Parenteral-Assisted Feeding

Rebecca L. Remillard

Korinn E. Saker

"When the facts change, I change my mind. What do you do?"
John Maynard Keynes

CLINICAL IMPORTANCE

Parenteral nutrition (PN) is valuable in meeting a patient's daily resting energy and amino acid requirements. In veterinary medicine, clinicians attempt to meet the patient's estimated resting energy requirement (RER) and most immediate requirements for essential amino and fatty acids, and selected water-soluble vitamins, electrolytes (macro) and trace minerals. PN does not consistently limit disease activity in patients and therefore is an adjunct (not a primary) therapy. PN support in veterinary patients may prevent nutrient deficiencies, preserve lean body mass and support the functional capacity of most body organs when nutrient intakes fall below requirements. The overriding rationale and criteria for using PN in veterinary patients is to treat subclinical undernutrition due to three or more days of decreased appetite and to avoid the development of clinical undernutrition resulting from insufficient energy intake in the face of increased energy needs (ASPEN, 2002). **Box 26-1** describes PN nomenclature.

Patient selection is very important to the successful use of PN support. Patients with impairment of the small intestine that is unlikely to resolve within three days are candidates for PN support. PN can be used initially to meet energy and amino acid requirements for cases in which enteral access cannot be safely acquired for several days. Depending on patient size, it may not be cost effective to use PN as a method of assisted feeding for less than a three-day course. There is a substantial startup cost

to preparing the parenteral solution. The procedure becomes cost effective when the cost is spread over several days or more than one patient.

There is evidence that 48 to 72 hours are required to reverse a catabolic state and begin anabolism (Zeiderman et al, 1989; Wernerman et al, 1986). Thus, proper patient selection mandates that the patient be hospitalized for at least three days because instituting PN for only one or two days is of questionable cost benefit. However, when PN is done in conjunction with enteral feeding, a course shorter than three days may be cost effective and provide nutritional benefit. PN support should not begin until the patient is hemodynamically stable and electrolyte and acid-base abnormalities, severe tachycardia, hypotension and volume deficits have been corrected (**Table 26-1**).

There are many published lists of diseases, disorders and case examples in which PN could or should be instituted. The number and type of veterinary patients that would benefit from PN is greatly expanded; however, if the goal in assisted feeding is to deliver the patient's energy and amino acid needs daily by any means (Remillard and Thatcher, 1989). Parenteral administration of nutrients has value in patients with inflammatory (small and large) bowel disease, parvoviral enteritis and other causes of impaired gastrointestinal (GI) motility, peritonitis, pancreatitis, intestinal lymphosarcoma and short-bowel syndrome (small bowel resection). Neurologic patients and those that are comatose or receiving large doses of pain-control medications that

Box 26-1. Nomenclature.

The term "parenteral nutrition (PN)" indicates administration of nutrients in a manner other than through the gastrointestinal (GI) tract. PN could therefore be administration by intravenous, intramuscular, subcutaneous, intraosseous or intraperitoneal routes. PN has been further characterized in human medicine as total or partial (relative to meeting all nutrient requirements) and central or peripheral (relative to venous access). A common misnomer associated with PN, originally from the human literature, is the term "hyperalimentation." This term incorrectly implies the administration of nutrients via the GI tract in excess of need. The term "parenteral nutrition" is used throughout this text because it simply and accurately identifies a general method of administering nutrients to a patient.

Another common misnomer is total parenteral nutrition (TPN). In veterinary medicine, PN is not total because there is no immediate need to meet all the amino and fatty acid, fat- and water-soluble vitamin and macro, trace and ultra-trace element requirements as there is in people dependent on PN for years.

There are several valid reasons why partial PN, rather than TPN, is used in veterinary medicine. The foremost reason is the comparatively short period PN is administered to animals (three to 14 days for animals vs. weeks to years in people). In people, long-term feeding implies 10 days or longer. The shorter time frame of assisted feeding of pets allows omission of less immediately essential nutrients (e.g., fat-soluble vitamins). Until there is a demand by pet owners for a longer period of support (weeks to months), PN support in animals will remain cost effective by providing only the most immediately essential nutrients (i.e., electrolytes, energy and amino acids).

Only some of the nutrients needed by animals are readily available in water-soluble form for PN solutions. Some water-soluble nutrients are available as multiple single nutrients in specially prepared water-insoluble products. Such nutrients (vitamins A and E) are cost prohibitive and difficult to justify on a short-term basis. As more nutrient preparations are added to PN solutions, the risk for incompatibility and formation of insoluble precipitates increases. PN solutions currently used in veterinary medicine contain only the less expensive essential nutrients. PN solutions are therefore limited by necessity, pharmacokinetics, cost and current nutritional knowledge.

Table 26-1. Patient criteria for administration of parenteral nutrition.

1. The patient is hemodynamically stable and major electrolyte and acid-base abnormalities, severe tachycardia, hypotension and volume deficits have been corrected.
2. Actual or anticipated food intake is less than calculated resting energy requirement for more than three days.
3. Concurrent small intestinal disorder is known or suspected to be present, or a safe enteral nutritional access cannot be established.
4. The patient is expected to be hospitalized for at least the next three days.

cause lateral recumbency with questionable swallowing reflexes and/or risk of aspiration when oral or tube feedings are attempted also benefit from PN. PN has been used successfully in complicated cases of feline hepatic lipidosis, in patients with facial fractures, pneumonia, lung lobe torsion or contusion and diaphragmatic hernias, and in other patients that are poor anesthetic risks.

PN can be administered until patients are more stable and can tolerate placement of a feeding tube. Septic and anemic patients and those with severe upper respiratory infections that cause persistently poor appetites may benefit from PN. Sometimes PN support may be as simple as augmenting oral intake with intravenous lipids to meet RER. Patients with a poor appetite that also have large heat and/or protein losses (e.g., continuous-suction chest or abdominal drains, large areas of skin loss due to burns, degloving injuries) benefit from PN in addition to voluntary oral food intake.

The goal of assisted feeding is to provide adequate nutrition to meet the patient's RER. The logistics of that support should be determined on a case-by-case basis. The guidelines presented here are to help establish a foundation. But never underestimate the need for attentiveness, initiative and ingenuity in meeting the patient's nutritional needs; no two cases are alike.

Because enteral nutrition and PN are often used in conjunction, the reader may want to refer to Chapter 25 for information about:
- Consequences of malnutrition
- Patient assessment, including physiologic state and history of malnutrition
- Anorexia, cachexia and accommodation
- Metabolic changes through days of starvation (simple starvation and disease states)
- Key nutritional and other factors.

PARENTERAL PRODUCTS

Compounding a PN solution is beyond the scope of most veterinary practices; however, most veterinary practices can administer PN to patients. Individual dextrose, lipid and amino acid solutions can be combined as a "three-in-one" solution, also called a total nutrient admixture (TNA). TNA in veterinary medicine refers to one fluid bag containing a sufficient mixture of parenteral solutions to meet a particular patient's fluid, energy, amino acid, electrolyte and B-vitamin needs for a 24-hour period. This is a very convenient method requiring only one bag, one infusion pump and one administration set. Any opaque liquid infusion pump can be used. The formulation is designed specifically for the patient based on its current RER, daily fluid and electrolyte requirements, approximate protein need and ability to handle dextrose vs. lipid.

The TNA solution should be calculated to first meet the patient's RER and protein needs with essential water-soluble vitamins and trace mineral products (if available). The total fluid volume should then be adjusted with a standard crystal-

Table 26-2. Standard total nutrient admixture (TNA) formulations.

PART A. CALCULATION WORKSHEET

Patient data needed	Feline example
1. Current body weight in kg	4.1 kg
2. Calculate resting energy requirement (RER) as kcal/day	200 kcal/day
3. Expected fluid volume in ml/kg/day	70 ml/kg
4. Calories from fat as a percent	80%
5. Protein-calorie ratio as g/100 kcal RER	4 g/100 kcal RER
6. Potassium concentration as mEq/l	30 mEq/l

Parenteral solution formula

1. Determine volume of fat and dextrose needed daily

Calculate RER calories from fat	200 x 0.80 = 160 kcal
Calculate volume of 20% lipid needed	160 kcal ÷ 2 kcal/ml = **80 ml/day**
Calculate RER calories from dextrose	200 - 160 = 40 kcal
Calculate volume of 50% dextrose needed	40 kcal ÷ 1.7 kcal/ml = **24 ml/day**

2. Determine volume of amino acid solution needed daily

Calculate g of protein needed	RER x 4 g/100 kcal = 8 g protein/day
Calculate volume of 8.5% amino acid needed	8 g ÷ 0.085 g/ml = **94 ml/day**

3. Determine volume of B vitamins and trace minerals needed daily

Calculate B vitamins needed	RER x 1 ml/100 kcal = **2 ml/day**
Calculate trace minerals needed	RER x 1 ml/100 kcal = **2 ml/day**
Daily parenteral nutrition formula	80 ml of 20% lipid emulsion
	24 ml of 50% dextrose
	94 ml of 8.5% amino acid with electrolytes
	2 ml of vitamin-B complex
	2 ml of trace elements
	Total = 202 ml

4. Determine volume of crystalloid solution needed to meet daily fluid requirement

Daily fluid volume requested	4.1 kg x 70 ml/kg = 287 ml/day
Volume required is daily total – PN total	287 – 202 = 85 ml

5. Determine phosphorus supplementation

Phosphorus from amino acids	94 x 30 mM/l = 2.8 mM
Desired final phosphorus concentration in the TNA	= 10 mM/l x 287 ml = 2.9 mM (no phosphorus is needed)

6. Determine potassium supplementation

K^+ from lactated Ringer's solution	85 ml x 4 mEq/l = 0.3 mEq
K^+ from amino acid solution	94 ml x 60 mEq/l = 5.6 mEq
Total K^+ in TNA solution	0.3 mEq + 5.6 mEq = 5.9 mEq
Desired final K^+ concentration in TNA	30 mEq/l x 287 ml = 8.6 mEq
KCl (2.0 mEq/ml) required	8.6 mEq – 5.9 mEq = 2.7 mEq ÷ 2.0 = 1.4 ml

PART B. FELINE FORMULA EXAMPLE

Animal data

Body weight	4.1 kg
RER	200 kcal/day
Calories from fat	80%
Calories from glucose	20%
Protein-calorie ratio	4 g/100 kcal (adequate for most cats)
Fluid volume	70 ml/kg (maintenance fluid volume)
Potassium concentration	30 mEq/l

Parenteral solution

50% dextrose	24 ml providing 41 kcal
20% lipid emulsion	80 ml providing 160 kcal
8.5% amino acids with electrolytes	94 ml providing 8 g of amino acids
Potassium chloride	1.4 ml
Vitamin-B complex	2 ml
Trace elements	2 ml
Lactated Ringer's solution	85 ml
Total fluid volume	288 ml

This final solution is a 500-ml bag containing 200 kcal (80% from fat), adequate nitrogen, major B vitamins with the following electrolyte profile

Sodium	61.6 mEq/l
Potassium	29.5 mEq/l
Magnesium	3.3 mEq/l
Phosphorus	9.8 mM/l
Chloride	55.4 mEq/l
Calcium	0.8 mEq/l
Zinc	2 mg
Copper	1 mg
Manganese	0.2 mg

Table 26-2 continued	
Chromium	8 mg
Final osmolarity	768
Approximate cost = $100 per day	
PART C. CANINE FORMULA EXAMPLE	
Animal data	
Body weight	14 kg
RER	507 kcal/day
Calories from fat	90%
Calories from glucose	10%
Protein-calorie ratio	3 g/100 kcal
Fluid volume	70 ml/kg
Potassium concentration	20 mEq/l
Parenteral solution	
50% dextrose	30 ml providing 51 kcal
20% lipid emulsion	227 ml providing 454 kcal
8.5% amino acids with electrolytes	176 ml providing 15 g of amino acids
Potassium phosphate	1.4 ml
Vitamin-B complex	5 ml
Trace elements	5 ml
NormaSol R	543 ml
Total fluid volume	987 ml
This final solution is a 1-liter bag containing 507 kcal (90% from fat), adequate nitrogen, major B vitamins with the following electrolyte profile	
Sodium	88.0 mEq/l
Potassium	20.3 mEq/l
Magnesium	3.5 mEq/l
Phosphorus	9.9 mM/l
Chloride	65.5 mEq/l
Calcium	0 mEq/l
Zinc	5 mg
Copper	2 mg
Chromium	20 mg
Manganese	0.5 mg
Final osmolarity	523 mOsm/l
Approximate cost = $100 per day	

loid solution (e.g., lactated Ringer's solution, Plasmalyte A) to meet the patient's daily fluid requirement. Then electrolytes are adjusted, if necessary (**Table 26-2**). Alternatively, crystalloid fluids with added potassium may be administered by a separate intravenous line piggybacked into the same catheter.

