\text{TBW} \times (\text{Na}_2/\text{Na}_1 - 1)]$$

TBW = total body water

Na₁ = desired serum sodium

Na₂ = actual serum sodium

4. Calculated Sodium Deficit (11):

$$(\text{Na}^+ \text{ desired} - \text{Na}^+ \text{ measured}) \times \text{estimated TBW}$$

5. Calculated Serum Anion Gap (12):

$$\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$$

6. Calculated Bicarbonate Deficit (11):

$$\begin{aligned} \text{HCO}_3^- \text{ deficit (mmol)} &= 0.5 \times \text{wt (kg)} \times [(\text{HCO}_3^- \text{ desired}) - (\text{HCO}_3^- \text{ measured})] \\ &\text{Replace } \frac{1}{2} \text{ of deficit first 24 hours and remainder over next 24 to 48 hours} \end{aligned}$$

7. Calculated Chloride Deficit (4):

$$\text{Chloride deficit (mmol)} = 0.5 \times \text{wt (kg)} \times (\text{Cl}^- \text{ normal} - \text{Cl}^- \text{ measured})$$

Sodium in PN is combined with chloride, acetate, phosphate, or lactate salt (18). PN solutions usually provide more than one of these components. The liver converts acetate to bicarbonate in a 1:1 ratio. Sodium requirements can vary widely, depending on the patient's fluid status, sodium requirements, and organ function. Sterile water or saline solutions may be added to the PN or provided in a separate intravenous infusion (19). The Safe Practices Committee recommends an average sodium provision of 1 to 2 mEq/kg/d (3).

Potassium

Potassium plays an important role in maintaining cell volume, enzyme function, protein synthesis, cell growth, neuromuscular activity, and hydrogen ion concentration (pH) (4). The total amount of body potassium is proportional to muscle mass and body weight. Therefore, the amount decreases with age, in females, and in those with depleted muscle mass (1). Approximately 98% of body potassium is contained intracellularly; only 2% is in the ECFV. Therefore, plasma potassium

is a limited indication of total body potassium stores. Normal serum potassium concentrations generally range from 3.5 to 5.5 mEq/L (11).

Hypokalemia

Hypokalemia occurs in degrees of significance: mild-to-moderate hypokalemia is a concentration of 2.5 to 3.5 mEq/L, and severe hypokalemia is a concentration of less than 2.5 mEq/L. Severe deficiencies can result in neuromuscular changes such as weakness, fatigue, and respiratory muscle dysfunction; gastrointestinal complications such as constipation or ileus; and electrocardiograph (ECG) changes (1).

The three primary causes of hypokalemia result from redistribution, extrarenal losses, or renal causes. Redistribution involves potassium moving from the plasma into the cells, which can occur with insulin administration, refeeding syndrome, anabolism, and alkalosis (1). Extrarenal losses result from severe secretory diarrhea, chronic laxative abuse, and fasting or inadequate dietary intake. Renal causes often arise from acid-base disorders or from recovery from acute renal failure, osmotic diuresis, and postobstructive diuresis. Magnesium depletion also causes potassium loss, so magnesium levels should be evaluated during repletion (1). Twenty-four-hour urine potassium levels greater than 40 mEq/d indicate renal losses; values less than 30 mEq/d reflect nonrenal losses (12).

In general, a potassium deficit of 10% total body potassium stores is expected for every 1-mEq/L decrease in serum potassium, or a 150- to 400-mEq deficit (1). Replacement should proceed more cautiously in states of renal insufficiency/failure (1). Oral supplementation with potassium gluconate or citrate is preferred (20). The appropriate salt is chosen based on the cause of potassium loss. If the loss is from emesis, nasogastric tube drainage, or diuretics, potassium chloride is appropriate. Use potassium phosphate if there is a coexisting phosphorus deficiency. If an acidosis is present, clinicians use potassium bicarbonate or its precursors citrate, acetate, or gluconate. Parenteral repletion is indicated if the

oral route cannot be used, if neuromuscular complications are present, or if there is a severe deficit. No more than 10 to 20 mEq/h of potassium should be infused. The total amount of potassium provided rarely exceeds 200 mEq/d. Repletion should occur over days or weeks to prevent hyperkalemia (20). Potassium in PN is available as chloride, acetate, and/or phosphate salt (18); 3 mmol potassium phosphate yields approximately 4.4 mEq of potassium (4). The Safe Practices Committee recommends an average provision of 1 to 2 mEq/kg/d, but requirements can vary widely (3).

Hyperkalemia

Hyperkalemia is defined as a serum potassium concentration greater than 5.5 mEq/L. Severe hyperkalemia at concentrations greater than 6.5 mEq/L can cause weakness, respiratory failure, ascending paralysis, and ECG changes (11).

Pseudohyperkalemia, redistribution, renal, and miscellaneous causes are all potential contributors to hyperkalemia. Pseudohyperkalemia occurs when serum platelets are greater than 1,000,000/mm³, white blood cells are greater than 200,000/mm³, or blood draws are ischemic or hemolyzed (1). Redistribution occurs with metabolic or respiratory acidosis, but not from lactic acidosis or other organic acidosis. Impaired potassium excretion accounts for most cases of hyperkalemia, such as type 4 renal tubular acidosis. Otherwise, a glomerular filtration rate of less than 10% is usually needed to produce hyperkalemia (1). Certain medications, such as angiotensin-converting enzyme inhibitors and potassium-sparing diuretics, can predispose a patient to hyperkalemia, especially when administered to those who have type 1 diabetes, chronic kidney disease, or heart failure (5). Hyperkalemia can also occur from crush injury, catabolism, rhabdomyolysis, gastrointestinal hemorrhage, and hypertonic states (4).

For hyperkalemia not caused by hemolysis, the appropriate treatment is to limit or discontinue all exogenous sources of potassium, including potassium supplements, salt substitutes, and IV fluids and/or PN with potassium

(1,14). It is important to evaluate medications that might contribute to hyperkalemia. Other treatments include removing potassium through the gastrointestinal tract with a potassium exchange resin, administration of diuretics with a high-salt diet for hyporeninemic hypoaldosteronism, and dialysis (11). Intracellular shift of potassium occurs via glucose administration with insulin by injecting one ampule of dextrose with 10 U of insulin, administering bicarbonate, and providing beta-2 agonists (salbutamol and albuterol). When the condition is life-threatening, calcium salts or hypertonic sodium solutions work the quickest by antagonizing the membrane effect of hyperkalemia (11).

Magnesium

Magnesium is the second most abundant intracellular cation. It serves as a cofactor in more than 3,000 enzyme reactions involving adenosine triphosphate (ATP) (4). It also regulates the movement of calcium into smooth muscle cells to maintain cardiac contractile strength and peripheral vascular tone. Only 0.3% of body magnesium is found in the plasma. Therefore, serum levels are not a good indication of total body stores (11). The normal concentration range for serum magnesium is 1.7 to 2.5 mEq/L (11).

Hypomagnesemia

Hypomagnesemia occurs in an estimated 10% to 20% of patients in general medicine wards and 60% to 65% of patients in intensive care units (11). Because serum values are of limited use, it is important to be aware of common clinical manifestations. Signs of hypomagnesemia include cardiac arrhythmias, muscle weakness, hyperreflexia, and hypokalemia that may be resistant to repletion (11). Hypomagnesemia is usually accompanied by depletion of potassium, phosphorus, and/or calcium (11). Hypomagnesemia can cause hypocalcemia. With severe magnesium depletion (<1.0 mEq/L) and the presence of hypokalemia and hypocalcemia, convulsions, stupor, and coma can occur (15).

