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An In-Depth Look:

PARENTERAL NUTRITION

CE Article #2

Parenteral Nutrition: Formulation, Monitoring, and Complications*

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ABSTRACT: Because decreased caloric and nutrient intake can complicate the course of both mild and serious illness, parenteral nutrition (PN) is an important feeding modality for patients unable to receive adequate enteral nutrition. Although the effectiveness of PN has not been proven in animals, human studies have shown that using PN in appropriately selected cases can improve clinical outcome, reduce hospitalization time, and even reduce the overall cost of patient care. PN formulations for animals are readily available through pharmacies. This article provides practitioners with basic information on calculating and using PN in patients. Information is also provided on monitoring patients receiving PN as well as ways to identify and overcome common complications in animals receiving PN.

Parenteral nutrition (PN) involves intravenous administration of nutrients to patients that require nutritional support and are anorectic despite correction of dehydration and other metabolic derangements. PN solutions are usually mixtures of dextrose solutions, lipid emulsions, and amino acid solutions that variably contain electrolytes, vitamins, and mineral supplements (see the companion article beginning on p. 76). When dextrose, lipids, and amino acids are used together in a PN formulation, the resulting mixture is called a *three-in-one solution* or *total nutrient admixture*. Three-in-one solutions are easy to administer; provide a patient's short-term amino acid, glucose, and energy needs in one solution; and are well tolerated by patients.[1] Dextrose and amino acid solutions—without lipids—are given to patients as well. The use of these solutions can help avoid negative side effects of lipid administration. Dextrose and amino acid solutions do not need to be replaced on a daily basis as with lipid-containing admixtures but, because they contain fewer kilocalories per milliliter, require substantially greater volumes of delivery to meet caloric needs (see the companion article beginning on p. 76 for the advantages and possible drawbacks of lipid supplementation).

*A companion article on uses, indications, and compounding begins on p. 76.
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Published opinions differ on the appropriate estimate of nutrient requirements for a patient. For the purposes of the following discussion, we will describe the formulation method used by the University of Missouri-Columbia Veterinary Teaching Hospital and several other veterinary colleges. The formulation is based on descriptions by Remillard and Thatcher[2] and Lippert and Armstrong[3] and is similar to other methods described in the veterinary literature.[4–6] However, research is ongoing in the field of veterinary nutrition, and the future may hold alterations to this formulation.

TOTAL PARENTERAL NUTRITION FORMULATION

To calculate total parenteral nutrition (TPN) rates, see Tables 1 and 2.

Step 1: Calculate the Basal Energy Requirement

The basal energy requirement (BER) represents the energy requirement of an animal maintained under conditions involving the least energy expenditure for sustaining life:

$$\text{BER (kcal/day)} = (30 \times \text{Body weight in kg } [BW_{kg}]) + 70$$
(for patients weighing 2–45 kg)

$$\text{BER (kcal/day)} = 70\ (BW_{kg})^{0.75}$$
(for patients weighing <2 and >45 kg)

BER is determined under experimental conditions when an animal is in a post–nutrient-absorptive state, not engaged in voluntary activity, and kept in a thermoneutral environment. BER is typically used as an approximation of a patient's resting energy requirement (RER), which is an animal's energy expenditure at rest under conditions less restricted than those used in measuring BER.[2] BER and RER are often used interchangeably in the literature describing energy requirement estimation. For the body weight range indicated, the first BER equation is a useful linear interpolation of the second equation, which is commonly known as the *Kleiber-Brody equation*.

A recent publication indicated that neither equation is a perfect estimation of BER for individual animals; the equations better represent the energy needs of populations of animals.[7] Nonetheless, they are commonly used as a starting point for BER estimation. Some sources propose using the following equation for feline energy requirements[8]:

$$\text{BER} = 40 \times BW_{kg}$$

Proponents of this equation argue that for "typical" adult cats weighing 4.4 to 13.2 lb (2 to 6 kg), the total calculated caloric intake is too great when $(30 \times BW_{kg}) + 70$ is used to estimate BER and, by extension, patients are being nutritionally oversupplemented.

Step 2: Determine the Total Energy Requirement

The total energy requirement (TER) is also called the *illness energy requirement* (IER).

$$\text{TER} = \text{BER} \times \text{Illness factor}^{2}$$

Traditionally, illness factors range from 1.0 to 2.0. In the current system at the University of Missouri-Columbia, a burn patient would be assigned an illness factor of 2.0 to provide for increased losses of protein and fluid through cutaneous wounds. A patient with a hypermetabolic condition, such as sepsis, would have an illness factor of 1.7, whereas a patient without severe trauma or body protein losses would require only the BER and thus an illness factor of 1.0.

These factors were initially derived from research in humans during the late 1970s and 1980s. The factors have been reported and repeated in the veterinary literature without direct verification of their use in animals and, therefore, may not be valid in animals.[2]

The validity of multiplying the BER by an illness factor has recently been questioned.[8,9] Human studies[9,10] have shown that during periods of illness or after trauma, the body naturally transitions to a catabolic state. Insulin resistance occurs, and transient hyperglycemia may result. In this state, regardless of the amount of dextrose infused, the body cannot make full use of it. This brings into question the formerly accepted idea that supplying large amounts of dextrose to stressed patients to meet their energy needs is appropriate in all cases.

More recent human studies[9,10] have also shown that increasing protein intake (as amino acids in PN) above the patient's basal metabolic needs does not effectively counter protein catabolism during periods of stress or illness. Amino acids that are unused for body protein needs are instead used to generate energy, resulting in proportionally increased metabolic urea and ammonia production.

