A common problem in veterinary medicine is maintenance of the nutrient and caloric requirements of patients that are malnourished, anorectic, or otherwise unable to use enteral nutrition. Although the goal is to discover and resolve the underlying condition, allowing the patient to go without food until the condition is resolved may contribute to morbidity and prolong therapy. In most if not all cases, providing nutrition is believed to be beneficial to patients and, based on human study findings, may improve clinical outcome, shorten hospital stay, and reduce the cost of care.¹

Parenteral nutrition (PN) is one potential modality of providing nutrition to animals for which enteral feeding is not indicated. PN typically involves intravenous administration of nutritional products² and has been used successfully in human medicine since 1966.³ Although the first published veterinary study demonstrating the provision of complete intravenous nutrition to dogs was in 1977,⁴ PN has become progressively more widely used in animals since the 1990s. PN is classified as either total parenteral nutrition (TPN) or peripheral (partial) parenteral nutrition (PPN).

**TOTAL PARENTERAL NUTRITION**

In human medicine, the strict definition of TPN refers to intravenous provision of the total nutrient needs of the patient. As practiced in veterinary medicine, TPN may not supply all nutrient needs because the specific requirements of critically ill dogs and cats have not been as thoroughly investigated as they have in humans. Thus it is controversial whether veterinary TPN formulations are appropriately supplemented

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¹A companion article on parenteral nutrition formulations, monitoring, and complications begins on p. 88.
²Dr. Thomovsky is conducting research funded by the Waltham Foundation.
³Dr. Reniker is now affiliated with First Regional Animal Hospital, Chandler, Arizona.
with the vitamins, macrominerals, and trace elements required for long-term nutritional maintenance. However, veterinary TPN typically does attempt to supply all the energy and protein needs of patients. Veterinary TPN has classically been administered through a central vein because of the high osmolarity of TPN solutions.

**PERIPHERAL VERSUS PARTIAL PARENTERAL NUTRITION**

The abbreviation PPN refers to either partial or peripheral PN. PPN solutions are less hyperosmolar than TPN solutions and, therefore, are safely administered into peripheral veins. PPN can be formulated to provide all daily energy, protein, vitamin, and mineral requirements; these solutions are referred to as *peripheral PN solutions* because they are supplied through a peripheral vein. However, in many cases, the volume of PPN required per day to meet the full energy needs of patients is excessive because PPN has a greatly reduced osmolarity versus that of TPN. Thus veterinary PPN is not commonly formulated to fully supply either the daily energy and protein requirements or vitamin and mineral requirements but rather seeks to provide a portion of the total energy requirements (i.e., commonly 50% of total daily energy requirements). Therefore, these solutions provide *partial PN*5,6 (Table 1).

### Table 1. A Comparison of Veterinary Total and Partial Parenteral Nutrition

<table>
<thead>
<tr>
<th>Total Parenteral Nutrition</th>
<th>Partial Parenteral Nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Marked hypertonicity (850–2,000 mOsm/L)</td>
<td>• Mild hypertonicity (500–600 mOsm/L)</td>
</tr>
<tr>
<td>• Supplies total patient energy needs</td>
<td>• Does not usually supply all patient energy needs</td>
</tr>
<tr>
<td>• Central venous administration required</td>
<td>• Peripheral venous administration possible</td>
</tr>
<tr>
<td>• May be deficient in total vitamin and mineral needs, depending on the formulation</td>
<td>• Typically deficient in vitamin and mineral needs</td>
</tr>
</tbody>
</table>

**FEEDING PATIENTS**

**Metabolic Changes When Food Intake Is Decreased**

Patients requiring nutritional support are experiencing either uncomplicated or stressed starvation.5,7 Uncomplicated starvation results when an animal is deprived of food sources but is not injured or ill. To decrease the nutrient needs of starving animals, their metabolic rates slow down, resulting in less protein use by the body and down-regulation of the release of catecholamines and other stress hormones.5 These animals have decreased insulin secretion and rely on gluconeogenesis and hepatic glycogenolysis to supply glucose to their tissues. Fatty acids are broken down to provide ketone bodies for skeletal muscle energy as well as gluconeogenesis, and body proteins are broken down to amino acids that in turn are used for gluconeogenesis. In cases of short-term uncomplicated starvation, providing food reverses the metabolic changes, allowing patients to shift back to a normal metabolic rate and begin to preferentially use carbohydrates for energy. In cases of prolonged uncomplicated starvation, reintroduction of food requires close patient monitoring. A possible side effect is a syndrome of hypophosphatemia, hypokalemia, and hypomagnesemia induced by the introduction of food. This “refeeding syndrome” is thoroughly discussed in the companion article beginning on p. 88.