Predisposing conditions include inadequate intake or gastrointestinal

(Continued on next page)

absorption, such as from poor intake, starvation/refeeding syndrome, malabsorption, inflammatory bowel disease, and severe diarrhea (15). Renal losses occur with volume expansion, diuretics, sodium loads, SIADH, and hypercalcemia. Among other causes are alcoholism, acute pancreatitis, and burns. Medications, including loop diuretics, especially furosemide, interfere with both sodium and magnesium reabsorption. Antibiotics, including aminoglycosides and amphotericin B, and the chemotherapy drugs cisplatin and cyclosporine all can cause magnesium loss (4,21).

Recommendations for magnesium repletion depend on the severity of the deficit. IV supplementation is indicated for moderate-to-severe hypomagnesemia, with the following guidelines: 2 to 4 mEq/kg of $MgSO_4$ in repeated doses of 25 mEq (3 g $MgSO_4$) over 2 to 6 hours for severe hypomagnesemia (4). Repletion is 1 mEq/kg in the first 24 hours for mild depletion, followed by 0.5 mEq/kg for the next 3 to 5 days. For patients with renal insufficiency, the doses are reduced by half. Serum magnesium concentrations may take up to 1 or 2 days to replete, but several days are required to replenish total body stores (11,17). Magnesium salts are sulfate and chloride salts. PN magnesium is usually in the form of magnesium sulfate in mEq. One gram of magnesium sulfate is equivalent to 8 mEq of magnesium (18). The Safe Practices Committee recommends an average provision of 8 to 20 mEq/d in PN (3).

Hypermagnesemia

This disorder is defined as serum magnesium concentrations greater than 2.5 mEq/L. Many cases are due to excess magnesium administration in the form of laxatives or antacids to patients who have advanced renal insufficiency (21). Other causes include severe dehydration, severe trauma or surgical stress, rhabdomyolysis, and severe acidosis (4). Treatment involves elimination or reduction of exogenous magnesium provision and correction of the acidosis or volume deficit (4).

Phosphorus

Phosphorus is the most abundant

intracellular anion. It is a cofactor in most enzyme systems and a major component in ATP production. About 1% of total body phosphorus is located in the ECFV. Therefore, serum levels are a limited indicator of total body stores. Normal plasma concentrations are 2.5 to 5.0 mg/dL (4,11).

Phosphate is provided as sodium or potassium salt. Additional amounts are provided in PN with careful consideration for calcium/phosphorus and calcium/magnesium concentrations (4). Deaths and injuries caused by calcium phosphate precipitation in 3-in-1 total nutrient admixtures have been reported (3). Among the numerous recommendations to prevent this problem are to avoid high calcium and phosphate concentrations and the use of calcium chloride. If the amount of calcium or phosphate added is suspected to cause a precipitate, some or all of the calcium should be administered separately. In addition, a filter should be used for all PN infusions (22). The ordering clinician should contact the compounding pharmacy for specific questions concerning total provision of these nutrients.

Hypophosphatemia

Hypophosphatemia is defined as serum concentrations less than 2.5 mg/dL. Causes of this disorder are intracellular shift, increased renal excretion, or decreased absorption from the gastrointestinal tract. Most acute cases result from intracellular shifts due to refeeding syndrome, recovery from diabetic ketoacidosis, or respiratory alkalosis (4). Intracellular shifts also occur with insulin or glucose administration and anabolism. Malabsorption, vitamin D deficiency, and phosphate-binding antacids affect absorption from the gastrointestinal tract. Increased renal excretion occurs with hyperparathyroidism and renal tubular defects. Phosphorus depletion can impair cardiac contractility, reduce cardiac output, and impair ATP production and oxygen release to tissues (4,11).

IV phosphorus replacement is indicated for all patients whose serum values are below 1.0 mg/dL and for patients with any hypophosphatemia who have cardiac dysfunction, respiratory

failure, muscle weakness, or impaired tissue oxygenation. When serum phosphorus values are more than 2.0 mg/dL, the element is repleted via the gastrointestinal tract, providing the tract is functional (11). Phosphorus in PN is provided as sodium and/or potassium phosphate (18). The Safe Practices Committee recommends an average provision of 20 to 40 mmol/d (3).

Hyperphosphatemia

Hyperphosphatemia is defined as a serum phosphorus value of more than 4.5 mg/dL and usually results from impaired excretion due to renal insufficiency or from widespread cell necrosis from rhabdomyolysis, tumor lysis, and hypercatabolic states (15). Cardiac, visceral, and peripheral soft-tissue calcification may occur when the calcium-phosphorus product exceeds 55 mg/dL (23).

Treatment includes limiting exogenous phosphorus sources, including that in PN, and providing phosphorus binders such as calcium carbonate, calcium acetate, or sevelamer, providing the gastrointestinal tract is functional (15,23).

Calcium

Calcium is the most common electrolyte in the body. Some 99% is in the bone, with the remainder primarily in the ECFV. Calcium plays an important role in blood coagulation, neuromuscular transmission, and smooth muscle contraction (11).

Fifty percent of plasma calcium is bound to protein, 5% to 10% is chelated to plasma ions, and the rest is free (ionized), which is the active form. Laboratory assays measure all three sources, which can be misleading if hypoalbuminemia is present. Although many clinicians use a correction factor, current recommendations are to measure ionized calcium (24). Normal ionized calcium values range from 4 to 4.6 mg/dL (11).

Hypocalcemia

The primary cause of hypocalcemia is alkalosis, occurring more with respiratory than metabolic alkalosis, which promotes binding of calcium to albumin. Other causes are vitamin D deficiency,

blood transfusions, magnesium depletion, renal insufficiency, sepsis, hypoparathyroidism, and medications such as aminoglycosides (11,24).

Hypocalcemia can result in hyporeflexia, generalized seizures, and tetany. An ionized calcium level of 3.2 to 4 mg/dL is considered a mild depletion; severe depletion is characterized as a level less than 2.6 mg/dL (11). Treatment includes oral supplementation to provide 1,000 to 1,500 mg/d elemental calcium. For symptomatic hypocalcemia, IV replacement with calcium chloride or calcium gluconate is required (24). Calcium gluconate is preferred for PN because it is most stable in solution (12). The Safe Practices Committee recommends an average provision of 10 to 15 mEq/d in PN (3).

Hypercalcemia

Hypercalcemia occurs in fewer than 1% of hospitalized patients, and 90% of cases are caused by hyperparathyroidism or malignancy (11). Other causes are prolonged immobilization, vitamin D intoxication, acute renal failure with rhabdomyolysis, and calcium carbonate ingestion (milk-alkali syndrome). A patient has severe hypercalcemia if the total serum value is greater than 11 mg/dL or the ionized measurement is more than 5.5 mg/dL. Clinical signs include nausea, vomiting, constipation, ileus, hypovolemia, hypotension, polyuria, confusion, decreased mental status, or coma. Treatment involves saline infusion with furosemide or administration of calcitonin or pamidronate (4,11). Calcium should be reduced or eliminated in the PN solution until the condition resolves (15).

Acid-Base Disturbances

Acid-base disturbances can affect plasma concentrations of electrolytes as they shift between intracellular and extracellular spaces to accommodate the disorder. Gastrointestinal losses or certain renal disorders also may affect acid-base balance (25). Understanding this can assist the practitioner in evaluating appropriate provision of electrolytes and adjustment of chloride and acetate provision.