Therefore, the practice of multiplying the BER by an

Table 1. Sample Calculation of Total Parenteral Nutrition for a 22-lb (10-kg) Dog with Pancreatitis

Step	Equation
1: Calculate the BER	30 × (10 kg) + 70 = 370 kcal/day
2: Calculate the TER	In this case, the illness factor is 1.0. TER = 370 kcal/day
3: Determine the daily protein requirement	4 g/100 TER kcal/day × 370 kcal/day = 14.8 g of protein/day
4: Determine the volume of nutrient solutions required	
Dextrose	The patient will receive 60% of its daily energy requirement as dextrose. 0.60 × TER = 0.60 × 370 kcal/day = 222 kcal/day as dextrose 222 kcal/day ÷ 1.7 kcal/ml of 50% dextrose = 130.5 ml/day (rounded to 131 ml/day) of 50% dextrose
Lipids	The patient will receive 40% of its daily energy requirement as lipids. 0.40 × TER = 0.40 × 370 kcal/day = 148 kcal/day as lipids 148 kcal/day ÷ 2 kcal/ml of 20% lipid solution = 74 ml/day of 20% lipid solution
Amino acids	14.8 g of protein/day ÷ 85 mg/ml of 8.5% amino acid solution = 174.1 ml/day (rounded to 174 ml/day) of amino acids
5: Determine the total volume and hourly rate of TPN solution administration	131 ml + 74 ml + 174 ml = 379 ml/day of TPN solution 379 ml/day ÷ 24 hr = 15.8 ml/hr of TPN solution
6: Determine the daily vitamin requirements	Vitamin K: 0.5 mg/kg × 10 kg = 5 mg SC once weekly, if needed Supplementation with vitamin B may be necessary. For example: 370 kcal/day ÷ 1 ml B complex/1,000 kcal = 0.37 ml/day
7: Administer TPN	Day 1: Administer one-third of the calculated requirement. ⅓ × (379 ml/day + 0.37 ml/day of B vitamins) ÷ 24 hr = 5.3 ml/hr Day 2: Administer two-thirds of the calculated requirement. ⅔ × (379 ml/day + 0.37 ml/day B vitamins) ÷ 24 hr = 10.5 ml/hr Day 3 and on: Administer the full calculated requirement plus 0.37 ml/day B vitamins. 379 ml/day + 0.37 ml/day B vitamins ÷ 24 hr = 15.8 ml/hr

illness factor to supply greater amounts of energy as protein (in the form of amino acids), dextrose, and lipids may not benefit a patient and may actually be detrimental. There is agreement within the human literature that during stress and illness, a human's energy requirements do not increase more than 1.2 × BER.[9] Thus the current movement in veterinary medicine is away from using illness factors in energy requirement calculations for all

Table 2. Total Parenteral Nutrition Worksheet

Step	Equation
1: Calculate the BER	30 × (_____ kg) +70 = _____ kcal/day
2: Calculate the TER	TER = illness factor × BER = _____ kcal/day
3: Determine the daily protein requirement	Protein requirement × _____ kcal/day = _____ g/day of protein
4: Determine the volume of nutrient solutions required	
Dextrose	The patient will receive _____ % of its daily energy requirement as dextrose. _____ % × TER = _____ kcal/day as dextrose _____ kcal/day dextrose ÷ 1.7 kcal/ml of 50% dextrose = _____ ml/day of 50% dextrose
Lipids	The patient will receive (100 − _____)% of its daily energy requirement as lipids. _____ % × TER = _____ kcal/day as lipids _____ kcal/day ÷ 2 kcal/ml of 20% lipid solution = _____ ml/day of 20% lipid solution
Amino acids	_____ g/day of protein ÷ 85 mg/ml of 8.5% amino acid solution = _____ ml/day of amino acids
5: Determine the total volume and hourly rate of TPN solution administration	_____ ml of dextrose + _____ ml of lipids + _____ ml of amino acids = _____ ml/day of TPN solution _____ ml/day ÷ 24 hr = _____ ml/hr of TPN solution
6: Determine the daily vitamin requirements	Vitamin K: 0.5 mg/kg × _____ kg = _____ mg SC once weekly, if needed Supplementation with vitamin B may be necessary. For example: BER ÷ 1 ml of B complex/1,000 kcal = _____ ml
7: Administer TPN	Day 1: Administer one-third of the calculated requirement. ⅓ × (_____ ml/day + _____ ml/day of B vitamins) ÷ 24 hr = _____ ml/hr Day 2: Administer two-thirds of the calculated requirement. ⅔ × (_____ ml/day + _____ ml/day of B vitamins) ÷ 24 hr = _____ ml/hr Day 3 and on: Administer the full calculated requirement plus _____ ml/day of B vitamins. _____ ml/day + _____ ml/day of B vitamins ÷ 24 hr = _____ ml/hr

but a few select patients. Limiting the use of illness factors to specific cases can help avoid patient oversupplementation, which can lead to hyperglycemia, liver dysfunction, or unwanted metabolic acid and ammonia production.[8] Most commonly, PN solutions are given at gradually increasing rates to meet the BER, and rate adjustments are made according to patient response as assessed during monitoring (see p. 97).

Step 3: Determine the Protein Requirement

As already discussed in this article and in the companion article beginning on p. 76, parenterally administered

Typical Protein Requirements

Adult cats	6 g/kg/day
Cats with renal/hepatic disease	3 g/kg/day
Adult dogs	4 g/100 TER kcal/day
Dogs with renal disease	1.5 g/kg/day
Dogs with extraordinary protein loss	6 g/100 TER kcal/day

amino acids are used to replace amino acids lost in protein turnover and other biochemical pathways.[2,3] It should be recognized that during both the fed and food-deprived states, amino acid catabolism is always occurring, albeit at different rates. Hence, regardless of whether protein requirements are met by amino acids given in PN admixtures, catabolism of amino acids always makes some contribution to body energy needs (see box on this page).