Energy Solutions

A TNA solution should supply sufficient energy to meet, but not exceed, the patient's daily RER. Negative consequences of PN administration (i.e., metabolic complications) are often due to administering energy in excess of the patient's expenditure (Deitel et al, 1983; Chang and Silvis, 1974; VA Study Group, 1991; Lippert et al, 1993). Early PN solutions for people contained dextrose and "liberal" amounts of protein. These solutions were administered at rates providing 3,000 to 5,000 kcal/day (12.55 to 20.92 MJ) to a 70-kg person (Solomon and Kirby, 1990). This "hyperalimentation" actually increased catabolism by exceeding the patients' endogenous usage of energy and produced multiple adverse metabolic effects. Human patients are given 1,000 to 2,400 kcal (4.2 to 10 MJ) with 75 to 100 g of protein per day with fewer metabolic complications (Woolfson, 1983). Currently, people are fed at RER instead of RER times a disease factor (McMahon, 1993; Forse,

1995; DeBiasse and Wilmore, 1994). Energy is routinely provided to veterinary patients receiving PN as a combination of dextrose and lipid. Several companies manufacture dextrose and lipid products of various strengths and attributes (**Table 26-3**). Most TNA solutions formulated for veterinary patients use 50% dextrose and 20% lipid. Dextrose solutions range from 2.5 to 70% glucose, which is usually derived from hydrolyzed cornstarch. Osmolarity ranges from 126 to 3,530 mOsm/l and is directly proportional to the glucose concentration (AHFS Drug Information, 1997). Dextrose solutions are maintained in the pH range of 3.5 to 5.5 and are sterilized by autoclave to prolong shelf life at room temperature.

Lipid (10, 20 or 30%) products (**Table 26-3**) contain emulsified fat particles (0.5 mm) of soybean oil and/or safflower oil, glycerin and linoleic and linolenic acids. Earlier formulations made with cottonseed oil were taken off the market in 1965 because they caused severe adverse reactions in people. Lipid emulsions are maintained in a pH range of 6.0 to 8.9 and have an osmolarity range of 260 to 310 mOsm/l, which effectively decreases the final osmolarity of the TNA (AHFS Drug Information, 1997). Dextrose and lipids are readily available and both are strongly recommended as sources of energy in a TNA solution.

Table 26-3. Nutritional comparison of parenteral products.

Products	Caloric density (kcal/ml)	Osmolarity (mOsm/l)	Amino acids (g/100 ml)	Fat (g/100 ml)	Carbohydrate (g/100 ml)	Electrolytes (kcal/ml)	Comments
Amino acids 8.5% without electrolytes	na	785-860	8.5	0	0	Few	Contains all essential amino acids except taurine, nitrogen 1.3 g/100 ml, pH 5.3-6.5, available in 500- and 1,000-ml sizes.
Amino acids 8.5% with electrolytes	na	1,160	8.5	0	0	Yes	Contains all essential amino acids except taurine, nitrogen 1.3 g/100 ml, pH 5.3-6.5, electrolytes Na, K, Mg, Cl, PO_4, available in 500- and 1,000-ml sizes.
ProcalAmine	0.25	735	3	0	3	Yes	Contains 3% glycerol and 3% amino acids, nitrogen 4.6 g/1,000 ml, pH 6.5-7.0, electrolytes Na, K, Mg, Cl, PO_4, available in 500- and 1,000-ml sizes. Contains 13 nonprotein kcal/ml and 22.5 g amino acids/100 nonprotein kcal as is. Mix 775 ml ProcalAmine with 300 ml 20% lipid to get 1,075 ml of a 3.2 g protein/100 nonprotein kcal solution.
Lipid 10%	1.1	268	0	10	0	No	Contains soybean and/or safflower oil, glycerin, linoleic and linolenic acids, egg yolk as phospholipid emulsifier, pH 6.0-8.9, available in 50-, 100-, 250- and 500-ml sizes.
Lipid 20%	2	268	0	20	0	No	Contains soybean and/or safflower oil, glycerin, linoleic and linolenic acids, egg yolk as phospholipid emulsifier, pH 6.0-8.9, available in 50-, 100-, 250- and 500-ml sizes.
Dextrose 2.5-70%	0.09-2.4	126-3,535	0	0	2.5-70	No	Contains hydrolyzed (various) cornstarch, pH 3.5-5.5, available in 50- and 500-ml sizes.

Key: na = not available.

Dextrose–Fat Ratio

When PN is begun, most patients have not consumed their daily RER for at least three days, and are more likely even further along in the course of food deprivation (Day 5 or more). The proportion of glucose to lipid in the PN solution should mirror the current metabolic condition of the liver. Fewer metabolic complications will arise if the liver tolerates the glucose-lipid ratio in the PN solution.

PN is rarely instituted during the early phases of food deprivation (fewer than three days of anorexia); however, if PN is indicated, canine patients should tolerate a moderate percentage of their calculated RER as dextrose. For example, dogs in

Box 26-2. Complications of Fat Administration.

LIVER PATHOLOGY

Administering parenteral total nutrient admixture (TNA) solutions to human adults and infants for long periods (weeks to months) has been reported to cause steatosis, intrahepatic cholestasis, periportal inflammation and even cirrhosis. Fatty infiltration of the liver is the earliest and most common change noted. This undesirable relationship between long-term parenteral feeding and hepatic changes is thought to be multifactorial, but is not yet well understood. These complications are not specific to parenteral nutrition (PN) or lipid emulsions. Lipid additions are now encouraged, even in patients with hepatic disease, because replacing a portion of the glucose with lipid ameliorates some hepatic pathology. Choline is not routinely included in TNA solutions but is a conditionally essential nutrient in people. Studies have correlated choline deficiency and hepatic steatosis in people receiving total parenteral nutrition (TPN). Investigators studying TPN-fed rats reported reversal of hepatic complications with both oral and intravenous choline administration. Today, it is extremely rare for a veterinary patient to receive a PN solution for more than two or three weeks; therefore, hepatic complications from prolonged PN administration are unlikely, although choline is an essential nutrient in dogs and cats.

COAGULOPATHIES AND THROMBOCYTOPENIA

Lipid infusions have been reported to cause fat overload syndrome in people and, in the past, were associated with hyperlipidemia, hemolytic anemia, coagulopathies, thrombocytopenia and respiratory impairment with liver and renal dysfunction. Most adverse reports were associated with the use of a cottonseed oil emulsion, which was withdrawn from the market in the 1960s. Only isolated cases have been reported to occur with the soybean or safflower oil emulsions used today, and no cases have been associated with the relatively limited use of medium-chain triglyceride (MCT) emulsions. Thrombocytopenia has been reported as a rare complication of soybean oil emulsions and is now considered an idiosyncratic reaction. In vitro, lipids have a limited effect on shortening prothrombin times, but this effect may be due to the phospholipids or vitamin K in emulsions. Reduced aggregation of platelets has also been produced in vitro and at high triglyceride concentrations. It is important to emphasize that slow continuous infusion of lipids has little or no effect on platelet numbers, aggregation or bleeding time. Fat infusion rates for people have been recommended at 0.10 to 0.15 g/kg body weight/hour. Infusing veterinary patients with PN solutions containing 80 to 90% of nonprotein calories as lipid over a 24-hour period is usually within these guidelines.

ALTERED IMMUNE FUNCTION

Lipid infusions have also been associated with altered and impaired immune function. Major controversies exist about the role lipid emulsions play in affecting reticuloendothelial cells and eicosanoid, cytokine and complement synthesis. Many of these effects have not been observed with slow infusion of pure soybean oil or during rapid infusion of MCT emulsions. One review of many studies concluded there was no evidence supporting the opinion that lipid infusions detrimentally alter immune function.

The Bibliography for **Box 26-2** can be found at www.markmorris.org.

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the early phase of food deprivation maintain blood glucose levels by glycogenolysis and therefore should receive 60 to 90% of the RER as dextrose. However, feline patients in the early phases of food deprivation maintain blood glucose levels by lipolysis and gluconeogenesis, and should receive 60 to 90% of their RER from lipid.

By Day 5 of food deprivation or longer, patients should receive the majority (60 to 90%) of their calculated RER as lipid because the liver is using glycerol from endogenous fat for gluconeogenesis. Giving high doses of glucose at a time when the patient's natural metabolic response is to minimize glucose usage is unlikely to result in optimal glucose use. This is the most likely cause of hyperglycemia. There is evidence to suggest the proportion of calories needed from fat increases greatly (>60%) in starving and diseased states. For example, in an acute sepsis model, rats given a fat-free glucose solution parenterally had increased and extensive mobilization of endogenous fat. Control, nonseptic rats had no mobilization of endogenous fat when a high glucose solution was given (Stein, 1986). A measurable shift in the preferred fuel (from glucose to endogenous fat) occurred in these septic patients. In people, fat is well oxidized in the septic state, and as the sepsis worsens the amount of fat oxidized increases and the glucose oxidative capacity decreases (Stoner et al, 1983). Dogs with a septic abdomen

receiving PN with both glucose and lipid maintained nitrogen balance better than dogs receiving glucose-only PN solutions (Iriyama et al, 1985).

The optimal caloric source is a mixture of glucose and fat; however, the precise ratio is unknown (Stein, 1986). A mixed fuel source should decrease the possibility of fat deposition in the liver when any metabolic pathway that handles either fat or glucose becomes overloaded. Studies have shown that serum glucose, lactate, pyruvate, free fatty acid, triglyceride and insulin concentrations were more stable and more closely approximated the normal postabsorptive state in people when all three substrates were administered (i.e., simultaneous lipid infusion with glucose and amino acids), as opposed to fat-free PN solutions (MacFie et al, 1991). The old recommendation that fat should not compose more than 4 g/kg body weight/day or 60% of the calories has been perpetuated many times.[a] Over the last decade or so, the recommended proportion of calories from fat supplied to burn victims has progressively increased from 5 to 15 to 50%. Furthermore, higher proportions of fat calories (75 to 80%) have been recommended in other disease states (Nordenstrom et al, 1983; Chiarelli et al, 1994; Deitel and Kaminsky, 1974).

The negative effects of high-fat infusions have included reports of liver pathology, coagulopathies, thrombocytopenia,

Table 26-4. Advantages to administering a high fat total nutrient admixture (TNA) solution.

1. The liver is metabolically geared for lipolysis and preferentially uses fat as a source of calories. Therefore, supplying a high-fat solution accommodates that profile, spares endogenous fat stores and does not raise insulin levels.[*]
2. The osmolarity of the fat solution is 260 mOsm/l and can be administered by peripheral catheter. Fat included in a TNA solution decreases the final osmolarity:

80% calories from 50% dextrose and 20% calories from 20% lipid	= 862 mOsm/l[**]
20% calories from 50% dextrose and 80% calories from 20% lipid	= 535 mOsm/l[**]
5% dextrose and lactated Ringer's solution	= 525 mOsm/l
Blood or plasma	= ~300 mOsm/l

3. The pH of the final TNA solution that includes fat is closer to 7.0 than solutions of dextrose and amino acids excluding fat, thus imposing less of an acid load.
4. Patients with compromised pulmonary function are prone to developing respiratory acidosis when given solutions containing a high dextrose concentration. High-fat solutions produce less carbon dioxide to be expelled than high dextrose solutions.[***]

[*]Stein TP. Protein metabolism and parenteral nutrition. In: Rombeau JL, Caldwell MD, eds. Clinical Nutrition; Parenteral Nutrition, 1st ed. Philadelphia, PA: WB Saunders Co, 1986; 100-134.
[**]These osmolarity examples are based on a total fluid volume of 70 ml/kg body weight, 3 g protein/100 kcal resting energy requirement and 30 mEq K^{+}/liter.
[***]Askanazi J, Nordenstrom J, Rosenbaum SH, et al. Nutrition for the patient with respiratory failure: Glucose vs. fat. Anesthesiology 1981; 54: 373-377.

altered immune function, atherosclerosis and the overall unknown effect of synthetic chylomicrons on blood vessels when administered to people for more than 10 days. These adverse effects occurred in people and other animals during high infusion rates in which lipids were provided in excess of energy need (Klein and Miles, 1994; Mashima, 1979; Meguid et al, 1984; Adamkin et al, 1984). In addition, some of the products used in these studies are no longer available (**Box 26-2**).