Stressed starvation occurs when ill or injured animals do not have adequate food intake.5,6 Many of these patients have elevated resting metabolic rates and an increase in protein catabolism proportional to the extent of disease.5 The production of catecholamines and other stress hormones is up-regulated, leading to increased cardiac output and systemic vascular resistance, insulin resistance, proliferation of inflammatory mediators, and rapid onset of malnutrition.5

Feeding patients with stressed starvation is challenging for multiple reasons.5,7 These animals have relative insulin resistance and do not use exogenous carbohydrate sources as efficiently as normal animals. It is also important to provide affected patients with sources of amino acids to help reverse protein catabolism. Moreover, it is difficult to determine the actual energy requirements for these animals because they may have increased resting metabolic rates associated with stress and disease. However, it is equally difficult to determine the exact degree of increase of the metabolic rate. In addition, as discussed more thoroughly later in this article, the underlying reason for a patient’s stressed state...
can be important in determining how the patient will respond to supplemental nutrition.

**Enteral Versus Parenteral Nutrition**

When clinicians are deciding whether to provide nutritional support to a patient, enteral nutritional support (i.e., orally or through feeding tubes placed directly in the gastrointestinal [GI] tract) is preferable to PN when enteral feeding is tolerable and not contraindicated. Enteral nutrition (EN) is more physiologic than PN and reduces GI tract atrophy that may otherwise develop from disuse. Histologic examination of liver and small intestine samples from normal cats before and after 2 weeks of complete nutritional support by TPN revealed swelling and vacuolization of hepatocytes and mild to moderate small intestinal villous atrophy. All changes were reversed 3 weeks after the animals resumed normal enteral feeding. There is also evidence of decreased muscular contraction of the gallbladder, stomach, and duodenum during TPN administration. In addition to contributing to gallbladder sludging, gut stasis may lead to bacterial overgrowth and predispose patients to bacterial translocation and sepsis.

Because PN administration is not without risk, it should be reserved for malnourished patients or patients unable to use the GI tract for prolonged periods. When patients are in good nutritional status before clinical presentation and interruption of feeding is anticipated to be brief, it is rational to delay the start of nutritional support for 3 to 5 days. It is important to take historical information into account when determining the need for nutritional support because many animals may have been anorectic or undernourished for 1 day or longer before admission to the veterinary hospital. On the other hand, if the patient was already undernourished before its current illness, immediate initiation of nutritional supplementation is important, regardless of the number of days of complete anorexia (see box on this page). For help in determining the best choice for a patient’s nutrient needs (i.e., PPN or TPN), specific indications for administering PPN and TPN are found in the box on p. 80.

** COMPONENTS OF PARENTERAL NUTRITION**

Veterinary PN solutions are primarily composed of carbohydrates, amino acids, electrolytes, and possibly a lipid substrate. Some formulations also include vitamins and minerals. The carbohydrate source used in most TPN formulations is 50% dextrose, which contributes to most of the osmolarity of the solution. PPN solutions contain a lesser concentration (i.e., typically 5%) of dextrose and thus have a greatly reduced osmolarity. Most PN solutions also contain synthetic amino acid formulations that may not contain electrolytes. The lipid component is supplied as a commercial lipid formulation made primarily of long-chain triglycerides derived from soybean and/or safflower sources.

**Carbohydrates**

A goal of using dextrose and lipid-based formulations is to provide nonprotein energy sources to patients. Dextrose is normally a readily usable energy source that can be transported from the bloodstream directly into the cells through the actions of insulin. Once in the cells, dextrose is readily converted into needed substrates and ATP by glycolytic oxidative metabolism.