Although energy production from amino acid catabolism is well recognized, many parenteral formulations currently used in veterinary medicine (including the present formulation) do not account for energy derived from the provided amino acids. Such formulations are prepared so that the animal's energy requirement is completely supplied as dextrose and lipids. This is done to address the concern that most supplemented amino acids will be converted into energy via gluconeogenesis rather than used for protein synthesis and other anabolic processes if insufficient energy is supplied to the patient from other sources.[2] Also, excessive amino acid supplementation may lead to the excretion of nitrogenous wastes, such as urea, which uses the energy derived from the supplemented dextrose and lipids.[2]

For optimal use of parenteral amino acids in anabolic processes, it is believed that amino acids should be given in a certain proportion with energy. Therefore, the protein requirement (in amino acids) is determined per 100 kcal of TER in dogs.[2] Because variation in body weight among adult cats is considerably less than that among adult dogs, the optimal protein:energy ratio in cats is suitably expressed as a ratio of grams of protein per kilogram of body weight.

A 2001 study[11] was conducted to determine the protein requirements of parenterally fed normal dogs using nitrogen balance methodology. It examined the presently used 4 g/kg/day estimation of canine protein requirements, which originated from a 1968 publication reporting research on PN in adult beagles.[12] The recent work[11] indicates that 2.3 g/kg/day is the intravenous amino acid requirement for clinically normal dogs fed their maintenance energy requirements (i.e., roughly equivalent to 2 × BER). At this time, it is unclear whether this amount of protein can be used in diseased dogs when supplying only BER, but it is possible that the protein requirement for dogs may be significantly less than the 4 to 6 g/kg/day traditionally used as the daily protein requirement.

A study[13] evaluating the effects of dietary protein restriction and amino acid deficiency on protein metabolism in dogs fed enterally concluded that a healthy dog's typical daily nitrogen requirement is 0.41 to 0.55 g/(kg$^{0.75}$). A recent study[14] conducted on healthy adult cats fed enterally concluded that they require 2.7 g/kg/day of crude protein to meet their needs. Both studies suggest that actual protein and amino acid requirements may be lower than current recommendations in cats and dogs. However, because both of these studies involved enteral provision of nutrients, it is difficult to know the relevance of these findings to PN formulation. In addition, these were healthy animals, and a direct correlation to systemically ill pets cannot be inferred.

Patients benefit from parenteral nutrition but frequently have at least transient hyperglycemia and may require insulin supplementation.

Step 4: Determine the Volume of Nutrient Solutions Required

Dextrose Solution

The dextrose solution most often used in TPN admixtures is 50% (500 mg/ml) dextrose and contains 1.7 kcal/ml. Patients typically receive 40% to 60% of their energy requirements from dextrose. If hyperglycemia or insulin resistance is an anticipated complication of PN, it may be better to provide closer to 40% of the energy requirements as dextrose. The remaining requirement for energy must be supplied through the

lipid portion of the PN solution. To deliver 60% of a patient's energy (i.e., TER) from dextrose, the volume of solution can be calculated using the following equation:

TER × 0.60 = ___ kcal/day of dextrose ÷ 1.7 kcal/ml = ___ ml of 50% dextrose per day

Lipid Emulsion

The lipid most commonly used in TPN admixtures is a 20% (200 mg/ml) vegetable oil emulsion containing 2 kcal/ml. Ten percent and 30% lipid emulsions are used in special cases. Patients typically receive 40% to 60% of their energy requirement as lipid. For 40% of the energy requirement (i.e., TER), calculate the volume of 20% lipid emulsion using the following equation:

TER × 0.40 = ___ kcal/day of lipids ÷ 2 kcal/ml = ___ ml of 20% lipid solution per day

Amino Acid Solution

As with dextrose solutions and lipid emulsions, amino acid solutions are available in a variety of concentrations. The most commonly used solution is 8.5% (85 mg/ml) amino acids available with and without electrolytes. With the use of an 8.5% solution, the following equation can be used to calculate the volume of amino acid solution:

_____ g protein/day ÷ 85 mg/ml × 1,000 mg/g = _____ ml/day

Step 5: Determine the Total Volume of Total Parenteral Nutrition Solution

(___ ml of dextrose + ___ ml of lipids + ___ ml of amino acids) ÷ 24 hr = ___ ml/hr

First day: Typically administer one-third of this rate
Second day: Typically administer two-thirds of this rate
Third day: Typically administer at the full calculated daily rate

Most patients are gradually introduced to TPN to avoid rebound hyperglycemia and other electrolyte abnormalities from the sudden infusion of large concentrations of dextrose (Figure 1; also, see the Patient Monitoring section on p. 97). The patient may also require additional intravenous crystalloid fluids through another intravenous port to meet daily maintenance fluid and electrolyte requirements. In patients with severe electrolyte disturbances (e.g., diabetic ketoacidosis), the use of amino acid formulations without electrolytes may simplify case management. In such cases, electrolyte-containing solutions can be administered through a separate intravenous catheter to allow more controlled titration and provision for electrolyte deficits.

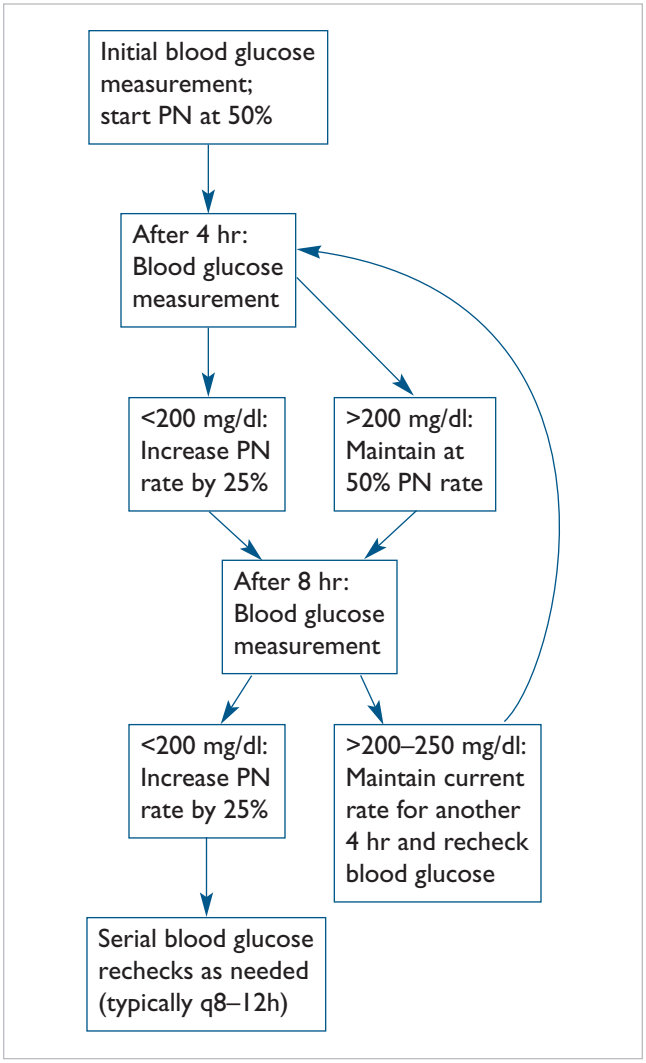

Figure 1. Strict blood glucose monitoring protocol.