To date, there appears to be little in the veterinary literature documenting why lipids could not or should not provide more than 60% of a dog's or cat's RER. In fact, when central venous access is limited and the patient requires fluid therapy at or below maintenance rates, administering a lipid emulsion by peripheral access (providing 100% of the caloric intake as fat) is well tolerated. The use of solutions containing high-fat concentrations (60 to 90%) has gained a wider acceptance with fewer complications as compared to those containing high-glucose concentrations. PN may be successfully administered to ferrets and rabbits using the same overall guidelines. No unusual metabolic or hematologic complications have been associated with these infusions (**Table 26-4**).

Unlike patients in earlier reports, most patients receiving high-fat solutions today do not develop hyperglycemia, based on regular urine glucose checks (VA Study Group, 1991; Lippert et al, 1993). Glycemia is better controlled in patients with diabetes mellitus, pancreatitis and septicemia when a TNA solution is used that provides most of the calories as fat. A TNA solution with 80% fat calories contains 1 to 3% dextrose. Intravenous infusion of a lipid emulsion routinely increases plasma triglyceride levels transiently. However, this should not be considered a true hyperlipidemia because most patients can clear these chylomicron-size lipid particles within 30 minutes. The half-life of chylomicrons in the plasma of dogs from either diet or intravenous infusion of soybean oil and safflower oil emulsions ranges from seven to 16 minutes (Edgren and Meng, 1962; Kesterson, 1978). Therefore, it is sometimes necessary to turn off the TNA infusion pump 20 to 30 minutes before blood is drawn if hyperlipidemia is a problem. Lipid from the TNA solution does interfere with certain serum biochemistry tests (Chapter 28).

The PN guidelines for people state that the role of intravenous artificial lipid emulsions in influencing the course of pancreatitis is not defined. Lipid emulsions are safely used in hyperlipidemic people when serum triglyceride concentrations remain below 400 mg/dl (ASPEN, 2002). PN solutions containing a lipid portion do not stimulate the pancreas (Konturek et al, 1979; Kelly and Nahrwold, 1976; Edelman and Valenzuela, 1983) and should be implemented when enteral nutrition is not tolerated (ASPEN, 2002). Most people tolerate glucose- and lipid-based formulas well because hypertriglyceridemia-induced pancreatitis is rare unless serum concentrations exceed 1,000 mg/dl (Silberman et al, 1982). PN administration without lipid emulsions beyond two weeks is not advised because of the risk for developing essential fatty acid deficiency. There are no similar data available for dogs or cats; however, patients with hypertriglyceridemia and/or pancreatitis have routinely received a high-fat TNA at their RER with no additional problems.[b]

Protein Solutions

Patients must receive a source of essential and nonessential amino acids. Solutions are available containing 3.5 to 15% amino acids. These solutions are maintained in the pH range of 5.3 to 6.5, have an osmolarity between 300 and 1,400 mOsm/l and may contain various combinations of electrolytes and/or dextrose (AHFS Drug Information, 1997). Modified formulas are available with disproportionate concentrations of branched-chained vs. aromatic amino acids. These formulas are designed for patients with renal or liver failure or multiple trauma, but have not been widely used in veterinary medicine due to expense. The most commonly used product in veterinary medicine is the conventional 8.5% amino acid solution either with or without electrolytes (**Table 26-3**). Most amino acid solutions contain all the essential amino acids for dogs and cats, except

Table 26-5. Drug incompatibility with B-complex vitamins.*

Known incompatible	Suspected incompatible
2-PAM (pralidoxime chloride)	4-methylpyrazole
Aminophylline	Adriamycin
Asparaginase	Carboplatin
Bicarbonate	Cisplatin
Calcium versenate	Dobutamine
Cefazolin	Dopamine
Diazepam	Fentanyl
Digoxin (injectable)	Propranolol
Mannitol	
Nitroprusside	
Penicillin G	
Quinidine	

*Plumb DC. Veterinary Drug Handbook, 3rd ed. White Bear, MN: Pharma Veterinary Publishing, 1999.

taurine. However, some specialized pediatric amino acid products contain taurine.

Protein should be provided to the patient within a ratio of 1 to 6 g protein/100 kcal of nonprotein energy provided. Adult dogs and cats do well on 2 to 3 g/100 kcal and 3 to 4 g/100 kcal, respectively. Ferrets should receive protein intakes similar to those for cats (4 to 5 g protein/100 kcal), whereas rabbits should receive lower protein intakes (1 to 2 g protein/100 kcal). The lower protein-calorie ratios are recommended for patients with renal or hepatic insufficiency. The higher protein intakes are recommended for patients with increased protein needs (e.g., albumin losses, chest-tube drains). The exact protein intake for each patient cannot be determined prospectively but may have a significant effect on outcome. Postoperative patients receiving 1 g amino acids/kg body weight parenterally had less negative nitrogen balance and greater transferrin concentrations and lymphocyte counts compared with people receiving an isocaloric intake of calories as glucose without amino acids (Hwang et al, 1993). Therefore, the ratios recommended here should be used as guidelines only. A reasonable estimate of a patient's protein needs should be made, the patient's response to that particular protein intake should be monitored and the intake should be adjusted accordingly. Patients are rarely azotemic due to PN administration when amino acids are provided within these protein-energy ratios and a product is used that provides mostly essential amino acids.

There are some combination amino acid/glycerin products that provide amino acids and an energy source in a fixed ratio (**Table 26-3**). Some of these combinations are provided as a two-compartment bag with dextrose and amino acid solutions separated by a breakable divider. Most of these prepackaged dextrose/amino-acid mixes contain very high protein-calorie ratios and do not contain fat.

Electrolyte Solutions
The more common electrolyte abnormalities associated with PN occur with the major intracellular cation potassium and the anion phosphorus. Potassium and phosphorus rapidly move

intracellularly with refeeding by either enteral or parenteral methods or with the administration of glucose or insulin (Forrester and Moreland, 1989). Potassium moves intracellularly when acidosis is corrected or when insulin is released. A TNA solution composed of 8.5% amino acids with electrolytes and lactated Ringer's solution contains approximately 12 mEq potassium/l, which is inadequate to maintain normal serum potassium levels. Potassium can be added to the PN solution using either a 2 mEq/ml potassium chloride solution or a 4.4 mEq/ml potassium phosphate solution.

If the patient is normokalemic when PN is initiated, 30 to 40 mEq potassium/l will usually maintain normokalemia. However, if the patient is hypokalemic when PN is started, 40 or more mEq potassium/l will be required. If the patient is hyperkalemic when PN is initiated, no additional potassium is recommended; however, serum potassium concentrations should be monitored daily. Administration of crystalloid solutions containing potassium by a second intravenous line is a convenient method of regulating serum potassium levels in difficult cases.

Phosphorus moves intracellularly with refeeding because of increased production of high-energy phosphate compounds (Hardy and Adams, 1989). Patients receiving PN rarely become hypophosphatemic. Sufficient quantities of phosphorus (10 mM/l) appear to be available in the TNA from lipid (15 mM/l) and amino acid/electrolyte (30 mM/l) solutions. However, adding a potassium phosphate solution containing 4.4 mEq potassium and 3 mM phosphorus/ml will increase the potassium and phosphorus content of the TNA. In cases of hyperphosphatemia, the quantity of amino acids, electrolytes and fat must be reduced to decrease phosphate concentrations in the TNA. Alternatively, an amino acid solution without electrolytes and potassium chloride can be used.

Vitamin Solutions
Very few veterinary patients receiving PN have a demonstrable need for fat-soluble vitamins unless there is a history of prolonged weight loss, inappetence and decreased fat absorption (diarrhea/steatorrhea). Dogs and cats usually have sufficient body stores of vitamins A, D, E, K and B_{12} to last several weeks to months if there is no increased demand or losses. Fat-soluble vitamin supplementation is warranted in cases with a history of long-term fat malabsorption (months). One-time administration of 1 ml of a vitamin A, D and E product,[c] divided into two intramuscular sites, is simple, cost effective and supplies fat-soluble vitamins for about three months. Vitamin K_1 injections (3 to 5 mg/cat, b.i.d., subcutaneously) reportedly improved abnormal coagulation times in cases of severe idiopathic hepatic lipidosis (Center, 1995, 1996). Most disease states are associated with increased oxidative stress and free radical-induced cell damage. Administering a PN solution with a high lipid concentration may provide nutritional support, but is also an oxide-rich nutrient source. Early work indicated patients administered highly oxidative nutrient solutions (lipids) may benefit from receiving the antioxidant d-α-tocopherol (24 to 48 IU/g lipid) (Becvarova et al, 2005).

Water-soluble vitamins, however, must be supplied daily by either the enteral or parenteral route. Most veterinary vitamin B-complex products do not contain all 11 B-complex vitamins, because some B vitamins are incompatible (e.g., folic acid and riboflavin in the same solution). Folic acid, therefore, must be administered separately if needed. Based on the National Research Council (NRC, 2006) daily vitamin recommendations for healthy dogs and cats and given the vitamin concentrations available in most solutions[d] the recommended dose of 1 ml of B vitamins/100 kcal exceeds daily B-vitamin requirements by several-fold, except for B_{12}. Most previously healthy patients, however, have sufficient hepatic stores of B_{12}.

Some B vitamins are light labile; therefore, most B-vitamin preparations should be kept in a light-resistant bottle and stored between 15 to 30°C (59 to 86°F). Riboflavin, perhaps the most light-labile B vitamin, still has 50% of its original activity after exposure to indoor fluorescent lighting for eight hours (Chen et al, 1983; Smith et al, 1988). Given the NRC (2006) recommended dose of riboflavin and the concentration of riboflavin in the TNA at 1 ml B vitamins/100 kcal, the patient would receive the daily recommended amount of riboflavin within the first two hours of TNA therapy. Thus, covering the intravenous fluid bag to protect B vitamins is unnecessary. Also, the addition of lipid increases the opacity of the final solution, reduces light penetration and precludes having to cover the PN solution from light (Smith et al, 1988). Adding B vitamins is a low-cost (pennies per day), effective means of improving energy metabolism. However, B vitamins are incompatible with some drugs commonly administered to veterinary patients by continuous intravenous infusion (**Table 26-5**).