The primary buffer system in the ECFV is bicarbonate (HCO_3^-), which the kidneys control, and PCO_2 , which the lungs control (1,4). Arterial blood gas tests, including PO_2 (arterial partial pressure of oxygen), PCO_2 (arterial partial pressure of carbon dioxide), and pH, measure the ECFV buffer system (1). Primary acid-base disorders alter one component of the $\text{PCO}_2/\text{HCO}_3^-$ ratio. When this occurs, there is a compensatory response to keep the $\text{PCO}_2/\text{HCO}_3^-$ ratio constant (11).

Respiratory Acidosis

Respiratory acidosis is defined as hypercapnia, or a PCO_2 value greater than 40 mm Hg. If a patient has inadequate renal compensation, the pH is less than 7.35. Chronic respiratory acidosis usually occurs with chronic obstructive pulmonary disease or restrictive pulmonary disease. Airway impairment or obstruction causes acute respiratory acidosis. Treatment focuses on correcting the cause of the defect. Nutritionally, it is important to avoid overfeeding, which increases CO_2 production and may worsen the acidosis (4).

Respiratory Alkalosis

Respiratory alkalosis is an acute reduction of plasma HCO_3^- with a proportionate reduction in plasma CO_2 . PCO_2 is less than 40 mm Hg, and pH is greater than 7.45 with inadequate renal compensation. Causes are hyperventilation due to hypoxia, anxiety, fever, salicylate intoxication, exercise, or excessive mechanical assist to breathing while receiving ventilator support (11). With severe respiratory alkalosis, plasma potassium moves into the cells in exchange for H^+ as the body attempts to compensate for the alkalosis. Treatment involves correcting the underlying cause and plasma deficits (4).

Metabolic Acidosis

Metabolic acidosis results from an increase in acids other than carbonic acid (1), which causes a decrease in the plasma HCO_3^- concentration. There is either a gain of acid or a loss of HCO_3^- . Gains of acid occur from the following: excessive ingestion of acid (salicylates, methanol, ethylene glycol, paraldehyde), excessive endogenous

production of acid (lactic acidosis, diabetic ketoacidosis/ketoacidosis, rhabdomyolysis), excessive provision of acidifying salts (ammonium chloride, lysine hydrochloride, hydrochloric acid, arginine hydrochloride), inability to excrete the acid load (in renal failure), or overfeeding protein in the presence of decreased ability to excrete the acid load. HCO_3^- is lost via the gastrointestinal tract with severe diarrhea, pancreatic or small bowel fistulas, biliary drainage, ureterosigmoidostomy, or from renal losses in type 2 renal tubular acidosis (1,4). Metabolic concerns arise because serum potassium increases due to a shift of H^+ into cells and potassium out of cells (4).

The anion gap (Table 4) helps to determine the type of metabolic acidosis. Normally, there is a 1:1 ratio. An anion gap of 6 to 12 mEq/L is normal. Hypoalbuminemia decreases the anion gap approximately 3 mEq/L for every 1-g/dL decrease in serum albumin because serum albumin is considered an unmeasured anion. If the anion gap is more than 26 mEq/L, metabolic acidosis is likely (25).

Treatment of metabolic acidosis always involves correcting the underlying disorder. Provision of exogenous sodium bicarbonate or its precursor sodium and/or potassium acetate (given in PN) is indicated for severe cases of acidosis (pH <7.1) or to replace ongoing gastrointestinal losses. For patients with metabolic acidosis due to organic acid production (such as ketoacidosis and lactic acidosis), HCO_3^- replacement is recommended only if the pH is <7.1 and HCO_3^- is <10 mEq/L. For nonanion gap acidosis, HCO_3^- may be indicated if the acidemia is less severe (2,10). Careful repletion and re-evaluation of the acid-base status is required to avoid "overshoot alkalosis" (25). Refer to Table 4 for calculating HCO_3^- deficit. Finally, close monitoring of plasma potassium is needed as the acidosis resolves and potassium moves intracellularly.

Metabolic Alkalosis

Metabolic alkalosis occurs with an increase in the plasma HCO_3^- concen-

(Continued on next page)

tration. This is due to either the loss of hydrogen or the gain of HCO_3^- and abnormal renal retention of HCO_3^- . Causes include ECFV depletion (also called contraction alkalosis) due to vomiting/nasogastric suction, diuretic therapy, and chronic diarrhea/laxative abuse; secondary hyperaldosteronism, renovascular disease, and malignant hypertension accompanied by severe vascular damage (9), congestive heart failure, or cirrhosis with diuretic therapy; and renal failure due to inability of the kidney to excrete HCO_3^- . Excess HCO_3^- can also be gained with oral or IV administration of HCO_3^- or administration of HCO_3^- precursors such as citrate, lactate, or acetate (4). Metabolic alterations usually include decreased plasma potassium, with hydrogen leaving the cell and potassium entering the cell in attempt to maintain electroneutrality (1,11).

Appropriate treatment is to correct the underlying disorder or cause. For ECFV depletion from diuretic therapy, the medical team should reassess the treatment strategy. With alkalosis due to vomiting/nasogastric suction, attempts should be made to reduce output with antiemetics and reduce acid loss with histamine₂-blockers or proton pump inhibitors. Most cases of metabolic alkalosis in hospitalized patients are chloride-responsive; chloride is replaced with isotonic fluid and chloride (0.9NS) (11). Refer to Table 4 for the equation used to calculate chloride deficit.

Usually, clinicians managing PN provide chloride and acetate in equal amounts to maintain normal acid-base balance. However, these components may require dosing adjustment based on the patient's clinical course (3).

Monitoring and Follow-Up

Close monitoring of patient tolerance to PN is essential, especially early after initiation. It is particularly important in the acutely ill patient to monitor daily input and output, edema, and vital signs such as blood pressure, temperature, and daily weights. Keeping a written daily care plan that includes all monitored variables is very helpful in assessing trends. Re-evaluation of actual provision of nutrients versus

recommended estimated or measured requirements is also important. Each follow-up should involve detecting and preventing complications, evaluating and documenting clinical outcomes, and monitoring for changes in the patient's condition. This includes transitioning to the enteral mode of nutrition as soon as indicated. Finally, it is helpful to discuss issues with appropriate team members who can assist with complex management concerns (3).

Jodi Kingley, MS, RD, CNSD, is a clinical dietitian at Newark Beth Israel Medical Center, Newark, NJ.

Jodi's mentor was Jennifer Muir Bowers, PhD, RD, CNSD, Department of Nutritional Sciences, University of Arizona, Tucson, Ariz.