Step 6: Determine the Daily Vitamin Requirements

If the patient will not receive enteral nutrition for more than 5 to 7 days, the clinician may also want to supplement the PN solution with vitamin K_1 (0.5 mg/kg SC once weekly).

Virtually all sources indicate that B vitamins should be supplemented in patients receiving TPN. B vitamins are essential in the use of the dextrose, lipids, and amino

acids delivered in the PN solution, and most patients ill enough to receive PN have B vitamin deficiencies. However, the actual amount of B vitamins required by critically ill animals and the amount added to PN solutions vary widely in the veterinary literature.

The exact formulation and dose of supplemental B vitamins are also rarely mentioned. Original sources recommend that the B vitamin preparations include at least five to seven of the "important" B vitamin types (i.e., folic acid, thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, B_{12}) but do not specify a particular preparation or dose.[2] A frequently published B vitamin supplementation recommendation is to add 1 ml of B complex vitamins per 1,000 kcal of energy supplied in the PN admixture; this amount can supply more than the minimum nutritional requirements of B vitamins for adult dogs and cats as determined by the National Research Council on the Nutritional Requirements of Dogs and Cats.[15] However, those recommendations reflect enteral nutrition requirements and may not be correct when nutrition is supplied parenterally.

Our institution uses a vitamin B complex solution containing (per milliliter) 12.5 mg of thiamine hydrochloric acid, 12.5 mg of niacinamide, 2 mg of riboflavin, 5 mg of D-panthenol, and 0.2 ppm cobalt as vitamin B_{12}. One milliliter of the solution per 1,000 kcal of TER is estimated to well exceed the dietary requirements of dogs and cats.

PARTIAL PARENTERAL NUTRITION FORMULATION

If three-in-one admixtures of partial parenteral nutrition (PPN) containing lipids, dextrose, and amino acids are being administered, the following guidelines apply[16] (Tables 3 and 4).

Step 1

Calculate the TER as detailed in Steps 1 and 2 on p. 89.

Step 2

Partial daily energy requirement (PER) = 50% × TER

Step 3: Determine the Calorie Sources for the Patient

- It is recommended that a dog or cat weighing less than 22 lb (10 kg) receives 25% of PER as dextrose, 25% as amino acids, and 50% as lipids.
- A dog weighing 22 to 55 lb (10 to 25 kg) can receive its energy requirements equally from dextrose, amino acids, and lipids (i.e., 33% of its energy requirements from dextrose, 33% from amino acid sources, and 33% from lipid sources).
- A dog heavier than 55 lb (25 kg) should receive 50% of its energy requirements from dextrose, 25% from amino acid sources, and 25% from lipid sources.

This variation in the composition of PPN solution is an attempt to keep the total volume consistent among patients of varying weights. However, patients weighing less than 6.6 lb (3 kg) will still receive a volume of fluid greater than their daily maintenance requirements to fulfill their daily energy requirements. In addition, it is interesting to note that this formulation of PPN uses amino acids to directly supply the patient's energy needs rather than to support muscle anabolism as with TPN. Patients receiving PPN should also receive enteral nutrition: the PPN solution should not be relied on to meet all nutritional requirements.

Step 4: Determine the Volume of Nutrient Solutions Required

Dextrose

5% (50 g/dl) Dextrose solution =
0.17 kcal/ml PER × % Calories as dextrose =
___ kcal/day dextrose ÷ 0.17 kcal/ml = ___ ml/day

With the use of 5% dextrose rather than 50% dextrose, the resulting osmolarity of the PN solution will be much less than that of TPN and, therefore, make the solution safe to administer through a peripheral vein. (For a more complete discussion of osmolarity, see the companion article beginning on p. 76.)

Lipid

20% (200 g/L) Lipid emulsion =
2 kcal/ml PER × % Calories as lipid =
___ kcal/day lipids ÷ 2 kcal/ml = ___ ml/day

Amino Acids

8.5% (8.5 g/L) Amino acid solution =
0.34 kcal/ml PER × % Calories as amino acids =
___ kcal/day ÷ 0.34 kcal/ml = ___ ml/day

An alternative method to reduce PPN osmolarity is to use a 3.5% amino acid solution instead of an 8.5% solution. These 3.5% solutions contain 3.5 g of protein equivalent in amino acids per deciliter and are of lower osmolarity than 8.5% amino acid solutions. Before PPN

Table 3. Sample Calculation of Partial Parenteral Nutrition for a 22-lb (10-kg) Dog That Will Undergo Surgery the Next Day for Gastrointestinal Foreign Body Removal and Enteral Feeding Tube Placement