However, in practice, there are limitations to dextrose use in PN. The proportion of dextrose in a PN admixture must be limited to prevent excessive osmolarity. High osmolarity may lead to thrombophlebitis, especially when solutions are administered through peripheral veins. Many animals with stressed starvation are insulin resistant and cannot completely use administered dextrose. In addition, malnourished patients commonly have protein malnutrition, which is not corrected by dextrose administration.

**Lipids**

Lipids are an efficient form of energy and a source of essential fatty acids that are often incorporated into PN formulations. Lipids are important for the production of certain hormones and for maintaining cell membranes. They also help to decrease the osmolarity of PN solutions. Some lipids are essential for proper function of the nervous system, liver, and kidneys.

**Guidelines for Initiating Nutritional Support**

- Acute weight loss of 5%, or chronic weight loss of 10% or more
- Anorexia or inappetence for 3 or more days, especially in patients already receiving intravenous fluids
- Indications of decreased protein intake, such as cachexia, poor body condition, overall weakness, and nonhealing wound

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9 As discussed in the text, it is appropriate to initiate nutritional support sooner than 3 days, especially if other physical examination or historical parameters indicate the need to do so.
Indications for Nutritional Support

**PPN**
- Short-term nutritional support in nondebilitated patients (no signs of malnutrition)
- Patients in which central venous catheterization is contraindicated or impossible
- A supplement to enteral feeding to provide complete nutrition

**TPN**
- Patients unable to enteraly absorb sufficient nutrients for more than 3–5 days, especially with apparent signs of malnutrition (e.g., massive small intestinal resections, chronic or intractable vomiting, severe diarrhea)
- Severe prolonged pancreatitis when enteral feeding tubes (especially jejunal tubes) are not an option
- Severe malnutrition with a nonfunctional GI tract
- Intolerance to enteral tube placement (including anemia required for feeding-tube placement) or force feeding

Lipid emulsions have several beneficial characteristics: they are isosmolar, provide energy through gluconeogenesis or ketone body production, and are the building blocks of cellular membranes. The addition of lipid substrates to the PN admixture reduces the volume of dextrose required to meet an animal’s energy requirements and thus reduces the solution’s osmolarity.

However, controversy exists regarding the inclusion of lipids in PN, especially PN administered to critically ill animals. Recent research suggests that concurrent administration of dextrose and lipids may result in inefficient lipid use when dextrose stimulates insulin release. However, research in healthy dogs indicates that despite an increase in insulin concentrations, PN solutions with lipids as the main source of energy do provide adequate energy. It is unknown whether these findings apply to patients with an altered metabolism during illness.

There is also concern that in conditions of widespread inflammation (i.e., sepsis), parenterally administered lipids may amplify the inflammatory response. Most commercial lipid preparations have a predominance of omega-6 fatty acids, including linoleic acid. Although linoleic acid is a nutritionally essential fatty acid, it is also a precursor of arachidonic acid in dogs, which in turn is a precursor of many proinflammatory mediators, such as thromboxanes, leukotrienes, and prostaglandins. The results of recent studies in species other than dogs and cats indicate that exogenous lipid administration could lead to deleterious effects in patients with medical conditions perpetuated by inflammation, such as sepsis.

One study has compared omega-6 fatty acids with omega-3 fatty acid preparations in humans with sepsis. The study demonstrated that omega-6 fatty acids (e.g., linoleic acid) up-regulated endotoxin-induced monocyte cytokine production during sepsis, worsening inflammation. Interestingly, patients who received omega-3 fatty acids showed suppression of proinflammatory cytokine production by monocytes, suggesting the possible value of lipid substrates rich in omega-3 fatty acids in the formulation of future PN solutions.

In addition, a retrospective human study showed that patients receiving parenteral lipids had decreased platelet-activating factor (PAF) acetylhydrolase versus patients who did not receive lipids parenterally. This enzyme normally inactivates PAF, which is another proinflammatory mediator that may be active in critically ill or stressed patients. Therefore, patients who receive parenteral lipid solutions may have an increased inflammatory response as a result of higher PAF activity. Despite this, lipids are still considered a useful component of PN, and further studies are needed to determine the clinical significance of these findings.