Trace-Element Solutions

Trace-element requirements have not been determined for catabolic veterinary patients and dosing recommendations for zinc and copper in PN solutions are still evolving. In studies, dogs receiving a zinc-free PN solution had serum levels 50% of normal after one week; therefore, some zinc supplementation is recommended (Iriyama et al, 1982). Supplementing PN solutions with at least 0.1 to 0.2 mg zinc/100 kcal has been suggested (Buffington, 1991; Hill, 1994). Piglets receiving PN for four weeks with a solution containing 5 mg zinc and 0.3 mg copper/100 kcal had toxic zinc but normal copper hepatic concentrations and evidence of pancreatic necrosis associated with zinc toxicosis. Piglets receiving a similar PN protocol with 1.2 mg zinc and 0.3 mg copper/100 kcal had normal hepatic zinc and copper concentrations and no pancreatic pathology (Gabrielson et al, 1996). Based on the NRC (2006) daily zinc and copper recommendations for dogs and cats and one author's (RLR) experience, PN solutions containing 2 mg zinc and 0.2 mg copper/100 kcal RER approximate the patient's needs or approximately 1 ml of a trace-element solution may be added per 100 kcal RER daily. These elements can be added to the PN solution most economically (pennies per day) using a multiple trace-elemente combination available in multiple-dose or single-dose vials.[e]

Table 26-6. Drugs compatible with total nutrient admixtures.*

Aminophylline	Furosemide
Ampicillin	Gentamicin
Cefazolin	Heparin
Chloramphenicol	Insulin (regular)
Cimetidine	Lidocaine
Clindamycin	Metoclopramide
Digoxin	Penicillin G
Diphenhydramine	Phytonadione
Dopamine	Ranitidine
Erythromycin	Ticarcillin

*Dickerson RN, Brown RO, White KG. Parenteral nutrition solutions. In: Rombeau JL, Caldwell MD, eds. Clinical Nutrition; Parenteral Nutrition, 2nd ed. Philadelphia, PA: WB Saunders Co, 1993; 310-333.

DRUG ADDITIONS

Although it is very convenient to administer drugs intravenously with the PN solution, *extreme caution must be taken before any medications are added to the TNA*. Drug and TNA solution compatibility studies are ongoing, and there are published lists of drugs known to be compatible and safe (Trissel et al, 1999). **Table 26-6** lists drugs of most interest to veterinarians that can be incorporated into a three-in-one mixture. The *Handbook on Injectable Drugs* is updated and published every two years and is a good source for current information about drug compatibility with PN solutions (Trissel, 2007). After a medication has been added to the day's PN solution, a decision to discontinue that medication can be costly, because a new bag of PN solution must be compounded. Therefore, use of a second peripheral catheter or a multi-lumen central catheter may be preferable to adding drugs to PN solutions.

COMPOUNDING

PN solutions can be obtained from several sources. Some human hospitals and independent pharmaceutical companies will compound TNA solutions for veterinarians. A prescription must be written indicating the volume or final concentration of each nutrient (fat, dextrose, amino acids and each electrolyte), and the person preparing the TNA is likely to refer to the solution as "TPN." Some veterinary schools, large referral practices and private veterinary hospitals have parenteral solution compounders and supplies for their own use and will compound and sell TNA bags directly to practitioners. Several bags of PN solution (up to 10 days' worth) can be sent by overnight mail services directly to the practice. This is often the safest, most convenient and economical method of obtaining an all-in-one PN solution for the occasional patient in most practices.

TNA solutions can be compounded by one of three basic methods: 1) syringe, 2) gravity flow or 3) computerized flow (Remillard and Thatcher, 1989). All-in-one PN or TNA supplies can be purchased from the same sources that provide
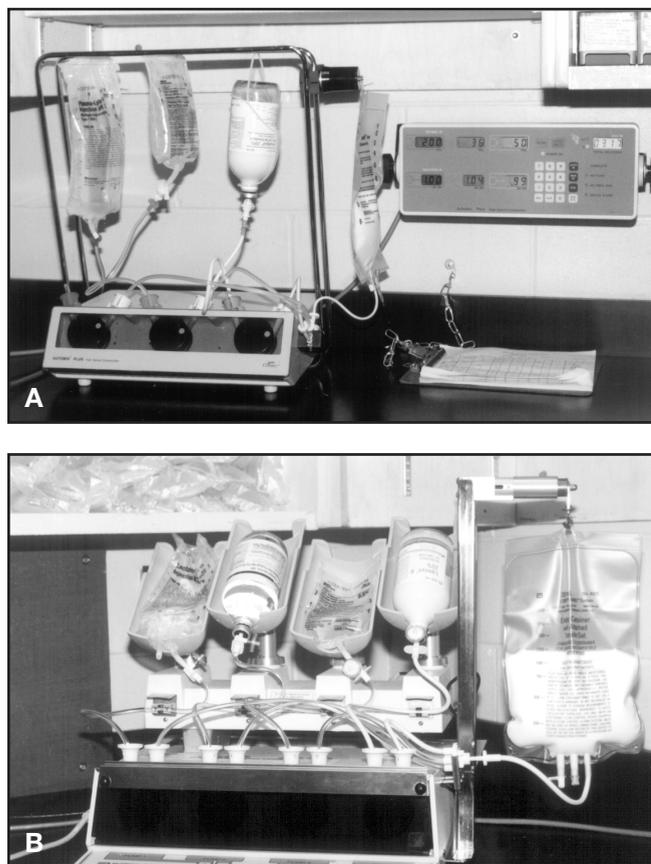
Figure 26-1. A three-station (A) and four-station (B) total nutrient admixture compounder.

nutrient solutions. The least desirable method uses a 35- or 60-ml syringe to transfer each nutrient solution (dextrose, amino acid and lipid) into a sterile, empty fluid bag. This method is the most time-consuming and carries the greatest risk of contamination because of the multiple transfers required. Transfers are ideally done under a laminar flow hood.

The second method uses a closed-circuit fluid system in which the all-in-one bag comes with a pre-attached three-lead transfer set. Each lead, with a vented filter spike, is inserted directly into the individual nutrient solutions (dextrose, amino acid and lipid), and the nutrients are transferred directly into the all-in-one bag by gravity flow. This method is faster and safer than the syringe method, but transfer of exact quantities is impossible. This method may be most economical when few patients require PN. Both syringe and gravity feed methods usually leave partially unused bottles of dextrose, lipid and amino acids.

The third and best method, used by most human hospitals and some large referral veterinary hospitals, employs a high-speed, closed-circuit fluid compounder that pumps three or four solutions (dextrose, amino acid, lipid and fluid) directly into one TNA bag within 60 seconds. Each solution is accurately transferred to within 1 ml. The method has a mean error of less than 3% (**Figure 26-1**). Multiple bags of TNA for several patients can be efficiently compounded at one time using

partial bottles of dextrose, fat and amino acids. Making TNA bags with a compounder is safe, fast, accurate and efficient. Veterinary technicians can routinely accomplish this task (McClendon, 1981). A computerized compounder has been used to formulate in one author's (RLR) practice since 1993. To date, no confirmed or suspected cases of microbial contamination have occurred during formulation.[f] All-in-one or TNA solutions can be refrigerated for seven to 14 days (**Box 26-3**).

ADMINISTRATION

The first practical technique for PN administration was demonstrated in the late 1960s (Franga, 2002). At that time, the only form of concentrated non-protein calories for intravenous use was hypertonic dextrose; therefore, a large-diameter, high-flow central vein was needed to avoid phlebothrombosis. Thus, infusion of this high osmolarity PN solution was best delivered into the superior vena cava. The predominant clinical complication with this feeding system was hyperalimentation and subsequent hyperglycemia. It was quickly realized that intravenous delivery of excessive dextrose calories commonly resulted in metabolic and infectious complications. Development and availability of crystalline amino acid and fat solutions helped to address these adverse PN-associated sequelae, because admixtures of lower osmolarity could be formulated for peripheral vein delivery. Additionally, there have been infrequent reports of PN solution delivery through either an intraosseous or intraperitoneal catheter. These alternatives offer additional options for short-term nutritional support.

The route of PN delivery is chosen after consideration of several factors including the underlying disorder and its severity, therapeutic goals for the patient, admixture composition, patient characteristics (e.g., body composition, species, age, vein accessibility), clinician experience and complication risk level (Hansen, 2006; Gallivan and Benotti, 1997). If management of the disease or disorder is thought to require prolonged (more than seven days) parenteral feeding, then the admixture delivery system should be initiated through or changed over to a central venous route. The peripheral route of admixture delivery is best suited to a short-term (less than seven days) nutritional support scenario or when central venous access is unavailable.

Central Vein Infusion

Traditionally, the right external jugular vein is the preferred access route for central venous catheters (CVC). From this site, the external jugular vein joins the cranial vena cava in a straighter line through the brachycephalic trunk, which facilitates catheter passage (Hansen, 2006). Body composition (obese, cachexia) can complicate CVC placement. Imaging techniques help reduce multiple attempts at placing CVCs, thereby minimizing coagulative states (Hunter, 2007; Franga, 2002). The large diameter of a central vein allows for delivery of a high osmolarity solution without concerns about phlebitis caused by fluid shifts in the vein lumen. Practically speaking,

the proportions of dextrose, lipid or amino acids in a PN admixture formulated for delivery through a central vein are not restricted. High- and low-dextrose admixtures are tolerated.

Central venous access can also be obtained by inserting a long catheter into the saphenous vein. This is commonly referred to as a peripherally inserted central catheter. Placing a 10- to 20-cm polyurethane[g] or silicone[h] catheter into the medial saphenous vein at the level of the tarsus and advancing the catheter up the vein places the tip of the catheter into the caudal vena cava of cats. A similar, but longer (20- to 30-cm) polyurethane or silicone catheter, placed in the lateral saphenous vein, is more useful in dogs weighing less than 20 kg. Parenteral admixtures can easily be administered to dogs and cats through a peripherally inserted central line. Cats, compared with most dogs, are smaller, have higher protein requirements and sometimes have restrictive fluid allowances. For cats (more so than for dogs), the final osmolarity of the PN solution will be greater than 600 mOsm/l; therefore, the solution should be administered into a large vein.

Catheters placed in a central vein can have a single lumen or multiple lumina. Although use of central catheters has not been adequately evaluated in veterinary patients, their use for PN administration in people is associated with an increase in septic complications (McCarthy et al, 1987). Many sources advocate that the central catheter must be "dedicated" to PN administration, and should not be used for blood sampling, medication or blood product administration or central venous pressure monitoring. However, when venous access is limited, the PN catheter may be used for blood sampling and administering medications if it is adequately flushed before and after PN administration is interrupted. It is imperative, as with any catheter, that proper aseptic handling technique be used during line interruptions. Likewise, the need for wiping PN lines after handling has not been substantiated; however, precautions are always warranted to reduce the risk of septic complications.

Peripheral Vein Infusion

The lateral saphenous (dog) and medial saphenous (cat) veins are most commonly used for peripheral catheter placement. These sites are preferred because the skin cover is thinner, thus providing better visualization and control over catheter insertion (Hansen, 2006). Less commonly used locations for catheter placement for delivery of PN include the cephalic and/or accessory cephalic veins, femoral veins in some dogs and cats and the ear veins in dogs with pendulous ears.

Based on peripheral vein diameter, there are limitations on the osmolarity of PN solutions that can be administered. In human patients, PN solutions with osmolarities ranging from 550 to 1,250 mOsm/l have been administered peripherally for short periods (three days) (Gazitua et al, 1979; Matsusue et al, 1995; Daly et al, 1985; Isaacs et al, 1977; Maden et al, 1992). Phlebitis, which occurred within the first 72 hours in 26 to 48% of human patients, was the principal complication (Bayer-Berger et al, 1989). Although peripheral vein administration of PN is not new in veterinary medicine, published studies are limited. One study of five dogs evaluated a 3-in-1

admixture delivered over various infusion time periods (Chandler and Payne-James, 2006). An 840 mOsm/l admixture was administered through a peripheral catheter for either 24 hours or 10 to 12 hours/day. Patency of the intravenous line was maintained for a median of 36 hours; no biochemical abnormalities were reported in study dogs. The incidence of line failure, due to thrombus or thrombophlebitis, was decreased by shorter infusion times. In another study, obese cats receiving a high-lipid, low-dextrose admixture through peripheral vein catheters for four days exhibited no mechanical, metabolic or septic complications (Becvarova et al, 2005).

Box 26-3. Complications of Total Nutrient Admixture Solutions.

The diverse composition of total nutrient admixture (TNA) solutions increases the risk of physiochemical incompatibilities. The most likely problem is deterioration of the lipid emulsion within the TNA in which individual fat particles collide forming larger particles creating a potentially dangerous intravenous mixture. TNA solutions containing 10 or 20% lipid have an osmolarity of about 300 mOsm/l, a pH of 7.0 and are stable when stored as directed at room temperature. An egg-yolk phospholipid emulsifier stabilizes the 4- to 5-mm lipid particles by giving the surface a negative charge to maintain a repulsive electrostatic force between particles. Fat breakdown in individual bottles of lipids rarely occurs.