Step	Equation
1: Calculate the TER	BER = 30 × (10 kg) + 70 = 370 kcal/day In this case, an illness factor of 1.0 is used. TER = 370 kcal/day
2: Calculate the PER	PER = TER × 50% = 370 kcal/day × 0.50 = 185 kcal/day
3: Determine the calorie sources for this patient	A 22-lb (10-kg) dog receives one-third of PER from protein, dextrose, and lipid sources. 185 kcal/day × 0.33 = 61.1 kcal/day Therefore, 61.1 kcal/day from amino acids, dextrose, and lipids, respectively
4: Determine the volume of nutrient solutions required	
Dextrose	61.1 kcal/day ÷ 0.17 kcal/ml of 5% dextrose = 359.4 ml/day (rounded to 360 ml/day) of 5% dextrose
Lipids	61.1 kcal/day ÷ 2 kcal/ml of 20% lipid solution = 30.6 ml/day (rounded to 31 ml/day) of 20% lipid solution
Amino acids	61.1 kcal/day ÷ 0.34 kcal/ml of 8.5% amino acid solution = 179.7 ml/day (rounded to 180 ml/day) of amino acids
5: Determine the total volume and hourly rate of PPN solution administration	360 ml + 31 ml + 180 ml = 571 ml/day of PPN solution (Note: This volume is greater than the daily maintenance fluid requirement estimated for a 22-lb [10-kg] dog) 571 ml/day ÷ 24 hr = 23.8 ml/hr of PPN solution
6: Determine the daily vitamin requirements	Vitamin K: not needed in this patient because it will receive enteral nutrition within the next 24 hr Vitamin B: possibly consider supplementing vitamin B For example: 185 kcal/day (PER) ÷ 1 ml B complex/1,000 kcal = 0.19 ml
7: Administer PPN	Give immediately at the full calculated rate. This patient will immediately receive 24 ml/hr of PPN.

formulations using 3.5% amino acid solutions are used, other sources can be consulted.

Step 5: Determine the Total Volume of PPN Solution Per Day

$$\left(\underset{\text{of dextrose}}{\text{\_\_\_ ml}} + \underset{\text{of lipids}}{\text{\_\_\_ ml}} + \underset{\text{of amino acids}}{\text{\_\_\_ ml}}\right) \div 24 \text{ hr} = \text{\_\_\_ ml/hr}$$

PPN is typically started immediately at the maintenance rate but can initially be given at half of the calculated rate for the first 6 to 12 hours and then increased to the full calculated rate.[8] PPN solutions are much less likely to induce hyperglycemia and the refeeding syndrome than are TPN solutions, and thus less importance is placed on gradually introducing the PPN solution to the patient.

Step 6: Add Vitamin Supplements

If the patient will not receive enteral nutrition for more than 5 to 7 days, the clinician may want to supplement the patient with vitamin K (0.5 mg/kg SC once weekly).

Most sources indicate that B vitamins should be supplemented in patients receiving PPN. However, this recommendation varies widely with each publication, and as already discussed with TPN formulations, the exact components of the B vitamin complex are not directly defined in any source. As with TPN, a typical B vitamin supplementation is to add 1 ml of B complex vitamins

Table 4. Partial Parenteral Nutrition Worksheet

Step	Equation
1: Calculate the TER	BER = 30 × (_____ kg) + 70 = _____ kcal/day
	TER = BER × Illness factor = _____ kcal/day
2: Calculate the PER	PER = TER × 50% = _____ kcal/day × 0.50 = _____ kcal/day
3: Determine the calorie sources for this patient	Determine the relative amounts of amino acids, dextrose, and lipids supplied per day: TER × proportion of dextrose = _____ kcal/day dextrose TER × proportion of amino acids = _____ kcal/day amino acids TER × proportion of lipid = _____ kcal/day lipid
4: Determine the volume of nutrient solutions required	
Dextrose	_____ kcal/day ÷ 0.17 kcal/ml of 5% dextrose = _____ ml/day of 5% dextrose
Lipids	_____ kcal/day ÷ 2 kcal/ml of 20% lipid solution = _____ ml/day of 20% lipid solution
Amino acids	_____ kcal/day ÷ 0.34 kcal/ml of 8.5% amino acid solution = _____ ml/day of amino acids
5: Determine the total volume and hourly rate of PPN solution administration	_____ ml dextrose + _____ ml lipids + _____ ml amino acids = _____ ml/day of PPN solution
	_____ ml/day ÷ 24 hr = ____ ml/hr of PPN solution
6: Determine the daily vitamin requirements	Vitamin K: may or may not be needed
	Vitamin B: possibly consider supplementing vitamin B
	PER ÷ 1 ml of B complex/1,000 kcal = _____ ml/day
7: Administer PPN	Give immediately at full calculated rate

per 1,000 kcal of energy supplied in the PN admixture.[15] Also, as with TPN, the assumption is made that vitamin requirements for PN are the same as those for enteral nutrition.

ALTERNATIVE PARTIAL PARENTERAL NUTRITION SOURCES

An alternative to the three-in-one admixtures with lipids, dextrose, and amino acids is the use of PPN solutions with only amino acids and/or dextrose. Several solutions are available commercially. One formulation is a mixture of 3% amino acids, glycerol, and electrolytes and is available commercially or created by mixing 300 ml of 8.5% amino acid solution with 700 ml of lactated Ringer's solution plus 5% dextrose. This solution can be administered continuously for longer than 24 hours because it does not contain lipids, which deteriorate over time. The published dosage for this solution is 40 to 45 ml/kg/day.[17] Downsides of this preparation are that it does not attempt to meet vitamin requirements in the patient and its osmolarity is higher than a three-in-one PPN admixture because it does not contain isosmolar lipids to dilute the hyperosmolar dextrose and amino acids. However, these PPN sources are advantageous in that the practitioner can either purchase the premixed solutions or easily prepare them using appropriate aseptic technique from supplies readily available.

It should be remembered that when dextrose, amino acids, and lipids in PPN and TPN solutions are metabolized, free water is produced. After metabolism, the volume of water delivered to a patient is roughly equivalent to the volume of solution administered. PPN calculations (especially for three-in-one admixtures) may require the use of a larger volume of solution than is

practical or safe to administer to a given patient. Conversely, larger patients may require additional electrolyte fluid solutions to completely meet their daily fluid requirements, especially if the patient needs a large volume of fluids. Also, if electrolytes are not added to PPN solutions or the patient has many electrolyte abnormalities, the patient will require concurrent administration of electrolyte-containing fluids through another intravenous catheter.