**Amino Acids**

Amino acids are added to PN solutions to slow muscle breakdown, help in the function of the immune system, play a role in wound healing, and aid in the function of many organs. Simply providing nonprotein energy in the form of glucose or lipids spares protein catabolism to an extent, but some form of protein or amino acid supplementation is also required. A study comparing nitrogen balance in healthy dogs administered electrolytes, dextrose-containing solutions, or amino acid-containing solutions demonstrated a negative nitrogen balance in all patients except those receiving amino acid supplementation.

**Other Components**

Electrolytes, vitamins, and trace minerals are added to PN solutions to provide nonenergy daily nutritional requirements. The Nutrition Advisory Group of the Department of Foods and Nutrition has published guidelines for vitamin, electrolyte, and trace element supplementation in humans receiving PN. Unfortunately, similar guidelines are unavailable to direct veterinary PN composition, making vitamin and mineral
supplementation of veterinary PN solutions variable. Components commonly added to veterinary PN solutions include B vitamins as well as vitamins D and A; these are often found as multivitamin supplements. Human formulations may also include iron, magnesium, or selenium, whereas veterinary PN mineral supplementation is less standardized.

Although long-term PN has been administered on an experimental basis to dogs, most clinical veterinary patients receive PN for only a short duration compared with humans. This minimizes the development of signs of mineral or vitamin deficiencies, which humans on long-term supplementation are more at risk of developing. Also, veterinary patients are typically placed on EN as soon as possible (usually within 7 days); EN is adequately supplemented with vitamins and minerals.

It is important that veterinary patients receive appropriate electrolyte supplementation while receiving PN. In some cases, amino acid solutions contain electrolytes such as sodium, chloride, magnesium, and potassium that typically supply the patient's needs. In other cases, amino acid solutions are not combined with electrolytes; in this situation, patients should receive electrolyte-containing fluids through a separate intravenous catheter or a different port on the central line. As discussed in the companion article beginning on p. 88, any patient receiving PN should have at least daily electrolyte panels conducted to ensure that the patient’s electrolyte needs have been appropriately supplied.

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Very few long-term studies investigating the clinical merits of parenteral nutrition administration exist in veterinary medicine; extrapolations from the human literature indicate that patients experience measurable improvement when administered parenteral nutrition.

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COMPOUNDING PARENTERAL NUTRITION SOLUTIONS

Asepsis is extremely important in the formulation and administration of PN solutions. Lipid-containing admixtures (e.g., dextrose, amino acids, lipids) are significantly more supportive of bacterial and fungal growth compared with dextrose or amino acid solutions alone. However, with the advent of sterile formulations of lipids and sterile technique used by pharmacists when compounding PN solutions, contamination can be minimized in today’s formulations. To ensure the safety of PN formulations, human and veterinary pharmacies must adhere to comprehensive guidelines regarding PN compounding and formulation.

Other concerns about the stability of PN formulations are minimized when PN is formulated by a pharmacist. The stability of the PN formulation depends on the techniques and order in which the components are added. The Maillard (browning) reaction refers to the negative interaction between amino acids (e.g., glycine) and carbohydrates. The brown color of the resulting solution is due to decomposition of carbohydrates. The pharmacist must separately prepare and combine amino acids and carbohydrates to avoid this reaction. Amino acid stability is also negatively affected by light; therefore, amino acid solutions must be carefully handled to avoid exposure to light during formulation of PN solutions. This includes keeping amino acid solutions covered both before and after they are added to the PN solution as well as when PN is administered to the patient. However, if properly prepared and stored, dextrose and amino acid solutions are stable for several months.

Precipitation of PN components can occur. The most commonly reported precipitation reaction is between calcium and phosphorus. Although calcium is not routinely used in veterinary PN solutions, calcium gluconate is used when needed because it is the least reactive formulation of calcium available. When calcium and phosphorus are needed, pharmacists add them separately in the compounding regimen to allow maximal dilution of the two nutrients in the PN solution, minimizing the chance of precipitation reactions. In veterinary medicine, the compositions of PN formulations vary widely and may not contain readily precipitant components, such as calcium and phosphorus.