References

1. Preston R. *Acid-Base, Fluids, and Electrolytes Made Ridiculously Simple*. Miami, Fla: MedMaster, Inc; 1997.
2. Luckey AE, Parsa CJ. Fluid and electrolytes in the aged. *Arch Surg*. 2003;138:1055-1060.
3. Task Force for the Revision of Safe Practices for Parenteral Nutrition. Safe practices for parenteral nutrition. *J Parenter Enteral Nutr*. 2004;28:S39-S70.
4. Whitmire SJ. Fluid, electrolytes and acid-base balance In: Matarese LE, Gottschlich MM, eds. *Contemporary Nutrition Support Practice*. New York, NY: Saunders; 2003:122-144.
5. Institute of Medicine (U.S.). Panel on Dietary Reference Intakes for Electrolytes and Water. *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate*. Washington, DC: National Academy Press; 2004.
6. Hassoun HT, Moore FA. Electrolyte disorders In: Cameron JL, ed. *Current Surgical Therapy*. 7th ed. Philadelphia, Pa: Mosby; 2001:1315-1326.
7. Chidester J, Spangler A. Fluid intake in the institutionalized elderly. *J Am Diet Assoc*. 1997(97):23-28.
8. Kee JL, Paulanka BJ, Purnell LD. *Handbook of Fluids, Electrolytes and Acid Base Imbalances*. 2nd ed. Clifton Park, NY: Thompson Learning™; 2004.
9. Thomas C, ed. *Taber's Cyclopedic Medical Dictionary*. Philadelphia, Pa: FA Davis Co; 1997.
10. Tawa NE, Maykel JA, Fischer JE. Metabolism in surgical patients In: Townsend CM, Beauchamp RD, Evers BM, Mattox KL, eds. *Sabiston Textbook of Surgery*. 17th ed. Philadelphia, Pa: Elsevier Saunders; 2004:137-181.
11. Marino P. *The ICU Book*. 2nd ed. Baltimore, Md: Lippincott Williams & Wilkins; 1998.
12. Man S, Uribarri J. Electrolytes, water, and acid-base balance In: Shils M, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*. Philadelphia, Pa: Williams & Wilkins; 1999:105-139.
13. Baumgartner TG. Enteral and parenteral electrolyte therapeutics. *Nutr Clin Pract*. 2001;16:226-235.
14. Adroge HJ, Madias NE. Hyponatremia. *N Engl J Med*. 2000;21:1581-1589.
15. Vanek VW. Assessment and management of fluid and electrolyte abnormalities. In: Shikora SA, Martindale RG, Schwaitzberg SD, eds. *Nutritional Considerations in the Intensive Care Unit: Science, Rationale, and Practice*. Dubuque, Ia: Kendall/Hunt; 2002:79-100.
16. Lobo, DN. Fluid, electrolytes and nutrition: physiological and clinical aspects. *Proceedings of the Nutrition Society*. 2004.63:453-466.
17. Yeates, KE, Singer M, and Morton AR. Salt and water: a simple approach to hyponatremia. *Can Med Assoc J*. 2004; 170:365-369.
18. Strausburg KM. Parenteral nutrition admixture. In: *The A.S.P.E.N. Nutrition Support Practice Manual*. Silver Spring, MD: American Society of Parenteral and Enteral Nutrition; 1998:8-1-8-12.
19. Fuhrman MP. Complication management in parenteral nutrition In: Matarese LE, Gottschlich MM, eds. *Contemporary Nutrition Support Practice*. New York, NY: Saunders; 2003:242-262.
20. Kim GH, Han JS. Therapeutic approach to hypokalemia. *Nephron*. 2002;92(suppl 1):28-32.
21. Alfrey AC. Disorders of magnesium metabolism In: Goldman L, Bennett JC, eds. *Cecil Textbook of Medicine*. Philadelphia, Pa: Saunders; 2000:1137-1139.
22. Trissel LA. *Calcium and Phosphate Compatibility in Parenteral Nutrition*. Houston, Tex: TriPharma Communications; 2001.
23. Block GA, Port FK. Re-evaluation of risks associated with hyperphosphatemia and hyperparathyroidism in dialysis patients: recommendations for a change in management. *Am J Kidney Dis*. 2000;35:1226-1237.
24. Spiegel AM. The parathyroid glands, hypercalcemia, and hypocalcemia In: Goldman L, Bennett JC, eds. *Cecil Textbook of Medicine*. Philadelphia, Pa: Saunders; 2000:1398-1406.
25. Vanek VW. Assessment and management of acid-base abnormalities In: Shikora SA, Martindale RG, Schwaitzberg SD, eds. *Nutritional Considerations in the Intensive Care Unit: Science, Rationale, and Practice*. Dubuque, Ia: Kendall/Hunt; 2002:101-109.

Parenteral Nutrition: Macronutrient Composition and Requirements

Emily Gasser, RD, CNSD Neha Parekh, MS, RD, CNSD

Abstract

Parenteral nutrition (PN) is a complex formulation designed to deliver fluid and nutrients in the absence of a functional gastrointestinal (GI) tract. The determination of whether a patient should receive PN rests on a thorough assessment of his or her clinical and nutritional status, with consideration given to the potential risks and benefits of PN. PN solutions can be classified by either route of infusion or by macronutrient content reflected in the inclusion or exclusion of intravenous fat emulsion. The preparation of a stable and safe PN formulation requires a series of careful calculations. This article addresses the appropriate use of PN, with a focus on macronutrient composition and requirements.

Introduction

Parenteral nutrition allows for the provision of energy, vitamins, minerals, electrolytes, fluid, and various medications via a peripheral or central vein. Since the introduction of PN in United States hospitals in the late 1960s, there has been a substantial increase in the demand for such specialized solutions. This has resulted in the diversification of health-care professionals prescribing PN, including physicians, pharmacists, nurse practitioners, and dietitians.

Today, more registered dietitians are faced with the task of not only recommending macronutrient provisions, but also prescribing the entire PN solution based on each patient's unique needs. Several publications provide evidence-based guidelines for the administration of PN (1–3). This article summarizes the standard practice guidelines and provides an overview of when to use PN, macronutrient composition and requirements, types of PN solutions, and calculations for designing the PN regimen.

Patient Selection

The determination of whether a patient should receive PN rests on a thorough assessment of his or her clinical condition and nutritional status. In cases of a nonfunctional GI tract, PN should be started within 7 to 14 days. However, severely malnourished or highly catabolic patients with GI dysfunction need PN within 1 to 3 days of hospital admission (2–4).

Before initiating PN, the clinician should consider the risks and weigh them against the potential benefits of PN. The routine use of PN in the acute setting places the patient at higher risk for fluid, nutrient, and electrolyte abnormalities as well as infectious and noninfectious catheter-related complications. Additional complications of PN extending to the long-term PN patient include metabolic bone disease and hepatobiliary dysfunction (5). The primary benefit of PN is the bypass of a nonfunctional GI tract via delivery of nutrients directly into the bloodstream. Of note, PN has not been shown to be superior to enteral nutrition (EN), and with careful administration, EN is safer, less expensive, and better tolerated than PN (6).

Indications for the use of PN are listed in Table 1. Perioperative PN is generally of most benefit in patients with moderate-to-severe malnutrition and high levels of metabolic stress (7). Very limited benefit has been shown with the use of PN in end-stage, metastatic cancer (8–10). Patients with anorexia or the inability to ingest enough nutrients orally should not receive PN unless enteral access is refused or impossible to obtain (11).

Macronutrient Composition

Dextrose

The primary energy source for the human body is carbohydrate. Brain and neural tissue, erythrocytes, leukocytes, the lens of the eye, and the renal

medulla exclusively require glucose or use glucose preferentially. Therefore, carbohydrates form the basis of all PN solutions. The most commonly used carbohydrate source in PN formulas is dextrose monohydrate. Dextrose provides 3.4 kcal/g in its hydrated form and is available in a wide range of concentrations from 5% to 70% (Table 2). Percent concentration refers to the grams of solute per 100 mL of solution. A 5% dextrose solution contains 5 g of dextrose per 100 mL of solution or 50 g/L. Higher dextrose concentrations are used to decrease total volume for patients requiring fluid restriction.