In a TNA, however, fat particles can aggregate and larger particles will migrate to the surface of the solution, creating a whiter band at the top of the TNA solution. This process is called "creaming." It can be easily reversed by gently mixing the TNA solution, and is of no danger to the patient. However, when the negative surface charge is neutralized, the emulsion destabilizes irreversibly and, with repeated collisions between fat particles, the emulsion completely destabilizes. This irreversible coalescence process creates two immiscible oil and water phases. Coalescence is associated with a dark yellow color, either in a line across the top portion of the TNA or as large yellow globules throughout the TNA solution. Adding B-vitamins to a TNA solution gives the solution a light but uniform yellow color, and should not be confused with coalescence. Bags with evidence of coalescence should not be administered to patients because the larger particles can become fat emboli that will plug 5-mm pulmonary capillaries.

Adding divalent cations (e.g., calcium or magnesium) to the TNA solution is not advisable because the positive charge can destabilize the negatively charged surface of fat, break the emulsion and cause coalescence. Adding solutions that reduce the final pH of the TNA to 5 or less will also cause the emulsion to breakdown. Individual dextrose solutions are kept at a pH of 5 to minimize microbial growth, whereas amino acid solutions are buffered and have a pH of 6. When mixing a TNA solution, it is important to add the lipid last when there is a large volume of fluid with a higher pH already in the parenteral nutrition bag.

The Bibliography for **Box 26-3** can be found at www.markmorris.org.

Observed physiologic alterations in study cats were associated with obesity-induced oxidative damage. Calories can easily and safely be administered peripherally to dogs and cats using a TNA of 400 to 650 mOsm/l or an isomolar 20% lipid solution piggybacked with standard fluid therapy at volumes sufficient to meet RER.[1]

Other Routes of PN Infusion

Intravascular complications associated with repeated catheter placements, insufficient blood flow or coagulation abnormalities can limit vascular accessibility. Alternatives for PN support include the intraosseous and intraperitoneal (IP) routes, as reported in several laboratory species, people (adults and children) and dogs. In two separate studies, rats were infused with PN solutions through IP catheters for seven or more days. No adverse effects from the placement or use of IP catheters were found. Weight maintenance was dependent on the caloric profile of the admixture; a PN solution approximating 600 to 700 mOsm/l was preferred (Rubin et al, 1988; LeLeiko et al, 1983). PN solutions (850 mOsm/l) have been infused by IP routes for more than 20 days in 19 normal dogs and in 12 normal dogs that had undergone intestinal resection (Moran et al, 1989; Garcia-Gamito et al, 1991). IP infusion of a 10% lipid solution into three-month-old beagles demonstrated that fat was quantitatively absorbed from the peritoneal cavity over a four-hour period (Klein et al, 1983). Despite this apparent success, the IP route for PN support isn't widely used in veterinary medicine. Intraosseous infusion of drugs and fluids is used as an emergency, last resort access site for human and veterinary patients. Reports of short-term PN infusion (e.g., bolus) are limited, but encouraging. Tibial intraosseous infusion is the preferred site for critically ill children (Koenig, 2000), whereas the sternum is reported to be the most effective site for infusion of lipids in adults (Koenig, 2000). Likewise, a solution containing electrolytes, amino acids, dextrose and vitamins has been successfully infused intraosseously in dogs (Otto et al, 1989). Several precautions exist for intraosseous infusions including appropriate catheter placement, avoiding compromised skin areas and growth plates and extravasation of fluid around bone cortices or vessel foramina (Moss et al, 2005). Although fat embolization is a reasonable consideration, it has yet to be reported in the literature.

Risks and Complications

Catheter placement and management come with potential risks. The most clinically significant problem in administering PN solutions involves the catheter, including loss of access, thrombophlebitis and infection generally in that order of occurrence. Parenteral feeding can introduce additional risks not associated with non-caloric fluid delivery. An overview of the risks and complications associated with central and peripheral vein PN delivery follows.

Infection

Infectious complications with intravenous infusions have been recognized for more than 40 years and are now primarily associated with substandard catheter care. Most catheter-related septicemias are due to microbial invasion at the catheter wound either during or after insertion, but other risk factors include poor patient and personnel hygiene, operator inexperience, method and site of catheter insertion, duration of catheterization and number of catheter manipulations (Bozzetti, 1985; Yilmaz et al, 2007).

Catheters for PN administration must be placed using meticulous aseptic technique. Bandage contamination increases the risk of infection; peripheral vein catheters are more likely to be exposed to and soiled by feces, urine and vomitus compared to CVCs (Hansen, 2006). For either peripherally- or centrally-placed catheters, bandage and administration sets should be changed at least every other day, and preferably daily. When the bandage is changed, the venipuncture site should be cleaned with an iodine solution and examined for redness, edema or swelling. A topical antibiotic ointment (e.g., povidone iodine) that contains antifungal properties should be applied to the catheter-skin junction. If redness, edema or swelling is noticed, the catheter should be removed and cultured and the site should be kept clean and hot packed, if necessary, to reduce swelling. Appropriate antibiotics should be given if culture and antimicrobial sensitivity testing show the catheter or PN solution is contaminated.

Cut-down incisions may be necessary for catheter placement at any location and can increase the risk of infection. Infected or wounded skin at the catheter placement site increases the risk of infection (Hansen, 2006). If there is no other option for a catheter insertion site other than in close proximity to wounded or infected skin, aseptic placement is absolutely necessary. Extreme care should be exercised when assembling and disassembling the admixture flow system and frequent bandage changes are highly recommended. Tunneling or the "indirect catheterization" method forms a subcutaneous tunnel between the point of entry through the skin and the point of entry into the vein. Catheter tunneling helps prevent infection. This technique is more commonly performed when placing a CVC for long-term use. Tunnels serve as a barrier to bacterial migration (Hansen, 2006; Franga, 2002).

In human intensive care units, catheter-related infections are the third most common cause of nosocomial infections (CDC, 1997). Although these data are not reported for veterinary patients, the findings most likely would be similar. Catheter infections are either related to cellulitis from contamination at the catheter exit site (type I) or microorganism contamination within the catheter lumen (type II). Both are due to a failure in aseptic technique (Kaminski, 1997). Adding extra lumina to the same catheter appears to potentiate the risk for type II infections (Kaminski, 1997; Early, 1990; Kemp, 1994). Data are controversial regarding the practice of maintaining a dedicated catheter line for PN administration. In the event a line cannot be dedicated to PN administration, stopping PN delivery, flushing the line adequately before and after delivery of medications, then restarting the PN delivery, will help minimize complications associated with potential solution incompatibilities.

CVCs vary in size and composition (i.e., polyethylene, polyurethane, polyvinyl, silicone, Teflon). Selection of catheter material has implications for catheter-related infections. Silicone catheters reduce the sensitivity of *Staphylococcus aureus* to antibiotics (Williams, 1997). CVCs impregnated with antibiotics reduce the incidence of catheter-related infections (Hanley, 2000). Reports indicate that minocycline/rifampin-coated catheters are less likely to become colonized and have a significantly decreased number of catheter-related infections compared to chlorhexidine/silver sulfadiazine-impregnated catheters (Darouiche, 1999).

Other sources of catheter-related infection include urinary tract infections, abscesses, pneumonia, bacterial translocation from the GI tract or other infected sites (Ryan et al, 1974), resulting in thrombus formation at the catheter tip. Infusion of contaminated fluid is another potential source of infection. Using a closed-circuit fluid system minimizes this route of contamination. Whether individual nutrient solutions within the PN solution promote bacterial or fungal growth if stored inappropriately is still controversial. The crystalline amino acid products now used in PN formulations prohibit bacterial growth (Goldmann et al, 1971; Wilkinson et al, 1973). As a safety precaution, the Centers for Disease Control and Prevention has recommended that lipid-only emulsions be administered for no longer than 12 hours, except in PN systems, which can be administered over a 24-hour period (Simmons et al, 1982). Infection associated with PN administration is a rare complication, most often attributed to substandard catheter care.

Thrombosis

Thrombophlebitis is a response of the vein intima to the unique combination of the infusate, the catheter material and placement and the ratio of catheter to vessel size. Ideally, the smallest catheter necessary to deliver the desired therapy should be selected. Cannulating a vein always poses a risk for thrombosis formation. The longer the catheter remains in place, the greater the risk. Any indwelling catheter becomes covered by a fibrin sheath and platelets within several hours of placement (Hansen, 2006). The likelihood of thrombosis increases in a small vein (i.e., peripheral vein relative to catheter size) that has lower blood flow; when a catheter traverses a mobile joint, when a pre-existing disease exists such as glomerulonephritis, protein-losing enteropathy, autoimmune hemolytic anemia, phlebitis or any disorder causing systemic inflammation. The catheter material is thought to be the single most important factor in the severity of infusion thrombophlebitis (Gaukroger et al, 1988; McKee et al, 1989). Three major characteristics of catheter material have been identified that contribute to thrombus formation: roughness, stiffness and propensity for platelet adhesion (Linder et al, 1984). Numerous studies comparing catheter types are available for review. Catheter choice is multifactorial; minimizing thrombus formation during PN administration should an important consideration. The primary complication from thrombosis is loss of vessel patency,

although other complications of deep venous thrombosis include septic thrombophlebitis, venous gangrene, extravasation of infusate, pulmonary embolism and death (Gallivan and Benotti, 1997). Although the risk of thrombosis in a catheterized jugular vein is much lower, the consequences are much more severe compared to those that might occur in a peripheral vein.

Extravasation

When a catheter is displaced, fluid leaks into or infiltrates surrounding tissues (extravasation) causing pain and swelling. Stiff plastic catheters are more likely to perforate vessels during and after placement compared to softer polyurethane or silicone catheters.

Complications with CVC extravasation may not become evident until large volumes of fluid are administered. Fluids (solution) tend to accumulate in the mediastinal and pleural spaces resulting in labored breathing. When catheters are advanced into the right atrium, blood and fluid will accumulate in the pericardial sac causing cardiac tamponade. Thoracic radiographs, physical signs and possibly fluid analysis can be used to document PN solution extravasation.

Swelling and tenderness at peripheral vein infusion sites may indicate extravasation of the PN admixture. The skin overlying the catheter tip may feel cool, and/or the catheter insertion site may be swollen, red and hot, and left unattended, may lead to tissue necrosis and sloughing.

Catheter Damage

Catheters placed in limbs are more accessible for patients to chew or tear. Placement of an Elizabethan collar may help prevent damage to the PN system after the catheter has been placed and the feeding system constructed. Catheters placed in an ear vein may be dislodged by scratching and head shaking. A well-fitted Elizabethan collar will minimize this concern. Catheters placed in the jugular vein are at least risk for damage because patients are less likely to disturb this site. Loss of venous access is caused by catheter kinking, catheter tip migration or blockage. In these instances, the catheter should be removed and a new catheter placed in another vein. Chewing and/or scratching at bandages that conceal a catheter may indicate that the catheter or bandage is irritating the patient. Check the bandage and catheter for tightness, wetness, inflammation or infection. Immediately remove the bandage if any of these problems arise. Assess catheter viability, vein patency, presence of inflammation or infection and immediately make changes to rectify the problem(s).

Guidelines for parenteral feeding of human patients clearly recommend central vein delivery for long-term (months) intravenous nutritional support. However, intravenous nutritional support for most companion animals lasts two to seven days; in some extreme cases, parenteral feeding may be used for several weeks. Catheter placement for PN delivery in small animals should be based on catheter complication risks, duration of feeding, catheter placement and monitoring experience and cost and solution composition (**Table 26-7**).

Table 26-7. Summary of catheter placement sites for parenteral nutrition administration in small animals.