PATIENT MONITORING

Careful monitoring of patients receiving PN is important to identify and rectify metabolic abnormalities that may develop.[2,5,6,8] Recommendations vary, but all sources agree that vital signs (i.e., temperature, pulse and respiratory rates, patient attitude) should be serially monitored every 4 to 6 hours for the first 2 to 3 days and at a decreasing frequency thereafter. Body weight should be measured every 12 to 24 hours.

Blood and urine glucose should be evaluated at least every 12 hours for the first 2 to 3 days for evidence of hyperglycemic complications. All sources agree that if the patient's blood glucose is persistently elevated over 200 mg/dl, steps should be taken to combat hyperglycemia.[2,6,8] Some clinicians might be more aggressive by addressing hyperglycemia at much lower blood glucose concentrations.

Steps to address hyperglycemia include initially decreasing the PN fluid administration rate and potentially administering regular insulin to bring the blood glucose concentration within the normal range.[2,8] Insulin can be

Future refinements in parenteral formulations for dogs and cats are expected and will probably result in evidence of improved clinical outcomes in dogs and cats.

administered by intermittent intramuscular or subcutaneous injections or by a constant-rate infusion of 1 to 2 U/kg/24 hr for dogs or at a starting dose of 1 U/cat/24 hr.[8] Regular insulin is preferred in these situations because of its short duration of action and the ease with which the dose can be altered. A third and perhaps less cost-effective option to combat persistent hyperglycemia is reformulation of the PN solution with a smaller percentage of dextrose and a greater percentage of lipids to provide energy requirements. Retrospective studies[18–21] in veterinary medicine reveal that although hyperglycemia is common and usually transient in most cases, many animals that become hyperglycemic require at least temporary insulin therapy.

Some authors feel that the blood glucose monitoring regimen should be very strict to avoid any chance of PN-induced hyperglycemia, especially for the first days of PN supplementation[8] (Figure 1). According to Figure 1, if the blood glucose concentration at subsequent rechecks remains greater than 200 to 250 mg/dl, the PN infusion rate should be decreased to the highest rate that maintains the blood glucose concentration below 250 mg/dl. If the blood glucose concentration rises above 300 mg/dl, the PN infusion rate should be decreased and the patient may need insulin therapy.

Tips to Reduce Infection When Administering Parenteral Nutrition

- Aseptically prepare the PN solution.
- Use sterile catheter placement and line handling.
- Change intravenous lines only as needed.
- Dedicate an intravenous port and line to PN.
- Limit handling of the PN line to a small number of staff members.

Serum electrolytes and renal parameters are also important to monitor at least every 24 hours for the first 2 to 3 days of PN administration and, if no complications occur, less regularly thereafter. Evidence of hypokalemia, hypophosphatemia, or other changes consistent with the refeeding syndrome can be handled as described in the Refeeding Syndrome section on p. 99. Azotemia, especially increases in blood urea nitrogen concentration, may be due to excessive protein supplementation and can be addressed by decreasing the amino acid content of the PN admixture.

Some authors feel that packed cell volume and total protein parameters should be serially monitored in patients receiving PN.[6] Others feel that a patient's blood should be checked at least every 12 to 24 hours for evidence of lipemia via visual inspection of the serum and/or examination of serial triglyceride measurements for the first 2 to 3 days and then with decreasing frequency thereafter.[2] Lipemia might indicate excessive administration of lipid sources and can be addressed by decreasing the lipid proportion of the feeding admixture.

It is clear from all sources that animals receiving PN should be closely and serially monitored to identify and correct metabolic abnormalities. Similarly, as dictated by common sense, a patient should slowly be weaned off PN over the course of at least 12 to 24 hours to decrease rebound hypoglycemia or other electrolyte changes that could be induced by abrupt cessation of nutritional support.[8]

Other parameters that are typically monitored in patients receiving PN at the University of Missouri include central venous pressure (CVP) measurements, especially in animals receiving additional isotonic crystalloids or electrolyte solutions with their PN. This is accomplished by using a multilumen central venous catheter in the patient: one lumen is dedicated to PN administration, and the other can be used for CVP monitoring. Serial CVP measurements are used to prevent volume overload while patients receive nutrition. Checking the patient's serum osmolarity every 24 hours also ensures that the PN solution is not causing the patient's serum to become hyperosmolar. Increases in CVP or serum osmolarity can be addressed by decreasing the rate of PN administration or the amount of dextrose administered in the solutions. In addition, the catheter site should be visually inspected at least every 12 hours. Extravasation of PN solutions leading to local tissue inflammation and necrosis is a potential complication of PN. If extravasation is detected, the PN catheter must be removed and replaced in another location. Ice packs and hydrotherapy can be administered to the affected region.

DISADVANTAGES OF PARENTERAL NUTRITION

The drawbacks of PN can be divided into four categories:

- Infection
- Mechanical complications
- Cost
- Metabolic complications

Infection occurs secondary to contamination and growth of bacteria and fungi in a PN bag, nosocomial bacterial or fungal contamination during administration of PN, or bacterial translocation from the patient's own body (specifically the gastrointestinal tract or skin at the catheter site). Contamination of the PN bag during compounding and nosocomial infection introduced during administration of PN can be controlled by careful preparation of PN and aseptic handling of the intravenous tubing as discussed in the companion article beginning on p. 76 (also, see box on this page).

Mechanical complications include intravenous line breakage or kinking, patient destruction of intravenous lines or catheters, clogging of intravenous lines, and thrombophlebitis. Careful monitoring of patients can help minimize these occurrences, and the use of polypropylene catheters has been shown to decrease the incidence of thrombophlebitis.[22–24] Metabolic complications such as biochemical or electrolyte abnormalities may be induced by PN administration and can include hyperglycemia, hypophosphatemia, and hypokalemia.