Amino Acids

Protein is provided in PN for the maintenance of cell structure, tissue repair, immune defense, and skeletal muscle mass. Crystalline amino acids are used as the protein source for PN. These solutions are commonly available in concentrations ranging from 8.5% to 20% and provide 4 kcal/g (Table 2). Standard amino acid solutions are a physiologic mixture of both essential

Table 1. Indications for the Use of Parenteral Nutrition

- Intractable vomiting or diarrhea
- Prolonged paralytic ileus
- Lower gastrointestinal tract perforation or leak
- High-output enterocutaneous fistula
- Bowel ischemia
- Short bowel syndrome with severe malabsorption
- Complete lower intestinal obstruction
- Diffuse peritonitis
- Persistent gastrointestinal bleeding
- Repeated failure of enteral feeding or inability to maintain enteral access

and nonessential amino acids and vary in composition among manufacturers. A 15% or 20% standard amino acid solution may be used to concentrate the PN formula for patients with marked fluid overload.

Several disease-specific amino acid solutions are also available, primarily for use in renal or hepatic disease exacerbated by severe stress or critical illness (Table 3). Patients with declining renal function who are not undergoing dialysis may experience accumulation of urea nitrogen in the blood stream upon infusion of nonessential amino acids. In light of this, parenteral amino acid solutions containing only essential amino acids have been developed for this population. However, clinical trials have failed to show definitive improvement in renal function with these specialized solutions, and nonessential amino acids may become conditionally essential during periods of severe stress (12–14). See Table 4 for the categorization of amino acids.

Patients with hepatic encephalopathy refractory to medical management may be candidates for the use of branched-chain amino acid (BCAA) parenteral solutions (Table 4). BCAAs are oxidized primarily in the muscle instead of the liver, which preserves appropriate metabolic pathways in cases of liver failure. This area of clinical therapy has been studied extensively, but few controlled trials have demonstrated a benefit over standard amino acid solutions (15,16). In general, disease-specific amino acid solutions should not be used for more than 2 weeks because they provide an incomplete amino acid profile (17). Additionally, routine use is not recommended due to lack of supporting research and substantial expense associated with these specialized amino acid solutions.

Lipids

Lipids are a concentrated, isotonic source of energy providing 9 kcal/g and are available for intravenous (IV) use as oil-in-water emulsions ranging in concentration from 10% to 30% (Table 2). Lipid emulsions currently available in the United States contain long-chain triglycerides (LCT) in the

form of soybean oil or safflower oil, egg phospholipids as an emulsifier, and water. Glycerol is added to create an isotonic solution.

The primary role of IV lipid emulsion is to prevent essential fatty acid (EFA)

deficiency. Daily EFA requirements can be met with 4% of total calories as linoleic acid or 10% of total calories as a safflower oil-based lipid emulsion.

Patients with a documented egg
(Continued on next page)

Table 2. Macronutrient Solutions

Nutrient	Concentration	Grams per Liter	Calories per Liter
Dextrose	5%	50	170
	10%	100	340
	20%	200	680
	50%	500	1,700
	70%	700	2,380
Amino Acids	8.5%	85	340
	10%	100	400
	15%	150	600
	20%	200	800
	Concentration	Calories per Milliliter	Calories per Liter
Lipid Emulsions	10%	1.1	1,100
	20%	2	2,000
	30%	3	3,000

Table 3. Disease-specific Amino Acid Solutions

Renal Failure	NephrAmine® 5.4% (B. Braun) RenAmin® 6.5% (Baxter) Aminosyn®-RF 5.2% (Hospira)	Essential amino acid solutions
Liver Disease	HepatAmine® 8% (B. Braun) BranchAmin® 4% (Baxter) Aminosyn®-HBC 7% (Hospira) FreAmine® HBC 6.9% (B. Braun)	Solutions high in branched-chain amino acids

B. Braun: Bethlehem, Pa.

Baxter: Deerfield, Ill.

Hospira: Lake Forest, Ill.

Table 4. Amino Acid Categorization

Essential	Nonessential	Conditionally Essential	Branched-chain
Isoleucine	Alanine	Arginine	Leucine
Leucine	Asparagine	Cysteine*	Isoleucine
Lysine	Aspartate	Glutamine*	Valine
Methionine	Glutamate	Histidine	
Phenylalanine	Glycine	Taurine	
Threonine	Hydroxyproline*	Tyrosine	
Tryptophan	Ornithine*		
Valine	Serine		

*Not routinely contained in parenteral nutrition amino acid formulations.

allergy should not receive IV lipids because of the egg phospholipid content. Patients with egg allergy who require PN as the sole source of nutrition for more than 3 weeks should be closely monitored for clinical and biochemical evidence of EFA deficiency. A triene: tetraene ratio of more than 0.2, in addition to excessive hair loss; poor wound healing; dry, scaly skin unresponsive to water-miscible creams; and/or alterations in platelet function can signify EFA deficiency (18).

In rare instances, cutaneous oil application may become necessary and is best used as a preventive measure in patients at risk for EFA deficiency. Miller and associates (18) reported successful prevention of EFA deficiency with 3 mg/kg/d safflower oil applied cutaneously over 4–6 weeks; Press and colleagues (19) reported correction of EFA deficiency with application of 2 to 3 mg/kg/d sunflower seed oil for 12 weeks.

In addition to providing a source of EFA, lipids are also useful for replacing excessive dextrose calories manifested by uncontrolled blood glucose levels or hypercapnia with delayed weaning from mechanical ventilation. Lipid emulsions containing medium-chain triglycerides (MCT), fish oil, and olive

oil have been used in Europe since 1984, but are currently available in the United States for research purposes only. When compared with pure LCT emulsions, mixed MCT-LCT lipid emulsions have been shown to exert less stress on the liver, improve plasma antioxidant capacity, reduce generation of proinflammatory cytokines, improve neutrophil function, and enhance oxygenation in stressed patients (20–22).

Types of Solutions

PN solutions can be broadly classified as either total or peripheral PN based on route of administration and more specifically as “2-in-1” or “3-in-1” solutions based on macronutrient composition. A patient’s clinical and nutrition status, estimated duration of therapy, and type of IV access are important considerations when determining the most appropriate form of PN.

Total Parenteral Nutrition

Total parenteral nutrition (TPN) refers to the administration of PN through a large-diameter central vein. Central access allows for the use of a highly concentrated, hypertonic solution, which can be tailored to meet the macronutrient and fluid requirements of individual patients. Patients requiring

PN for longer than 2 weeks generally are candidates for PN via a central vein, using either a temporary central venous catheter (CVC) or a long-term CVC such as a tunneled catheter, an implanted port, or a peripherally inserted central catheter (PICC). Although TPN does offer greater freedom in formula preparation, CVCs can increase the risk of catheter-related blood stream infections, particularly when used for PN (23).

Peripheral Parenteral Nutrition

Peripheral parenteral nutrition (PPN) avoids the use of a central vein and associated complications. Because PPN is administered into a peripheral vein, the osmolarity of a PPN solution should not exceed 900 mOsm/L (Table 5). Patients receiving PPN are at risk for vein damage and thrombophlebitis if this osmolarity level is exceeded (24). Generally, PPN solutions are lipid-based because lipids are a concentrated calorie source and contribute fewer mOsm/g. Due to the lower dextrose concentration of PPN, there is less risk of hyperglycemia. However, PPN solutions provide fewer total calories, protein, and electrolytes per liter than hypertonic TPN solutions. PPN is an acceptable form of parenteral support when a patient is not hypermetabolic,

Table 5. Calculating the Osmolarity of PN Solutions

A. Total grams of amino acids per liter of solution	× 10	= _____	mOsm
B. Total grams of dextrose per liter of solution	× 5	= _____	mOsm
C. Total grams of fat (using 30% emulsion) per liter of solution	× 0.67	= _____	mOsm
D. Total mEq of calcium, magnesium, potassium, and sodium per liter of solution	× 2	= _____	mOsm
Add A, B, C, and D to derive total osmolarity of the PN solution		= _____	mOsm

(For peripheral vein tolerance, total osmolarity **per liter** should be 900 mOsm/kg or less.)