A third compatibility issue is the stability of lipid particles. Over time, lipid particles begin to associate together, forming a layer at the surface of the admixture. This phenomenon is known as 'creaming' and can be
reversed by agitating the admixture. Creaming occurs almost immediately after the lipid-containing admixture is compounded. If particle association is unimpeded, lipid particles in the cream layer will begin to associate in aggregates (i.e., flocculation), eventually leading to coalescence of lipid particles into larger particles.

In human medicine, it is accepted that when lipid particles greater than 5 µm make up more than 0.4% of a PN solution, embolization of pulmonary capillaries can occur.\(^{2,25,27}\) The exact time point of flocculation and coalescence varies, depending on the temperature of the solution, the components of the solution, the hang time of the PN bag, and whether the bag has been agitated. However, it is believed that unacceptable levels of coalescence do not occur until the PN solution has been kept at room temperature for at least 24 hours.

Lipid particulate association is increased with decreasing pH and when admixtures contain more cations than anions.\(^{2,24–29}\) Increased cation concentration neutralizes the negative charge on lipid particles, decreases electrostatic repulsion between lipids, and increases the likelihood of coalescence. Appropriate formulation of PN solutions by a pharmacist is the best way to minimize the chance of these reactions.

PN should be compounded only in specialized bags. PN bags are composed of several layers of ethylene vinyl acetate and other components to make them poorly permeable to air. Air trapped in the bag during compound- ing or diffusion of air into the bag can result in air bubbles that oxidize PN components as well as trigger alarms in the intravenous pumps used to administer PN.\(^{25,28,30}\) Ethylene vinyl acetate is also less likely to bind to components of PN (e.g., vitamins and lipids), which helps to protect the components of PN from oxidation reactions.\(^{25,28}\) In addition, bags not made of ethylene vinyl acetate may release carcinogens into the PN solution.\(^{25}\)

### Obtaining and Administering Parenteral Nutrition

Veterinary PN can be compounded at most pharmacies that prepare human PN solutions because all components are the same. Some large veterinary referral institutions formulate and ship PN to private practices, as do commercial pharmacies. PN solutions can be formulated and stored for days or weeks at refrigerated temperatures (35.6°F to 46.4°F [2°C to 8°C]).\(^{2,23,25–28,31,32}\) However, once the PN formulation warms to room temperature, most institutions recommend changing PN bags daily as per FDA recommendations to avoid

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**Technical Guidelines for Administering Parenteral Nutrition**

- Place intravenous lines (central or peripheral) in aseptic fashion:
  - Clean and prepare skin as for surgery.
  - Wear sterile gloves when placing and handling intravenous catheter, intravenous line, PN bag, etc.
  - Maintain sterility of catheter, intravenous tubing, and PN bag.
- Cover all connections between intravenous catheter, intravenous lines, and PN bag with sterile dressing to prevent bacterial or fungal contamination.
- Do not disconnect the patient from the PN bag unless attaching a new bag; transport the patient at all times (including outdoors) with the intravenous lines and PN bag attached.
- Do not use the intravenous catheter through which PN is being administered for any other solution (e.g., no drugs or fluids should be administered through the PN tubing or intravenous ports).
- Minimize handling of the PN system.
contamination and lipid particle destabilization. There is some debate regarding the longest amount of time that a PN bag can be administered at room temperature, with some institutions administering a single bag of PN for 48 hours or more. However, there are little published data to support the safety of this deviation from FDA guidelines.

PN solutions in veterinary medicine have traditionally been administered continuously over 24 hours largely because of their use at referral institutions where 24-hour care is available. However, the calculated daily energy requirements can safely be administered over shorter periods of time without adverse effects. One investigation demonstrated complete daily nutrient infusion over 10 hours in healthy dogs. The shorter administration time improves convenience of administration when 24-hour monitoring is not readily available. A case study described the accidental administration of 1,800 ml of TPN solution within 2 hours to a German shepherd (the calculated rate for this patient was 50 ml/hr), resulting in transient hyperglycemia, hyperlipidemia, and osmotic diuresis, which were reversed with aggressive intravenous fluid therapy. Obviously, this infusion rate exceeds recommendations, but this case study demonstrates that TPN can be given without lasting negative effects at faster rates than those during a 24-hour continuous-rate infusion.