Site/Technique	Pros	Cons	Indications
External jugular	Central vein (large) access Exchangeable High osmolar solution compatible Long-term use (>7 days) Less bandage damage	Placement technically difficult Infection rate higher Intensive patient monitoring required	Inability to use GI tract for nutritional support Electrolytes stable Interruption of oral alimentations for >7 days; catabolic <7 days Non-septic patients Hospitalization required
Tunneled catheters	Lower infection rate of CVC Long-term use (>7 days) Central venous access Hospitalization compatible	Operative placement recommended Placement technically difficult	Long-term CVC required for PN
PICC (femoral vein)	Central vein access Hospitalization compatible Exchangeable	Thrombophlebitis risk higher Infection rate higher Short-term use (<3 days) Blood draws not predictable	To accommodate hospitalization in cats and small dogs No jugular access
Peripheral (saphenous, cephalic)	Easy insertion Lower infection rate Amendable to 3-in-1 solutions Less intensive patient monitoring Exchangeable Lower cost	Requires low osmolar solution (<650 mOsm/l) Short-term use (<7 days) Increase risk of bandage damage Elizabethan collar recommended	High risk of catheter sepsis from CVC Patient can tolerate lipid emulsions Patient in mild metabolic stress/ malnutrition Central vein access not available/ contraindicated Short duration PN Adjunct to enteral or oral nutrition on short-term basis
IO, IP	Venous access not required	Ultra short-term use (IO) Placement technically difficulty (IO) Limited documentation	Emergency situations when venous access is unavailable

Key: GI = gastrointestinal, CVC = central venous catheter, PN = parenteral nutrition, PICC = peripherally inserted central catheter, IO = intraosseous, IP = intraperitoneal.

COMBINED ENTERAL AND PARENTERAL FEEDING

In human medicine, there has been increased acceptance and use of PN in combination with tube feeding (Adams et al, 1986; Moore and Jones, 1986). Feeding enterally minimizes the disadvantages of PN. Prolonged fasting (more than three days) results in enterocyte deterioration and decreased GI immunity (Alverdy et al, 1985). Translocation of enteric bacteria due to a compromised intestinal mucosal barrier represents a possible source of infection with PN administration. Enteral infusion of small quantities of a liquid diet helped prevent intestinal mucosal deterioration during PN administration in piglets (2 ml/kg body weight b.i.d.), human infants (4 to 5 ml/kg body weight/hour) and adults (0.7 ml/kg body weight/hour) (Remillard et al, 1998; Andrassy et al, 1979, 1985). Intestinal adaptations after disease and intestinal hypertrophy after surgery require intraluminal nutrients. Food intake promotes intestinal hyperplasia and brush border enzyme activity (Herman-Zaidius, 1986). Therefore, current recommendations encourage some enteral feeding for patients receiving PN support, if at all possible. Feeding both the small bowel and the patient is important (Daley and Bistrian, 1994).

Either central or peripheral vein delivery systems can be used together with enteral feeding (voluntary or assisted). If PN complements a tube feeding system, avoid the central vein-esophagostomy feeding tube combination. Close proximity of the jugular vein catheter and the feeding tube insertion site may increase the risk of infection and mechanical problems. Other PN and enteral feeding combinations work predictably to optimize nutritional support and GI health.

REASSESSMENT

Regular reassessment is a critical step in successful nutritional management of hospitalized patients, regardless of whether the enteral route, the parenteral route or both are used. Malnutrition in the form of insufficient nutrient intake to support tissue metabolism undermines medical and/or surgical management of a case. Malnutrition is far more common in veterinary patients than is currently recognized. Patients resting in a cage have been mistakenly assumed to require little or no caloric intake when, in fact, the nutrient costs of tissue repair, immunocompetence and drug metabolism are significant. Therefore, reassessment of nutritional status is important whether the patient remains in the hospital or recovers at home.

Monitoring Parameters
Food intake or administration of nutritional support for hospi-

Table 26-8. Metabolic complications of parenteral-nutrition administration, treatment and potential patient considerations.

Complications are listed in descending order of likely occurrence and treatments are listed from immediate to longer term solutions. To minimize complications, patients should be hemodynamically stable and any electrolyte and acid-base abnormalities, severe tachycardia, hypotension and volume deficits should be corrected before starting PN.

Complication	Treatment	Patient considerations

Hyperglycemia	Stop infusion, recheck in two to four hours, decrease PN infusion by 50% until normal, then increase infusion rate slowly
	Subcutaneous insulin therapy
	Change caloric sources:
	    Increase lipid fraction of calories
	    Decrease glucose fraction of calories
		Glucose intolerance

Hypokalemia	Add KCl or KPO_4 to PN bag
	Correct serum magnesium as needed
	Change caloric sources:
	    Increase lipid fraction of calories
	    Decrease glucose fraction of calories
		GI or renal losses
		Drug therapies that increase urinary excretion
		Insulin therapy

Hypophosphatemia	Add $NaPO_4$ or KPO_4 to PN bag	Diabetic ketoacidosis

Hyperlipidemia	Stop infusion, recheck in two to four hours, decrease infusion by 50% until normal, then increase infusion rate slowly
	Change caloric sources:
	    Decrease lipid fraction of calories
	    Increase glucose fraction of calories
		Decreased lipid clearance

Phlebitis	Change catheter and infusion site
	Lower PN osmolality:
	    Increase lipid fraction of calories
	    Decrease glucose fraction of calories
	    Add heparin to PN bag
		Proper hydration
		Endogenous site of infection

Hyperkalemia	Change PN bag and decrease potassium	Acidosis, renal failure, sepsis Drug therapies that decrease urinary excretion
Hyperammonemia	Decrease PN infusion by 50% until normal Change PN bag, decrease amino acid concentration Use branched-chain amino acid sources	Liver dysfunction, GI bleeding
Hypomagnesemia	Add $MgSO_4$ to PN bag	GI or renal losses Drug therapies that increase urinary excretion

Hypoglycemia	Piggyback 50% dextrose drip until normal
	Change caloric sources:
	    Decrease lipid fraction of calories
	    Increase glucose fraction of calories
		Sepsis
		Insulin therapy
		Insulinoma

Infected catheter site	Change catheter and infusion site Culture catheter and PN solution Give antibiotics based on culture and antimicrobial sensitivity tests Hot pack the site	Substandard catheter care Endogenous site of infection Properly hydrated

Key: PN = parenteral nutrition, GI = gastrointestinal.

talized patients should be reviewed at least daily. Body weight should be recorded daily. Body condition should be noted; however, an animal's body condition score is unlikely to change during the course of a hospital stay. Laboratory assessments specifically for patients receiving nutritional support are generally not necessary beyond those tests already routinely performed for critically ill patients. The most common alterations that occur in laboratory parameters associated with nutrient administration are decreases in serum potassium and phosphate levels, increases in serum glucose concentrations and hypertriglyceridemia (**Table 26-8**). Even apparently stable patients might develop metabolic complications as a result of ongoing disease processes or from undiagnosed subclinical disease states. However, most patients' attitude improves subjectively within 36 hours of refeeding.[j]

Most parameters used to assess the nutritional status of patients will not change as a result of assisted feeding during the course of hospitalization. Laboratory parameters (e.g., albumin and total protein concentrations, RBC count and hemoglobin content) are unlikely to change in less than two weeks. The patient's body weight and condition and some laboratory parameters (albumin and total protein concentrations) should improve over the course of weeks (McAdams et al, 1996). Laboratory parameters that change during a hospital stay as a result of assisted feeding may be detected when acute-phase proteins with half-lives between two and 12 hours can be measured reliably in dogs and cats.

Changing Foods
Parenterally fed patients should be fed enterally as soon as pos-

sible, but may continue to receive PN as enteral intake increases to meet RER. The food offered enterally may be a fixed-formula therapeutic food intended as the food to be fed to the patient at home because of an ongoing disease condition (Chapter 25). When the patient has a decreased appetite, a highly palatable, fixed-formula food may be offered initially to stimulate oral consumption. This food may then be mixed in gradually decreasing proportions with the food to be fed on a long-term basis (Chapter 1). Vomiting and diarrhea are the most common problems seen when refeeding patients orally. Foods should be introduced in amounts equal to RER in small frequent meals, and the amounts increased if well tolerated over several days.

ENDNOTES

a. Prescribing information for Intralipid Intravenous Fat Emulsion, 1981. Cutter Laboratories, Berkeley, CA, USA.

b. Remillard RL, Angell Animal Medical Center, Boston, MA, USA. Unpublished data.

c. Vital E-A+D containing 100 IU of D and 300 IU of alpha-tocopherol per ml. Schering-Plough Animal Health Corp., Kenilworth, NJ, USA.

d. B-Vitamin Complex containing 50 mg thiamin, 2 mg riboflavin, 100 mg niacin, 2 mg pyridoxine, 10 mg pantothenic acid, 0.4 µg B12 per ml. Butler Co., Columbus, OH, USA.

e. MTE-4 contains 1.7 mg zinc, 0.42 mg copper, 0.37 mg manganese and 6 µg chromium per ml containing the preservative benzyl alcohol. Abbott Laboratories, Chicago, IL, USA.

f. Remillard RL, Angell Animal Medical Center, Boston, MA, USA. Unpublished data.

g. L-Cath (16 and 18 ga.). Luther Medical Products, Inc., Santa Ana, CA, USA. Central venous (20 to 16 ga.) catheters. Cook Veterinary Products, Bloomington, IL, USA.

h. Silicone (20 to 16 ga.) catheters (50 to 60 cm) can be cut to appropriate lengths. Cook Critical Care, Bloomington, IL, USA.

i. Remillard RL, Angell Animal Medical Center, Boston, MA, USA; Saker K, North Carolina State University, Raleigh, NC, USA. Unpublished data.

j. Remillard RL, Armstrong PJ, Guilford WG. Personal clinical experience.

REFERENCES

The references for **Chapter 26** can be found at www.markmorris.org.

CASE 26-1

Peripheral Parenteral Nutrition in a Dog

Korinn E. Saker, MS, DVM, PhD, Dipl. ACVN
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina, USA

Patient Assessment

A six-year-old, intact male, mixed-breed dog weighing 29.5 kg with a body condition score (BCS) of 3/5 was presented for evaluation of suspected sepsis following a severe neck wound. A large open wound on the right side of the dog's neck was first noticed five days earlier. The local veterinarian flushed and closed the wound and initiated antibiotic therapy (enrofloxacin[a], amoxicillin[b] and a single dose of cephalexin[c]). The dog's clinical condition continued to deteriorate; therefore, the dog was referred for further evaluation.

On physical examination, the dog was depressed and laterally recumbent. The wound on the right side of the dog's neck extended from the dorsal margin of the ear pinna to the ventral midline. There was a necrotic odor originating from the wound. A fluid-filled pocket ventral to the wound was incised, releasing a large volume of purulent material. Specimens were collected for bacteriologic studies. When skin sutures were removed, a large wound extending deep into the tissues on the left side of the neck was found. The trachea, jugular vein and several nerves were visible at the wound margins, along with large amounts of green necrotic tissue. Skin surrounding the wound was indurated and necrotic. The dog's right ear was swollen and edematous with a creamy exudate originating from wounds on the medial aspect. Crackles could be auscultated in the right caudal lung field and the patient was mildly dyspneic.

Laboratory abnormalities included neutrophilia with a left shift, thrombocytopenia, decreased total protein (5.2 g/dl [normal 5.5 to 7.4 g/dl]) and albumin (2.3 g/dl [normal 2.8 to 3.6 g/dl]) values, lymphopenia, elevated bilirubin (5.0 mg/dl [normal 0.1 to 0.5 mg/dl]) concentration and increased alanine aminotransferase (367 U/l [normal 13 to 100 U/l]) and alkaline phosphatase (2,954 [normal 20 to 167 U/l]) activities.

After initial presentation to the teaching hospital, the dog was sedated twice daily for aggressive wound management and bandage care with wet-to-dry bandages. Aerobic and anaerobic wound cultures grew *Pseudomonas aeruginosa*, *Eubacterium aureofaciens*, *Bacteroides bivius* and *Clostridium perfringens*. The patient regurgitated white foam numerous times during the first three days of hospitalization and was dysphagic.