Example: PPN solution containing 1,800 kcal, 80 g amino acids (AA), 130 g dextrose, and 115 g lipid in 2,400 mL volume plus 200 total mEq of calcium, magnesium, potassium, and sodium.

A. 80 g AA ÷ 2.4 L =	33 g AA/L	× 10	= 330 mOsm
B. 130 g dextrose ÷ 2.4 L =	55 g dextrose/L	× 5	= 275 mOsm
C. 115 g lipid ÷ 2.4 L =	48 g lipid/L	× 0.67	= 32 mOsm
D. 200 mEq electrolytes ÷ 2.4 L =	83 mEq/L	× 2	= <u>167 mOsm</u>
Total Osmolarity			= 804 mOsm

Reprinted with permission from Parekh NR, DeChicco RS, eds. *Nutrition Support Handbook*. Cleveland, Ohio: The Cleveland Clinic Foundation; 2004.

Table 6. Compatibility Ranges for Total Nutrient Admixtures

Macronutrient	Acceptable Range per Liter
Standard amino acids	20 to 60 g
Dextrose	35 to 253 g (119 to 860 kcal)
Fat	13 to 67 g (130 to 670 kcal)

Reprinted with permission from Parekh NR, DeChicco RS, eds. *Nutrition Support Handbook*. Cleveland, Ohio: The Cleveland Clinic Foundation, 2004.

requires therapy for fewer than 2 weeks, has and can maintain adequate peripheral venous access, and does not require fluid restriction.

“2-in-1” Versus “3-in-1” Solutions

PN solutions are routinely comprised of carbohydrate, protein, electrolytes, vitamins, minerals, trace elements, medications, and sterile water. Such solutions are referred to as “2-in-1” solutions. Lipids can be infused separately or added to the PN solution to form a total nutrient admixture (TNA) or “3-in-1” solution. A 2-in-1 solution is favorable when patients have high protein or minimal fluid needs and can maintain euglycemia with the addition of a modest insulin dose.

TNAs that include lipids are convenient and require less nursing time for administration. A TNA may be especially advantageous in patients who have increased energy needs or who would benefit from reduced carbohydrate provisions due to persistent hyperglycemia or hypercapnia (2). The phospholipid outer layer imparts stability to intravenous lipids when provided in a 3-in-1 admixture. However, macronutrient components must fall within acceptable ranges per liter for the 3-in-1 solution to remain stable (Table 6). If one component falls outside of the acceptable range, the stability of the solution cannot be guaranteed for 24 hours. Disruption of stability can present as either distinctive creaming or “oiling out” in which the lipid portion separates from the aqueous phase of the solution containing dextrose and protein. In this case, the TNA cannot be infused due to risk of fat embolus with unemulsified lipid.

Macronutrient Requirements

Daily macronutrient requirements are individualized based on age, sex, anthropometrics, body composition, activity level, medical diagnoses, degree of metabolic stress, and clinical circumstances. Several techniques are available for the estimation and measurement of energy expenditure. The accuracy of predictive equations in hospitalized patients remains an area of debate due to physiologic differences among patients and the multitude of factors affecting the ability to obtain a valid body weight.

A retrospective review by Barak and colleagues (25) used indirect calorimetry measurements to uncover disease-specific stress factors useful in estimating calorie needs for hospitalized patients. When multiplied by the Harris-Benedict equation, estimated energy expenditure using these stress factors closely approximated established literature values. The authors recommended using actual weight of normal and underweight patients and an adjusted body weight equal to ideal body weight plus 50% of excess body weight for estimating energy expenditure of obese patients requiring nutrition support.

Indirect calorimetry is used to derive energy expenditure through measurements of O₂ consumption, substrate oxidation, and CO₂ production. Substrate utilization is reflected in the ratio of CO₂ produced to O₂ consumed or the respiratory quotient (RQ) (Table 7). In general, an RQ greater than 1.0 suggests administration of excess carbohydrate or total calories with ensuing lipogenesis. An ideal RQ is between 0.85 and 0.95, indicating protein sparing and mixed utilization of carbohydrate and fat (26). Despite

the need to use protein for wound healing and maintenance of muscle mass, when estimating total daily energy requirements and prescribing PN, calories from all three substrates should be included (27).

Carbohydrate

The average adult requires approximately 100 g/d carbohydrate or 1 mg/kg/min to meet minimum daily requirements for central nervous system function. Without this daily requirement, protein is broken down to obtain the necessary fuel through gluconeogenesis. A minimum of 130 g/d carbohydrate is recommended for healthy adults and children as part of the Dietary Reference Intakes (DRI) (28). Prolonged underfeeding of carbohydrate and total calories via the enteral or parenteral route has been associated with poor wound healing, increased risk of infection, respiratory dysfunction, and an overall poor prognosis (29).

In cases of chronic underfeeding, the body adapts by decreasing reliance on carbohydrate and gluconeogenesis pathways and increasing utilization of ketones and fatty acids for energy. An increase in ketone body formation puts the patient at risk for ketoacidosis, a disruption of acid-base balance within the body (30). The reintroduction of carbohydrate loads causes a rapid shift to glucose as the primary fuel, thereby increasing the demand for insulin, which may not be available in adequate amounts to meet the demand. Hyperglycemia, hypophosphatemia, hypokalemia, hypomagnesemia, hypotension, dehydration, fluid retention, and

(Continued on next page)

Table 7. Respiratory Quotients for Various Substrates

Substrate	Respiratory Quotient
Alcohol	0.67
Fat	0.71
Protein	0.82
Mixed substrate	0.85
Carbohydrate	1.00
Lipogenesis	1.01 to 1.20

metabolic acidosis can occur with rapid refeeding of carbohydrate after prolonged starvation, known as the refeeding syndrome. Any existing electrolyte deficiencies should be corrected before initiating PN at 50% of caloric requirements or approximately 15 to 20 kcal/kg. PN can then be advanced over the next few days while closely monitoring electrolytes, blood glucose, and body weight.

Overfeeding is also of concern because excess carbohydrate administration has been associated with hyperglycemia, hepatic steatosis, and increased CO₂ production, which may preclude weaning of the ventilator-dependent patient (31). Continuous dextrose infusion rates greater than 4 mg/kg/min led to an increased incidence of hyperglycemia in a study of 37 nondiabetic PN patients (32). Intravenous carbohydrate administration, therefore, should not exceed 4 mg/kg/min in critically ill patients and 7 mg/kg/min in stable hospitalized patients, unless they are undergoing cycling of PN with careful monitoring of blood glucose levels (33). Replacement of excess carbohydrate with lipid calories may aid in the maintenance of euglycemia, the prevention of excess CO₂ production, and the reduction of lipogenesis.

Protein

Daily protein needs are based on the patient's age, weight, and nutritional and clinical status. Inadequate protein intake can result in negative nitrogen balance, depleted hepatic proteins, and delayed wound healing. The Recommended Dietary Allowance (RDA) for

protein for healthy adults is 0.8 g/kg/d. In periods of acute illness, muscle breakdown is accelerated and exceeds protein synthesis, which results in a net negative nitrogen balance.