In a retrospective study[21] of PPN administration in dogs and cats, metabolic, mechanical, and septic complications were reported. In this study, hyperglycemia (blood [serum] glucose concentration: >120 mg/dl) was

the most frequent metabolic complication. Other noted complications included hyperbilirubinemia, lipemia, and azotemia. No patients required insulin therapy, and hyperglycemia improved within 1 to 3 days. The likelihood of metabolic complications was not found to be significantly different between cats and dogs. Mechanical complications were more common in dogs (26% of dogs versus 9% of cats had complications) and included occlusion of catheters, line breakage, disconnections, and thrombophlebitis. There was only a 3% reported rate of septic complications in both species.

In two retrospective studies[18,19] of TPN use in both dogs and cats, mechanical complications were frequent. Forty-six percent of the mixed canine and feline population described by Lippert et al[18] had mechanical complications compared with 21% of the feline-only population described by Pyle et al.[19] Hyperglycemia was another common complication in 75% of all cats[18] and 47% of nondiabetic cats[19] (>140 mg/dl[18] and >134 mg/dl,[19] respectively). Similarly, 46% of all dogs[18] had high blood glucose values (>140 mg/dl) while receiving TPN. Other metabolic derangements detected in animals receiving TPN were hypo- and hypernatremia, hypo- and hyperkalemia, hypo- and hypercalcemia, and hypo- and hyperphosphatemia. However, these abnormalities were much less common than hyperglycemia—at the most, 10% of Lippert et al's[18] canine and feline populations and 34% of Pyle et al's[19] feline-only population. Lipemia was noted in 46% of cats and dogs[18] and 24% of cats.[19]

Clinical signs attributable to metabolic complications were rare in both studies,[18,19] although some patients required insulin administration for persistent (i.e., longer than 3 days) hyperglycemia. Lippert et al[18] reported that 36% of hyperglycemic dogs and 67% of hyperglycemic cats required insulin therapy. Although Pyle et al[19] did not report a percentage of cats requiring insulin, most hyperglycemic cats required insulin therapy. There was an overall low rate of septic complications, with Lippert et al[18] showing no septic complications in either cats or dogs and Pyle et al[19] finding TPN-associated sepsis in only five of 84 cats.

PN is not an inexpensive feeding modality. PN components are fairly inexpensive individually, but when they are combined into admixtures, the cost of each component is additive. In addition, when PN is formulated by a pharmacy, there is a dispensing and formulation charge for costs associated with the use of the laminar flow hood, the materials (e.g., syringes, needles, tubing) needed to compound the solution, and the expertise and time of the pharmacist. The specialized ethylene vinyl acetate PN bag is also a substantial cost. At the University of Missouri-Columbia Veterinary Medical Teaching Hospital, the bag itself represents 33% of the daily cost of PN. When all factors are taken into account, the cost of PN can be $100/day or more for the client and, therefore, may be cost prohibitive or limit the duration that PN can be provided to a patient.

REFEEDING SYNDROME

Refeeding syndrome is a complication of nutritional supplementation that, although it can occur in animals, is more commonly reported in humans. It is a syndrome of severe hypophosphatemia, hypokalemia, hypomagnesemia, and other electrolyte derangements that can be induced in an anorectic, mal-

Table 5. Recommended Potassium Supplementation for Hypokalemic Patients[29]

Patient's Measured Serum Potassium Concentration (mmol/L)	Recommended Volume (mEq/L) of Potassium Chloride Added to 1 L of Fluids	Maximum Rate (ml/kg/hr) of Potassium Chloride Administration
<2	80	6
2–2.5	60	8
2.5–3	40	12
3.1–3.5	30	17

nourished patient by providing nutrient supplementation[25,26] (oral, enteric, or parenteral). Patients typically have hyperglycemia as well. Hyperglycemia and concurrent glucosuria can lead to osmotic diuresis, resulting in sodium and water loss. However, in other cases, especially in patients fed mainly carbohydrate sources, feeding leads to reduced sodium and water excretion and, in some cases, can lead to increases in extracellular fluid volume and eventually peripheral edema.[26]

Refeeding syndrome can be induced in a patient fed enterally or parenterally; all patients need to be monitored for this potential (albeit rare) side effect.

Hypophosphatemia is the most significant feature of refeeding syndrome in humans.[25–27] It occurs when there has been starvation-induced loss of lean muscle mass, minerals, and water. The patient's whole body phosphorus is depleted in this stage, although blood work results typically do not reflect this. When nutrition is provided to such a patient, the presence of carbohydrates causes the release of insulin, which induces an intracellular shift of phosphorus, causing clinically measurable serum hypophosphatemia. As the patient is fed, conversion from catabolism to anabolism occurs, and the body begins to create cell membranes, nucleic acids, ATP, and 2,3-diphosphoglycerate (2,3-DPG), all of which require phosphorus. This demand for phosphorus magnifies the preexisting hypophosphatemia.

Refeeding syndrome is clinically recognized and typically occurs about 3 days after initiation of nutritional intervention.[25,26] Hypophosphatemia leads to decreased cardiac contractility through an undefined mechanism as well as decreased leukocyte function. A wide spectrum of neuromuscular dysfunction can occur, ranging from muscular paralysis to cranial nerve deficits and ventilatory dysfunction. These neuromuscular changes may be due to hypoxic cellular injury resulting from decreased oxygen delivery to tissues caused by decreased 2,3-DPG in erythrocytes. Hypoxia may also result from decreased erythrocyte delivery to tissues through capillary beds as erythrocyte membranes lose their pliability when the patient is hypophosphatemic. Severe hypophosphatemia may also lead to hemolytic anemia.

Hypomagnesemia and hypokalemia can cause clinical signs similar to those of hypophosphatemia, including cardiac arrhythmias, weakness, seizures, and ataxia.[26,27] The functions of magnesium are not completely characterized but seem to parallel those of phosphorus and potassium. Both hypokalemia and hypomagnesemia occur in the refeeding syndrome due mainly to the increase in insulin and accompanying shifting of potassium, magnesium, and phosphorus into the cells.[25–27]

Patients with prolonged anorexia or starvation should be gradually introduced to parenteral and enteral feeding over the course of 2 to 3 days to acclimate the body to the infusion of calories. This gradual introduction to calories minimizes the chance of inducing the refeeding syndrome. The patient should be carefully monitored, including serial electrolyte and blood glucose monitoring, during the first days of supplementation. Not every patient undergoes this syndrome, but every patient is at risk.