As already mentioned, veterinary TPN should be administered through a central vein because of the high osmolarity of the solution. TPN solutions are always hyperosmolar compared with plasma. Normal plasma osmolarity is approximately 300 mOsm/L, whereas that of TPN solutions is typically at least 850 mOsm/L and commonly 1,500 to 2,000 mOsm/L. Hyperosmolar solutions can directly damage the tunica intima of blood vessels. Also, erythrocytes and other cells can lyse when they are exposed to a hyperosmolar environment in the bloodstream. Therefore, TPN solutions must be administered through a central venous catheter (typically placed into or terminating in the jugular vein) to allow dilution to an isosmolar solution. This dilution occurs when TPN quickly mixes with a relatively large volume of blood in a central vein. Early studies in beagles proved the safety of administering hyperosmolar solutions through a central vein; hyperosmolar solutions up to 2,400 mOsm/L were diluted by the bloodstream to isotonicity within 1.5 to 2.5 cm from the point of infusion into the central vein.

Another significant issue in PN administration is catheter-related infection introduced by catheter placement or improper handling of intravenous tubing or ports. Human medicine adheres to strict guidelines to prevent
such complications, and most of these guidelines have been adapted to veterinary medicine\(^7\) (see box on p. 82). Figures 1 through 3 demonstrate the sterility and technique needed when handling and administering PN solutions.

Minimizing manipulation of and contact with the intravenous catheter, the administration set, and the PN bag itself, including routine line changes, can lower the risk for catheter-related infections. Human studies\(^9\) of 24- versus 72-hour PN line changes revealed a significant decrease in the incidence of nosocomial septicemia when changes were prolonged to 72 hours. The authors of the study speculated that decreased septicemia was due to the fact that most of the contamination was introduced through the open catheter hub during intravenous line changes. In the case of patients receiving PN through a central catheter, multilumen central catheters do not have an increased risk for infection versus single-lumen catheters as long as the lumen dedicated to PN is kept sterile as outlined in the box on p. 82 and is dedicated solely to PN.\(^{37,39,40}\)

**CONCLUSION**

PN is a viable nutritional choice for small animal patients that cannot receive nutrition enterally. It is possible to both obtain and administer PN in a private practice setting. PN formulations should be obtained from a pharmacy where appropriate protocols are followed to safely compound the solution. However, once the PN has been formulated, special equipment—other than an aseptically placed and maintained catheter dedicated specifically to PN—is not required for administration.

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

**REFERENCES**


4. EN is _____ PN.
   a. less physiologic than   c. as physiologic as
   b. more physiologic than   d. none of the above

5. Patients should begin receiving PN
   a. immediately if they were undernourished before their current illness.
   b. after 3 to 5 days of decreased or absent nutritional intake if they were appropriately nourished before their current illness.
   c. after more than 7 days of decreased or absent nutritional intake.
   d. all of the above

6. Which patient would be the best candidate for PN?
   a. a cat with hepatic lipidosis that has not been vomiting
   b. a patient after GI resection and anastomosis
   c. a patient with prolonged pancreatitis
   d. an anorectic patient that has undergone exploratory abdominal surgery for biopsies

7. Which component of parenteral solutions contributes the most to the osmolarity of the solution?
   a. dextrose   c. lipids
   b. amino acids   d. vitamin additives

8. Which is not a possible negative consequence of lipid administration?
   a. inhibition of lipolysis in the presence of insulin
   b. proinflammatory effects
   c. provision of energy via gluconeogenesis
   d. There are no negative consequences of lipid administration.

9. Which is(are) a possible sequela(e) of the formulation of PN?
   a. the Maillard reaction
   b. precipitation of calcium and phosphorus
   c. lipid particle coalescence
   d. all of the above

10. Which is an important procedure for PN administration?
    a. Clean and aseptically prepare the skin before intravenous catheterization.
    b. Change the intravenous lines every 12 hours.
    c. Disconnect the intravenous lines when the patient is removed from the cage.
    d. Mix all intravenous drugs in the PN solution before administration.