Hospitalized patients requiring PN generally need 1.5 to 2.0 g/kg/d protein, with adjustments made according to tolerance, clinical course, nitrogen balance, and monitoring of hepatic protein status (34). Critically ill patients receiving continuous venovenous hemodialysis may require up to 2.5 g protein per kilogram of dry body weight daily to promote nitrogen balance (17). Prerenal azotemia may develop as a result of dehydration or excess protein intake, although a mild increase in blood urea nitrogen (BUN) values can be expected with moderate-to-high amounts of protein infusion via PN. IV protein provisions should be decreased when BUN levels exceed 100 mg/dL (35).

Fat

Daily lipid requirements are met by providing adequate EFA in the form of linoleic acid. For healthy adults, the DRI for linoleic acid is 17 g/d for men and 12 g/d for women (28). This equates to about 10% of total calories as a commercial IV lipid emulsion of soybean or safflower oil. Lipid emulsions currently available in the United States are composed principally of LCT, which may have an immunosuppressive effect when administered in large amounts over short periods of time. Rapid infusion of IV lipids has been associated with the impairment of neutrophil production and the reduction

of endotoxin clearance (36,37). An attempt should be made to limit IV lipid administration to 1 g/kg/d or 25% to 30% of total calories to avoid adverse reactions such as respiratory insufficiency, fever, chills, headache, back or chest pain, nausea, and vomiting.

PPN solutions are commonly lipid-based because of the low contribution of IV lipid to the osmolarity of the solution. Because PPN solutions have osmolarity restrictions and generally cannot meet total calorie requirements, patients receiving such solutions may be fed up to 50% of total calories as lipid safely. However, care must be taken to attempt to limit lipid administration to 1 g/kg/d. The overfeeding of lipids can also result in hypertriglyceridemia or reduced lipid clearance. In cases of suspected altered lipid metabolism, as in pancreatitis, sepsis, and moderate-to-severe liver disease, serum triglyceride levels should be monitored before and 6 hours after PN infusion (5). Lipid administration should be held when serum triglyceride levels exceed 400 mg/dL (2).

Designing the PN Solution

The route and nutrient composition of a PN solution governs the calculations needed for preparation of a safe PN formula. Most institutions have a standardized order protocol used by all clinicians prescribing PN. In addition, an expert panel representing the American Society for Parenteral and Enteral Nutrition recently published updated guidelines on safe practices for PN formulations (3). The panel recommends standardized ordering

Table 8. Guidelines for Dosing Macronutrients and Fluid in PN

	Normal Range	Minimum Dose	Maximum Dose
Total Calories (kcal/kg/d)	25 to 35	10 (for morbid obesity)	45 to 55 (for severe malnutrition)
Protein (g/kg/d)	0.8 to 1.5	0.8	2.5
Dextrose (mg/kg/min)	2 to 3.5	1	4 to 7
Fat (% total calories)	25 to 30	10% as commercial IV fat emulsion (4% as linoleic acid)	30
Fluid (mL/kg/d)	30 to 40	As per compatibility/ osmolarity guidelines	Variable, depending on fluid losses and need for repletion

and labeling of PN solutions to display dextrose, amino acids, and IV fat emulsion as grams per total daily volume to support the use of a 24-hour nutrient infusion system.

Preparation of a stable and safe PN formulation requires a series of careful calculations. Once central venous access has been established, the process of designing the PN prescription begins. Table 8 provides an overview of dosage guidelines for macronutrient and fluid content of PN solutions. Protein is usually the first macronutrient to be addressed, and the first bag of TPN should provide full protein needs. The first bag of TPN also should deliver a reduced dextrose level (about 50% of total requirements or 150 to 200 g) to prevent complications such as hyperglycemia or fluid and electrolyte abnormalities. Assuming that the first bag of TPN administers full fluid needs, lipids are generally excluded to avoid difficulties in maintaining compatibility of the solution (Table 6).

Once laboratory values are within normal limits, TPN calories can be advanced to full requirements, with lipids infused concurrently or separately, based on patient tolerance. The minimal volume required to maintain all nutrients in solution may be calculated for those patients in need of fluid restriction (Table 9). Given the osmolarity restrictions of PPN, nutrient provisions generally depend on the patient's fluid allowance. Once this is determined, macronutrients can be calculated to maximize nutrient provisions for the given PPN volume (Table 5). Table 10 provides sample TPN and PPN solutions for an average 70-kg patient. The level of macronutrients provided in PN solutions should be modified from the standard based on individual patient tolerance and requirements.

Conclusion

PN is a complex formulation of macronutrients, electrolytes, vitamins, trace elements, water, and medications used in the absence of a functioning GI tract. A thorough evaluation of each patient's clinical and nutritional status forms the basis for deciding when to initiate PN, what form of PN to

Table 9. Calculating Minimum Volume for PN Solutions*

A. Total grams of amino acids	× 10 = _____ mL
B. Total dextrose calories	÷ 2.38 = _____ mL
C. Total lipid calories	÷ 3.0 = _____ mL
D. Estimate 200 mL for electrolytes and additives	= _____ mL
Add A, B, C, and D to derive total volume of the PN solution	= _____ mL

Example: PN solution containing 2,000 kcal, 100 g amino acids, 1,120 dextrose calories, and 480 lipid calories.

A. 100 g amino acids	× 10 = 1000 mL
B. 1,120 dextrose calories	÷ 2.38 = 471 mL
C. 480 lipid calories	÷ 3.0 = 160 mL
D. 200 mL electrolytes and additives	= 200 mL
Total Minimum Volume	= 1831 mL

*Using a 10% amino acid solution, 70% dextrose solution, and 30% lipid emulsion.

Table 10. Sample PN Solutions (for an Average 70-kg Patient)

	TPN	PPN
Total Volume (mL)	2,000	2,000
Total Calories	2,100	1,400
kcal/kg	30	20
Protein		
g	110	60
g/L	55	30
g/kg/d	1.6	0.9
Dextrose		
g	342	137
g/L	171	68.5
mg/kg/min	3.4	1.36
Fat		
g	55	77
g/L	27.5	38.5
g/kg/d	0.4	1.1
Percentage of total calories	24	50

PN=parenteral nutrition, TPN=total parenteral nutrition, PPN=peripheral parenteral nutrition

administer, and how to design the PN prescription. Adherence to evidence-based guidelines involving PN macronutrient composition can ensure provision of a safe and stable PN solution.

Emily Gasser, RD, CNSD, is a metabolic support clinician in the Nutrition Support

and Vascular Access Department of the Cleveland Clinic Foundation, Cleveland, Ohio.

Neba Parekh, MS, RD, CNSD, is nutrition coordinator of the Intestinal Rehabilitation Program at the Cleveland Clinic Foundation, Cleveland, Ohio.