Although the refeeding syndrome is recognized and reported in humans, few veterinary publications have explicitly addressed the syndrome. As noted previously, both hypo- and hyperphosphatemia were reported in animals administered TPN and PPN.[18,19] These studies had a slightly greater prevalence of hyperphosphatemic than hypophosphatemic complications, although the total numbers were very small in both studies. These studies were retrospective and did not directly address reasons for these electrolyte abnormalities. A single veterinary case

How to Get Started

Many veterinary schools, large referral hospital pharmacies, and human hospital pharmacies routinely make PN solutions and are willing to sell them to local practitioners. Check with the nearest school or hospital pharmacy for details.

PN solutions can also be obtained from private compounding pharmacies. An example of a company that ships PN solutions is Diamondback Drugs (diamondbackdrugs.com; phone 866-646-2223).

study[28] describing the refeeding syndrome in a chronically anorectic cat was characterized by severe hypokalemia and normal phosphorus concentrations.

If persistent hypophosphatemia results from PN administration, the patient can receive intravenous phosphorus supplementation. The recommended phosphorus dosage is 0.003 mmol/kg/hr IV for the first 24 hours or 0.03 mmol/kg/hr for a total of 6 hours.[27] Hypokalemia is best treated using oral supplementation, although this is typically impossible in animals receiving PN. However, potassium can be added to the patient's intravenous fluids[29] (Table 5).

Magnesium should be administered to patients with total serum magnesium concentrations below 1.2 mg/dl (normal: 1.7 to 2.4 mg/dl).[30] Magnesium supplementation should be administered as a 20% dilution by combining magnesium sulfate or magnesium chloride with 50% dextrose. This solution can be given as a constant-rate infusion of 0.75 to 1 mEq/kg/day for the first day, followed by 0.3 to 0.5 mEq/kg/day of the diluted magnesium solution for an additional 3 to 5 days. As an alternative in certain patients, oral supplementation of magnesium (magnesium oxide or hydroxide supplements) may be given at a dose of 1 to 2 mEq/kg/day.

CONCLUSION

Although the effectiveness of PN has not been proven in animals, human studies have shown that using PN in appropriately selected cases can improve clinical outcomes, reduce hospitalization time, and even reduce the overall cost of patient care.[31] Parenteral feeding through TPN and PPN administration provides nutrition to improve clinical outcome but also has a substantive cost and inherent complications. Careful monitoring of patients while they are receiving PN can help identify and correct these complications. It is important to have a dedicated nursing staff that closely monitors patients receiving PN to avoid mechanical complications. Frequent blood draws and biochemical analyses over the first 2 to 3 days of PN administration can help identify metabolic complications. Careful compounding and sterility when handling PN can reduce infectious complications. Overall, PN is a viable option for patients that cannot receive food enterally.

See p. 74 for a *Veterinary Therapeutics* abstract related to this topic.

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ARTICLE #2 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. ***Subscribers may purchase individual CE tests or sign up for our annual CE program.*** *Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. CE subscribers can take CE tests online and get real-time scores at* ***CompendiumVet.com****.*

1. What is the most important role of protein (as amino acids) in TPN?
a. providing another energy source to the body
b. providing a substrate for glucose metabolism
c. providing a substrate for muscle anabolism
d. reducing the osmolarity of the PN solution

2. Which statement regarding PN is correct?
a. In a TPN solution, patients typically receive 40% of their energy requirements from amino acids.
b. All patients routinely receive vitamin C supplementation in PN solutions.
c. The PN line and tubing should be changed every 12 hours to preserve asepsis.
d. TPN solution delivery should be initiated at a reduced rate and adjusted upward to the full calculated administration rate over the course of 1 to 2 days if the patient is tolerating the solution.

3. Which set of parameters is important to routinely monitor in *all* patients when administering PN?
a. blood glucose level, body temperature, and pulse and respiratory rates
b. glucose, phosphorus, and amylase levels
c. glucose and creatinine levels as well as urine specific gravity
d. glucose, sodium, and chloride levels

4. What are three common metabolic complications of PN administration?
a. hyperglycemia, hyperphosphatemia, and lipemia
b. hyperglycemia, hypophosphatemia, and lipemia
c. hypoglycemia, hyperphosphatemia, and hypoalbuminemia
d. hypoglycemia, hyperphosphatemia, and hyperalbuminemia

AN IN-DEPTH LOOK

5. Which is(are) an important disadvantage(s) of PN described in the veterinary literature?

a. infection
b. cost
c. metabolic abnormalities
d. all of the above

6. According to the literature, which is the most common complication of PN administration?

a. hyperglycemia
b. mechanical complications
c. infection introduced into the PN bag during compounding
d. sepsis

7. Which step(s) should be taken when there is extravasation of PN solution at the catheter site?

a. Continue to administer PN but at a lower rate.
b. Remove the catheter from the affected site, and place it in another site.
c. Remove the catheter from the affected site, and place it proximal to the affected site.
d. none of the above

8. Which electrolyte abnormalities are noted in the classic refeeding syndrome in humans?

a. hyperphosphatemia, hyperkalemia, and hypermagnesemia
b. hyperphosphatemia, hypokalemia, and hypomagnesemia
c. hypophosphatemia, hypokalemia, and hypomagnesemia
d. hypophosphatemia, hyperkalemia, and hypomagnesemia

9. Phosphorus is used by the body to make

a. 2,3-DPG (2,3-diphosphoglycerate).
b. ATP.
c. cell membranes.
d. all of the above

10. Cardiac arrhythmias, weakness, seizures, and ataxia are commonly associated with

a. hypomagnesemia.
b. hypophosphatemia.
c. hypokalemia.
d. all of the above