Assess the Food and Feeding Method

The dog had not eaten during the five days before presentation and was not offered food for the first three days of hospitalization while undergoing wound exploration and débridement and diagnostic cultures, radiography, bronchoscopy and esophagoscopy. Although nutritional support was not offered, a physiologic replacement fluid (lactated Ringer's solution) containing 20 mEq of potassium chloride/l was administered in the first 12 hours to replace an estimated fluid deficit of 10%. Fluids were reduced to maintenance rates thereafter.

Questions

1. What techniques and parameters could be used to assess the nutritional status of this patient?
2. Which nutrients would be beneficial in enhancing tissue repair and immunocompetence?
3. When and by what method should nutritional support be initiated?

Answers and Discussion

1. Currently, nutritional assessment is limited to the veterinary equivalent of anthropometric measures (i.e., body weight and condition), routine laboratory tests (e.g., total protein and albumin levels, lymphocyte counts) and clinical examination. Weight loss of more than 10% in sick or injured patients is considered a guideline for implementing nutritional support. Albumin has a half-life of eight days in normal dogs, thus it may remain within the normal range during short-term (one week) nutritional deprivation. The albumin concentration will decrease as the period of anorexia and lack of nutritional support is prolonged. The lymphocyte count also is altered in a relatively short period (days) as a result of nutrient deprivation. However, both hypoalbuminemia and lymphopenia can result from non-nutritionally related causes.

2. The patient's immune system was not responding optimally because of the infection and sepsis related to the neck injury. As a result of eight days of nutritional deprivation, the patient's body was now metabolizing fat and protein stores for energy and tissue repair. The labile protein pool (free amino acids) was becoming depleted and visceral and muscle protein was mobilized, which will result in atrophy and wasting in prolonged states of food deprivation in the face of accelerated catabolism. Immune cells and damaged muscle tissue benefit from dietary protein and fat. Research has shown that protein-energy malnutrition (PEM) results in immune system dysfunction. PEM increases the risk of mortality from infection, because it compromises innate and adaptive barriers to disease challenges. Specific alterations include: 1) a decreased marrow pool of neutrophils, 2) depressed neutrophil and monocyte phagocytic activity, 3) depressed antigen-presenting capacity of macrophages, 4) atrophy of lymphoid organs, 5) alterations in critical CD4 and CD8 cell subsets, 6) increased adhesion of organisms to mucosal epithelia and 7) alterations in regulation of inflammatory mediators. Micronutrients such as zinc, copper, iron, selenium and vitamins A, E and C should also be supplied because they are integral components in enzyme systems that promote antioxidant activity, antibody formation, cell activation and proliferation and protein synthesis.

3. Nutritional support should be instituted immediately. The twice daily wound débridement and bandage changes with sedation limit the time this patient is alert enough to assimilate oral nutrients. Additionally, this patient has a history of regurgitation and dysphagia since being admitted to the teaching hospital. In light of these factors, as well as the physical inaccessibility to the neck region because of the wound and bandages, this patient is an excellent candidate for peripheral parenteral feeding. The peripheral route of intravenous feeding can supply 100% of resting energy requirement (RER), amino acids plus maintenance electrolytes, minerals, vitamins and trace elements.

   The intravenous admixture should be formulated as a high-fat, low-carbohydrate solution to mirror the patient's current metabolic profile. A total admixture containing 3 g protein/100 kcal with 80 to 90% fat calories and 10 to 20% dextrose calories plus maintenance fluid therapy will ensure an osmolarity less than 600 mOsm/l and that the admixture can be administered peripherally. This high-fat admixture will also reduce the incidence of hyperglycemia and hyperinsulinemia, and improve nitrogen balance, which is particularly important in this case because of the patient's extensive tissue necrosis. A high-fat diet has also been recommended in cases with pulmonary compromise as observed in this patient. Metabolism of fat calories produces less carbon dioxide for excretion than carbohydrate metabolism. Feeding fat decreases the pulmonary work to excrete carbon dioxide and thereby reduces ventilatory work.

   This nutrient admixture, administered through a peripheral access, should be done using a silicone or polyurethane catheter. Sodium heparin can be added to the admixture (0.5 to 1 U/ml of total admixture) to prevent formation of fibrin clots around the catheter tip when it is placed in a small vessel. To promote or maintain gastrointestinal health, the patient should also be fed small amounts of a high-protein, high-fat liquid or moist food per os as soon as clinically possible. The oral food should be enriched with glutamine, arginine and omega-3 fatty acids to enhance enterocyte proliferation and immune cell function.

Progress Notes

The patient received peripheral parenteral feeding (**Table 1**) for eight days during which time the frequency of wound débridement and bandage changes was decreased to once daily. The patient's food assimilation and swallowing reflex improved so that the patient was able to eat a food with high protein, fat and moisture content (Prescription Diet a/d Canine/Feline[d] gruel and then Prescription Diet p/d Canine[d] meatballs) to meet its RER. Just before the patient was discharged, its laboratory values were normal except for mild hypoalbuminemia (2.4 g/dl). The patient was discharged with antibiotic therapy and instructions to the owners for daily wound care. The dog returned for weekly evaluations. Tissue healing was marked but not complete four weeks after hospitalization. The owners were advised to feed 4.5 cups of a moderately high-protein, calorie-dense food (Science Diet Puppy Original[d] dry) to meet the dog's daily energy requirement (DER) of 1,595 kcal (DER = 1.8 x RER) (6.67 MJ) until tissue healing was complete.

Endnotes

a. Baytril. Bayer Animal Health, Shawnee, KS, USA.
b. Amoxi-Tabs. Pfizer Animal Health, Exton, PA, USA.
c. Cephalexin. Teva Pharm, Sellersville, PA, USA.
d. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

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Neuvonen PT, Salvo M. Effects of short-term starvation on the immune response. Nutrition Research 1984; 4: 771-776.

Zaloga G, Ackerman MH. A review of disease-specific formulas. American Association of Critical-Care Nurses: Clinical Issues 1994; 421-435.

Table 1. Peripheral parenteral TNA for one day.[*]

Nutrients/fluids	Quantities (ml)
50% dextrose	52
20% lipid emulsion	400
8.5% amino acids (with electrolytes)	312
Potassium phosphate (4.4 mEq K, 3 mM P/ml)	4.9
Potassium chloride (2 mEq/ml)	7.5
Vitamin-B complex[**]	9
Trace elements[***]	9
Lactated Ringer's solution	1,252

[*]RER ($[29.5]^{0.75}$ x 70) = 886 kcal ME/day (3.7 MJ). Calories from lipid = 90%. Calories from dextrose = 10%. Protein-calorie ratio = 3 g/100 kcal. [K] = 29.6 mEq/l. [P] = 11.8 mM/l. Osmolarity = 486 mOsm/l.
[**]B-vitamin complex contains 50 mg thiamin, 2 mg riboflavin, 100 mg niacin, 2 mg pyridoxine, 10 mg pantothenic acid and 0.4 μg B_{12} per ml. Butler Co., Columbus, OH, USA.
[***]MTE-4 contains 1.7 mg zinc, 0.42 mg copper, 0.37 mg manganese and 6 μg chromium per ml containing the preservative benzyl alcohol. Abbott Laboratories, Chicago, IL, USA.

CASE 26-2

Central Parenteral Nutrition in a Cat

Kathryn E. Michel, DVM, MS, Dipl. ACVN
School of Veterinary Medicine
University of Pennsylvania
Philadelphia, Pennsylvania, USA

Patient Assessment

A 10-year-old, spayed female, domestic shorthair cat presented to the emergency service with a three-week history of poor appetite and weight loss. The chief complaint was facial swelling (especially around the nose) and nasal discoloration. The cat's problems were originally associated with an episode of pollakiuria and inappropriate urination, which resolved with antimicrobial therapy

(sulfadimethoxine[a]). About two weeks before presentation, the cat became lethargic and tachypneic and its appetite deteriorated further. At that time the owners noticed that the cat's normally pink nose had become discolored. They initially observed a small bloody spot on the bridge of the nose overlying bluish skin. Over the course of a week the nose became progressively swollen and the skin blackened. The cat developed mild epistaxis.

On physical examination, the patient was depressed, moderately dehydrated (8 to 10%) and hypothermic (36.7°C [98.2°F]). The cat weighed 3 kg and its body condition was considered cachectic (body condition score [BCS] of 1/5). Mucous membranes were pale and slightly tacky. Ecchymoses and petechiae were present on the sclera, pinnae and gingiva. Harsh lung sounds were auscultated bilaterally. Swelling and discoloration were noted on the nose, upper lip and tail.

Initial laboratory work included a serum biochemistry analysis, a complete blood count (CBC), a coagulation profile, activated clotting time (ACT) and blood typing. The cat had previously tested negative for feline leukemia virus and feline immunodeficiency virus. Results of the serum biochemistry profile were within normal limits. Abnormalities on the CBC included a hematocrit of 11% (normal 27 to 45%), hemoglobin of 3.5 g/dl (normal 8 to 15 g/dl) and an inflammatory leukogram with a left shift. The cat had a platelet count of 88,000/µl (normal 175,000 to 425,000/µl) and a corrected reticulocyte count of 8.28% (normal 1 to 10%). The coagulation profile was within normal limits, although the ACT was abnormal and the blood never completely clotted. Thoracic radiographs revealed an alveolar pattern in the cranioventral lung fields and overall increased density in the caudodorsal lung fields. Active inflammation and hemorrhage were noted on the tracheal wash. Biopsy specimens were submitted from the nose and upper lip. A cardiac consult revealed no evidence of primary heart disease and an occult heartworm test was negative.

The problem list included cachexia, anemia, neutrophilia, thrombocytopenia and alveolar disease. The differential diagnosis included thromboembolic disease, pneumonia and cold agglutinin disease. Microscopic thrombi consistent with cold agglutinin disease were found on biopsy specimens. Cold agglutinin disease was confirmed by a positive Coomb's test at 7°C (44.6°F).

Assess the Food and Feeding Method

The cat showed no interest in food even though a variety of foods were offered and efforts were made to coax it to eat. The cat had been fed a commercial grocery brand dry cat food (Purina Cat Chow[b]) free choice for several years. It would accept only a small amount of food when given by syringe. The necrotic condition of the cat's nose probably affected its ability to smell food and that in combination with dyspnea and anemia caused the lack of appetite. The cat's poor body condition, the severity of its illness and the likelihood of a prolonged clinical course prompted a more aggressive approach for providing nutrition to this patient.

Initial therapy included a maintenance infusion (65 ml/kg body weight/day) of 0.9% NaCl with 20 mEq K/l, antibiotic therapy (enrofloxacin[c] and ampicillin[d]) and a transfusion with whole blood and fresh frozen plasma. The cat was admitted to the intensive care unit where it was placed in an oxygen cage with orders to keep it warm. The cat was started on cyproheptadine[e] (2 mg per os, t.i.d.) with orders to offer a variety of warmed foods and to coax it to eat. A central venous polyurethane catheter was placed in the left femoral vein and a parenteral nutrition (PN) admixture containing 50% dextrose, 20% lipid emulsion, 8.5% amino acid solution without electrolytes, potassium phosphate, potassium chloride, trace elements and injectable B complex was begun (**Table 1**). The PN solution was delivered at a rate of 5 ml/hour for the first 24 hours to deliver two-thirds of the calculated resting energy requirement (RER). On subsequent days, it was delivered at a rate of 7 ml/hour (56 ml/kg body weight/day) to deliver 100% of the RER ($[3.0]^{0.75}$ x 70 = 160 kcal/day [670 kJ/day]). The peripheral catheter infusion rate of the NaCl solution was reduced to 9 ml/kg body weight/day to accommodate the central PN infusion and meet the cat's daily maintenance fluid requirement.