(Continued on next page)

References

- Barber JR, Miller SJ, Sacks GS. Parenteral feeding formulations. In: Gottschlich MM, Fuhrman MP, Hammond KA, Holcombe BJ, Seidner DL, eds. *The Science and Practice of Nutrition Support. A Case-Based Core Curriculum*. Dubuque, Ia: Kendall/Hunt Publishing; 2001:251–268.
- A.S.P.E.N. Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *J Parenter Enteral Nutr*. 2002;26:1SA–138SA.
- Mirtallo J, Canada T, Johnson D, et al. Safe practices for parenteral nutrition. Task Force for the Revision of Safe Practices for Parenteral Nutrition. *J Parenter Enteral Nutr*. 2004;26:S39–S70.
- Mirtallo JM. Introduction to parenteral nutrition. In: Gottschlich MM, Fuhrman MP, Hammond KA, Holcombe BJ, Seidner DL, eds. *The Science and Practice of Nutrition Support. A Case-Based Core Curriculum*. Dubuque, Ia: Kendall/Hunt Publishing; 2001:211–223.
- Maratese LE. Metabolic complications of parenteral nutrition therapy. In: Gottschlich MM, Fuhrman MP, Hammond KA, Holcombe BJ, Seidner DL, eds. *The Science and Practice of Nutrition Support. A Case-Based Core Curriculum*. Dubuque, Ia: Kendall/Hunt Publishing; 2001:269–286.
- Moore FA, Feliciano DV, Andrassy RJ, et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. *Ann Surg*. 1992;216:172–183.
- The Veterans Affairs Total Parenteral Nutrition Cooperative Group. Perioperative total parenteral nutrition in surgical patients. *N Engl J Med*. 1991;325:525–532.
- Bozzetti F, Cozzaglio L, Biganzoli E, et al. Quality of life and length of survival in advanced cancer patients on home parenteral nutrition. *Clin Nutr*. 2002;21:281–288.
- Sharp JW, Roncagli T. HPN in advanced malignancies. *J Parenter Enteral Nutr*. 1992;16:190–191.
- King LA, Carson LF, Konstantinides N, et al. Outcome assessment of home parenteral nutrition in patients with gynecologic malignancies: what have we learned in a decade of experience? *Gynecol Oncol*. 1993;51:377–382.
- DeChicco R, Trew A, Seidner D. What to do when a patient refuses a feeding tube. *Nutr Clin Pract*. 1997;12:228–230.
- Feinstein EI, Blumenkrantz MJ, Healy M, et al. Clinical and metabolic responses to parenteral nutrition in acute renal failure. A controlled double-blind study. *Medicine*. 1981;60:124–137.
- Naylor CD, Detsky AS, O'Rourke K, Fonberg E. Does treatment with essential amino acids and hypertonic glucose improve survival in acute renal failure? A meta-analysis. *Renal Failure*. 1988;10:141–152.
- Freund H, Atamian S, Fischer JE. Comparative study of parenteral nutrition in renal failure using essential and nonessential amino acid containing solutions. *Surg Gynecol Obstet*. 1980;151:652–656.
- Rocchi E, Cassanelli M, Gilbertini P, Pietrangelo A, Casalgrandi G, Ventura E. Standard or branched-chain amino acid infusions as short-term nutritional support in liver cirrhosis? *J Parenter Enteral Nutr*. 1985;9:447–451.
- Kanematsu T, Koyanagi N, Matsumata T, Kitano S, Takenaka K, Sugimachi K. Lack of preventative effect of branched-chain amino acid solution on postoperative hepatic encephalopathy in patients with cirrhosis: a randomized, prospective trial. *Surgery*. 1988;104:482–488.
- Parekh NR, Seidner DL. Disease-specific nutrition. In: Irwin RS, Rippe JM, eds. *Irwin and Rippe's Intensive Care Medicine*. 5th ed. Philadelphia, Pa: Lippincott, Williams & Wilkins; 2003:2069–2080.
- Miller DG, Williams SK, Palombo JD, Griffin RE, Bistran BR, Blackburn GL. Cutaneous application of safflower oil in preventing essential fatty acid deficiency in patients on home parenteral nutrition. *Am J Clin Nutr*. 1987;46:419–423.
- Press M, Hartop PJ, Prottey C. Correction of essential fatty acid deficiency in man by the cutaneous application of sunflower-seed oil. *Lancet*. 1974;1:596–598.
- Antebi H, Mansoor O, Ferrier C, et al. Liver function and plasma antioxidant status in intensive care unit patients requiring total parenteral nutrition: comparison of 2 fat emulsions. *J Parenter Enteral Nutr*. 2004;28:142–148.
- Mayer K, Fegbeutel C, Hattar K, et al. Omega-3 vs. omega-6 lipid emulsions exert differential influence on neutrophils in septic shock patients: impact on plasma fatty acids and lipid mediator generation. *Intensive Care Med*. 2003;29:1472–1481.
- Faucher M, Bregeon F, Gainnier M, Thirion X, Auffray JP, Papazian L. Cardiopulmonary effects of lipid emulsions in patients with ARDS. *Chest*. 2003;124:285–291.
- Centers for Disease Control and Prevention. Guidelines for the prevention of intravascular catheter-related infection. *J Infusion Nurs*. 2002;25:S37–S65.
- Isaacs JW, Millikan WJ, Stackhouse J, Hersh T, Rudman D. Parenteral nutrition of adults with a 900 milliosmolar solution via peripheral veins. *Am J Clin Nutr*. 1977;30:552–559.
- Barak N, Wall-Alonso E, Sitrin MD. Evaluation of stress factors and body weight adjustments currently used to estimate energy expenditure in hospitalized patients. *J Parenter Enteral Nutr*. 2002;26:231–238.
- Hester DD, Lawson K. Suggested guidelines for use by dietitians in the interpretation of indirect calorimetry data. *J Am Diet Assoc*. 1989;89:100–101.
- Skipper A, Tupesis N. Is there a role for nonprotein calories in developing and evaluating the nutrient prescription? *Nutr Clin Pract*. 2005;20:321–324.
- Institute of Medicine, Food and Nutrition Board. *Dietary Reference Intakes: Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids*. Washington, DC: National Academy Press; 2002.
- Fuhrman MP. Complication management in parenteral nutrition. In: Matarese LE, Gottschlich MM, eds. *Contemporary Nutrition Support Practice*. Philadelphia, Pa: WB Saunders; 2003:242–262.
- Groff JL, Sareen SG. *Advanced Nutrition and Human Metabolism*. 3rd ed. Belmont, Calif: Wadsworth/Thomson Learning; 2000:123–162.
- McClave SA, Lowen CC, Kleber MJ. Are patients fed appropriately according to their caloric requirements? *J Parenter Enteral Nutr*. 1998;22:375–381.
- Rosmarin DK, Wardlaw GM, Mirtallo J. Hyperglycemia associated with high, continuous infusion rates of PN dextrose. *Nutr Clin Pract*. 1996;11:151–156.
- Wolfe RR, O'Donnell TF Jr, Stone MD. Investigation of factors determining the optimal glucose infusion rate in total parenteral nutrition. *Metabolism*. 1980;29:892–900.
- Lennon E, Speerhas R. Estimating nutritional requirements. In: Parekh NR, DeChicco RS, eds. *Nutrition Support Handbook*. Cleveland, Ohio: The Cleveland Clinic Foundation; 2004:34–60.
- Hamilton C, Speerhas R, Steiger E. Recognition and management of complications of parenteral nutrition. In: Parekh NR, DeChicco RS, eds. *Nutrition Support Handbook*. Cleveland, Ohio: The Cleveland Clinic Foundation; 2004:93–106.
- Seidner DL, Mascioli EA, Istfan NW, et al. Effects of long-chain triglyceride emulsions on reticuloendothelial system function in humans. *J Parenter Enteral Nutr*. 1989;13:614–619.
- Jensen GL, Mascioli EA, Seidner DL, et al. Parenteral infusion of long- and medium-chain triglycerides and reticuloendothelial system function in man. *J Parenter Enteral Nutr*. 1990;14:467–471.