Table 1. Central parenteral TNA for one day.*

Nutrients/fluids	Quantities (ml)
50% dextrose	38
20% lipid emulsion	48
8.5% amino acids (without electrolytes)	113
Potassium phosphate (4.4 mEq K, 3 mM P/ml)	1.4
Potassium chloride (2 mEq/ml)	1.4
Vitamin-B complex**	1
Trace elements***	0.1

*RER ($[3.0]^{0.75}$ x 70) = 160 kcal ME/day (670 kJ/day). Calories from lipid = 60%. Calories from dextrose = 40%. Protein-calorie ratio = 6 g/100 kcal. [K] = 29.7 mEq/l. [P] = 11.8 mM/l. Osmolarity = 1,188 mOsm/l.
**B-vitamin complex contains 50 mg thiamin, 2 mg riboflavin, 100 mg niacin, 2 mg pyridoxine, 10 mg pantothenic acid and 0.4 µg B_{12} per ml. Butler Co., Columbus, OH, USA.
***MTE-4 contains 1.7 mg zinc, 0.42 mg copper, 0.37 mg manganese and 6 µg chromium per ml. Abbott Laboratories, Chicago, IL, USA.

Questions

1. Which other feeding routes might have been considered to support this patient and why were they rejected in favor of centrally administered PN?
2. Were any micronutrients absent from the PN formulation that might be important for erythropoiesis?
3. What types of metabolic complications should be anticipated in a critically ill patient receiving PN?

Answers and Discussion

1. A number of enteral feeding routes and PN infusion via peripheral venous access were considered for this patient. The nasoesophageal route was rejected for several reasons. The most obvious reason was the condition of the patient's nares, which were partially obstructed due to necrosis. Also, there was the concern of provoking epistaxis in a thrombocytopenic and severely anemic patient as the tube was advanced through the nose. Finally, there was the issue of blocking the nares in an animal already experiencing difficulty breathing through its nose. All other routes of enteral feeding (i.e., esophagostomy, pharyngostomy, gastrostomy and enterostomy) require heavy sedation or general anesthesia with varying degrees of surgical intervention. The cat's compromised pulmonary function and thrombocytopenia were considered contraindications for these procedures. (There was a missed opportunity later on in this

Figure 1. A 10-year-old, domestic shorthair cat with cold agglutinin disease on Day 19 of hospitalization.

case to place a less invasive type of enteral feeding tube [e.g., an esophagostomy tube]. On Day 10 of hospitalization the cat was anesthetized for a bronchioalveolar lavage and a bone marrow aspirate). Central infusion of PN was selected instead of peripheral infusion because there was a concern of fluid overload, given the extent of alveolar disease in this patient. Therefore, a more concentrated, smaller volume admixture was conservatively infused via a central vein rather than peripherally.

2. Two micronutrients important for red blood cell production, and which are associated with anemia when deficient, were omitted from the PN admixture because of noncompatibility issues. The first was iron. Parenteral iron solutions are not approved for mixing with any vehicle including PN admixtures and are therefore commonly given separately by intramuscular or intravenous routes. However, the concern that this patient would become iron deficient was minor because the cat had received multiple red blood cell transfusions during the course of hospitalization.

    The other missing nutrient was folic acid. Folic acid is omitted from standard veterinary parenteral B-complex formulations because of noncompatibility and stability issues. Some human parenteral vitamin formulations contain folic acid; however, at the time this case presented, there was a severe shortage of these products and their use in a veterinary patient could not be justified. Although omission of folic acid from this cat's nutritional support was not optimal, the extent of folic acid deficiency may have been limited due to ongoing efforts to feed the cat per os throughout the time it received PN.

3. Common metabolic complications associated with PN include hyperglycemia, lipemia and electrolyte disturbances. Hyperglycemia and lipemia were not noted at any time during PN infusion in this patient, probably due in part to the conservative estimate of its caloric requirements and because the cat received only 40% of its nonprotein calories as dextrose. Serum potassium, sodium, chloride and ionized calcium levels were monitored daily. Serum phosphorus and magnesium levels were monitored two or three times per week.

Progress Notes

The patient continued to require oxygen therapy. The thrombocytopenia resolved, but the anemia persisted with a poor regenerative response. *Pasteurella multocida* was cultured from a tracheal wash but it was unknown whether this isolate was the cause of the alveolar disease or a contaminant. The patient's appetite was poor despite continued efforts to coax the cat to eat. The cyproheptadine was discontinued after four days. On Day 4 of PN, a low serum magnesium concentration was detected and corrected with an infusion of magnesium sulfate at a rate of 1 mg/kg body weight/day via the peripheral catheter. The serum magnesium level returned to normal within 24 hours and the magnesium sulfate infusion was discontinued. Mild hypokalemia also occurred and was corrected by increasing the admixture potassium concentration to 30 mEq/l. Low serum phosphorus levels were not detected in this patient.

On Day 7, the cat was still receiving most of its nutrition parenterally. Therefore, injections of fat-soluble vitamins were given (1,000 IU vitamin A, 100 IU vitamin D, 3 IU vitamin E intramuscularly and 7.5 mg vitamin K subcutaneously). On Day 10, the cat was anesthetized for bronchoscopy, an ultrasound-guided fine-needle lung aspirate and a bone marrow aspirate. There were no abnormalities found grossly at bronchoscopy and when the bone marrow aspirate was examined. Cultures of the bronchoalveolar lavage revealed different organisms from the tracheal wash; however, the pulmonary disease seemed to be improving. The decision was made to start immunosuppressive therapy (prednisolone acetate 1 mg/kg, subcutaneously, b.i.d.) because the cat's red blood cells were still agglutinating.

The patient started to improve, and by Day 13 no longer required oxygen therapy. The necrotic tissue on the cat's nose had begun to scab over. By Day 19 (**Figure 1**), the Coomb's test was negative at 4°C (39.2°F), the nares became clear of scabs and the cat's appetite returned. The patient started to eat a maintenance dry cat food (Science Diet Feline Maintenance[f]) voluntarily with an excellent appetite and consumed sufficient quantities of food to exceed its RER. On Day 20, central venous access was lost, but

because the cat was eating well, there was no concern about continuing PN. On Day 22, the necrotic portion of the cat's tail was removed using local ring-block anesthesia. The patient continued to improve and was discharged from the hospital on Day 25. At the time of discharge, the cat weighed 3.2 kg and had a hematocrit of 19%. The cat continued to do well at home. At two weeks after discharge it weighed 3.4 kg, was still thin (BCS 2/5) but no longer cachectic and had a hematocrit of 22% with a corrected reticulocyte count of 6.2%. One year later on a routine annual examination, the cat weighed 4.1 kg (BCS 3/5), had a normal PCV with no reticulocytes and was reportedly doing very well.

Endnotes

a. Albon. Pfizer Animal Health, Exton, PA, USA.
b. Ralston Purina Co., St. Louis, MO, USA.
c. Baytril. Bayer Animal Health, Shawnee, KS, USA.
d. Amoxi-Tabs. Pfizer Animal Health, Exton, PA, USA.
e. Periactin. Merck and Company, Inc., Rahway, NJ, USA.
f. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

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CASE 26-3

Combined Parenteral and Enteral Feeding in a Cat

Donna Raditic, DVM
MSPCA Angell Animal Medical Center
Boston, Massachusetts, USA

Patient Assessment

A five-year-old, neutered male, domestic shorthair cat was presented for anorexia and weight loss. The patient lived in a large multiple-cat household and had been missing for one week. The owners found the cat and thought it had lost weight, but couldn't coax the cat to eat. On physical examination, the cat was lethargic, dehydrated with a body weight of 4.5 kg and a body condition score of 2/5. The cat had excessive skin folds, which supported the owner's report of recent weight loss. The cat was icteric with palpable liver enlargement. All cats in the household were fed a dry grocery brand cat food fed free choice.

Results of a complete blood count included a regenerative anemia; *Bartonella* was detected on a blood smear. The patient also had elevated liver enzyme activities, increased blood urea nitrogen values and hypoalbuminemia. Serum electrolytes were within normal limits.

The patient was stabilized with an intravenous bolus of crystalloid solution followed by appropriate fluid management, antibiotics and antiemetics. Although therapy stabilized the cat's laboratory values, the patient continued to vomit bilious fluid throughout the day and evening. Plans included radiography, ultrasonography and liver biopsy.

Abdominal ultrasonography showed hepatic enlargement. An ultrasound-guided liver biopsy was performed. Histopathology revealed neutrophilic and lipid infiltrates. A diagnosis of hepatic lipidosis with *Bartonella* infection was made.

Because the patient's vomiting was unresponsive to antiemetics, a parenteral solution of Aminosyn II (a parenteral nutrition [PN] admixture containing 3.5% amino acids and 5% dextrose solution) was started. The PN was given at a rate of 20 ml per hour and supplied 144 kcal/day. The patient became more alert and seemed to be responding positively to PN feeding.

Two days later the cat was sedated for placement of an esophagotomy tube for possible home care. Feeding instructions were given early afternoon, to start a continuous rate infusion of a monomeric solution[a] that contained 1.3 kcal/ml. This solution was given at a rate of 5 ml/hour, providing the cat with 156 kcal/day (653 kJ/day). PN and supportive care were continued. The next day the cat was unresponsive, febrile, more anemic and had increased liver enzyme activities. An electrolyte panel was performed (**Table 1**).

Questions

1. What is this cat's resting energy requirement (RER)?
2. How many kcal did the combination of PN and enteral feedings provide?
3. How should the serum electrolyte abnormalities, seen after 24 hours of enteral feedings, be interpreted?
4. How should these electrolyte imbalances be addressed given the patient's deterioration?

Answers and Discussion

1. RER is calculated as 70(weight in kg)$^{0.75}$. This cat's RER was 216 kcal/day. PN and/or enteral feeding should begin at the patient's RER. No "illness factors" should be used to avoid possible complications.
2. The PN supplied 144 kcal/day and the enteral feedings added 156 kcal/day. Therefore, the patient was receiving 300 kcal/day or 1.4 times above its RER.
3. Potassium decreased to 2.7 mg/dl (normal = 3.5 to 5.2) and phosphorus decreased to 1.2 mg/dl (normal = 2.6 to 8.3), whereas sodium, chloride and magnesium remained normal.

   This cat's hypophosphatemia and hypokalemia are classic signs of refeeding syndrome. These electrolyte changes occur most commonly when a patient is force fed an amount that is greater than is needed (i.e., above RER). Initially the cat was fed below RER with PN alone, and then total caloric intake increased above RER with the addition of enteral feedings. All patients fed with PN, enteral nutrition or both should initially be fed at RER. Glycogen stores are first rapidly depleted in cats with anorexia. With ongoing anorexia, fat mobilization and skeletal muscle degradation provide energy and support blood glucose.

   When refeeding, potassium and phosphorus move into intracellular spaces as normal cellular function (gluconeogenesis and ATP production) returns. Providing calories in excess of whole body potassium and phosphorous stores drives these electrolytes into intracellular spaces creating a deficient in the vascular space. Hypophosphatemia is the most serious electrolyte imbalance because it can result in hemolytic anemia and even death.
4. The patient's PN was discontinued and an intravenous crystalloid solution supplemented with potassium and phosphorous was started to replete body stores and normal serum levels. Enteral nutrition was continued at 25% of RER for two days simultaneously to maintain intestinal integrity until serum electrolyte levels returned to normal. Intestinal absorption of potassium and phosphorus should not cause electrolyte imbalances at a flow rate below RER. **Table 2** depicts the electrolyte panel 24 hours after feeding adjustments were made.

Progress Notes

Phosphorus was delivered by intravenous administration for another 24 hours to correct deficits. The patient continued to eat well in the hospital and was discharged three days later.

Endnote

a. Perative. Abbott Laboratories, Abbott Park, IL, USA.

Table 1. Electrolyte values after presentation.

Electrolyte	Value	Reference range
Sodium (mEq/l)	147	146-158
Potassium (mEq/l)	2.7	3.5-5.2
Phosphorus (mg/dl)	1.2	2.6-8.3
Chloride (mEq/l)	125	114-126
Magnesium (mEq/l)	2.1	1.9-2.28

Table 2. Electrolyte values after feeding adjustments were made.

Electrolyte	Value	Reference range
Sodium (mEq/l)	148	146-158
Potassium (mEq/l)	3.1	3.5-5.2
Phosphorus (mg/dl)	2.4	2.6-8.3
Chloride (mEq/l)	122	114-126
Magnesium (mEq/l)	2.3	1.9-2.28