CHAPTER 11

Parenteral nutrition in small animals

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Introduction

The provision of nutrition to animals via the parenteral route is an important therapeutic modality for hospitalized animals that cannot tolerate enteral nutrition (EN). Although parenteral nutrition (PN) can be an effective means of providing animals with calories, protein and other nutrients, there are a number of possible complications associated with its use that requires careful patient selection, appropriate formulation, safe and effective administration practices, and close patient monitoring. In most cases hospitalized patients that do not consume adequate quantities of food voluntarily should be supported with EN as it is the safest, most convenient, most physiologically sound and least expensive method of nutritional support (see Chapter 3). While EN support is the preferred method of nutritional support in hospitalized patients, PN is the established method of providing nutritional support to patients whose gastrointestinal tracts cannot tolerate enteral feedings (Barton, 1994; Braunschweig et al., 2001; Biffl et al., 2002).

While the use of PN support has certainly increased in recent years, there is a perception that this technique is technically difficult, associated with many complications and limited to university hospitals and major referral centers. In reality, PN support can be adopted in many practices and complications can be significantly reduced with proper and meticulous care. The goals of this chapter are to outline the proper identification of patients most likely to benefit from PN, to review the process of formulating, implementing, and monitoring parenteral nutritional support, and discuss how PN can be incorporated into many practices.

Indications for PN support

Studies in people have shown that the use of PN in some patient populations actually increases the risk of complications and worsens outcome (Braunschweig et al., 2001; Gramlich et al., 2004; Simpson and Doig, 2005). Moreover, some

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studies have demonstrated worse morbidity (e.g., increased risk of infectious complications, greater dependence on mechanical ventilation) in intensive care unit (ICU) patients when PN was initiated within the first 48 hours of ICU admission compared with delayed initiation of PN until day 8 of ICU admission. (Casaer and et al., 2011). The increase in complications may be related to early initiation of PN in well-nourished ICU patients and, therefore, careful patient selection may be particularly important when considering implementing PN (Lee et al., 2014). However, there are conflicting reports on the subject regarding the impact of PN on ICU outcome. A recent large prospective controlled study found that early PN in critically ill patients with relative contraindications to early EN was not associated with any negative impact on survival and in fact identified decreased dependence on mechanical ventilation and better preservation of lean muscle mass (Doig et al., 2013). Furthermore, a new study compared initiation of EN or PN within 36 hours of ICU admission and found significant reductions in rates of hypoglycemia and vomiting in the PN group and no differences in the rates of infectious complications, 30- or 90-day mortality or rates of 14 other secondary endpoints (Harvey et al., 2014). In light of these conflicting findings, perhaps the sensible first step in considering patients for nutritional support is to perform a nutritional assessment (see Chapter 1). Following the nutritional assessment of the patient, the most appropriate route of nutritional support should be selected. The indications for PN support include situations in which malnourished animals cannot voluntarily or safely consume food (i.e., animals unable to protect their airways) or those that cannot tolerate EN despite attempts to improve tolerance to EN. Persistent hyporexia or anorexia is not sufficient justification for PN and should be considered an inappropriate use of PN. In patients that require nutritional support but have contraindications for placement of feeding tubes (e.g., coagulopathic, presence of cardiovascular or cardiopulmonary instability), short term (e.g., <3 days) administration of PN may be considered.

Parenteral nutrition

The terminology used to describe the use of PN in veterinary patients has evolved and so it is worth reviewing the current terminology. Total parenteral nutrition (TPN) was previously defined as the provision of all of the patient's protein, calorie and micronutrient requirements intravenously, whereas partial parenteral nutrition (PPN) was defined as the provision of only a part of this requirement (typically 40–70% of the energy requirement) (Chan and Freeman, 2012). More recently, there has been a shift away from describing PN in terms of 'meeting energy and nutrient requirements' as they remain largely unknown in animals and so recent recommendations emphasize categorizing PN by the mode of delivery such that PN delivered into a central vein is described as 'central PN' and PN delivered into a peripheral vein is described as 'peripheral PN. (Queau et al., 2011; Perea, 2012). For the purposes of this chapter, 'PPN' will refer to peripheral PN.

To enable safe administration of PN solutions using peripheral veins the osmolarity of the solutions is decreased because osmolarity is believed to be one

of the main contributing factors for the development of thrombophlebitis. A recent study in paediatric human patients found that PN solutions with osmolarity >1000 mOsm/L was associated with greater risk of phlebitis and infiltration of PN as compared with solutions <1000 mOsm/L when administered via a peripheral vein (Dugan, Le and Jew, 2014). Although similar studies in animals have not been reported, a recent veterinary study evaluated the administration of a PN product with an osmolarity of 1350 mOsm/L to dogs and the authors did not report high rates of phlebitis or infiltration of PN (Gajanayake, Wylie and Chan, 2013). Interestingly, the majority of dogs (66% of 70 dogs) received this high-osmolarity solution peripherally, with a single occurrence of thrombophlebitis and only two incidents of infiltration noted in this study. Nevertheless, some authors recommend that PN solutions administered peripherally should have osmolarities <950 mOsm/L. In order to achieve these lower osmolarities (e.g., <1000 mOsm/L), the concentrations of amino acids and dextrose are reduced and this also decreases the caloric density of these solutions. As such, because PPN only provides a portion of the patient's RER, it should be used for short-term nutritional support in non-debilitated patients with average nutritional requirements.

The administration of PN always requires a dedicated catheter that is newly placed using an aseptic technique (see Chapter 10). Once placed, this catheter should not be used for anything other than PN administration. The use of long catheters composed of silicone or polyurethane is recommended for use with PN to reduce the risk of thrombophlebitis. Multi-lumen catheters are often recommended for PN because they can remain in place for longer periods of time (as compared with normal jugular catheters) and provide other ports for blood sampling and administration of additional fluids and IV medications.

Components of parenteral nutrition

Amino acids

Most PN solutions are composed of amino acids, a carbohydrate source (dextrose or glycerol) and lipids. Amino acid solutions vary from 3–10% concentrations. The most commonly cited concentration of amino acids used in veterinary patients is 8.5%, with an energy density of 0.34 kcal/ml and osmolarity of approximately 880 mOsm/L. Amino acid solutions are typically available with and without added electrolytes. The amino acid profile of these solutions is intended to meet the essential amino acid requirements in people. Currently, there are no amino acid solutions made specifically for dogs or cats and, therefore, these solutions do not meet all amino acid requirements in these species. However, when used for short-term nutritional support, their use is unlikely to result in clinically relevant deficiencies. The minimal protein requirement of healthy dogs supported via parenteral nutrition has been estimated to be 3 g/100 kcal (Mauldin et al., 2001). While the protein requirement of ill veterinary patients has not been extensively investigated, in order to support hospitalized animals with PN the standard recommendations for protein provision are 4–6 g/100 kcal (15–25% of total energy requirements) for dogs and 6–8 g/100 kcal

(25–35%) for cats (Michel and Eirmann, 2014; Chan and Freeman, 2012; Chan, 2012). The presumed increase in protein requirements in ill animals relates to inadequate food intake that accompanies many diseases, increased protein losses and altered metabolic and inflammatory pathways (Michel, King and Ostro, 1997; Chan, 2004).

Given the risk of protein malnutrition in hospitalized animals, the goal of PN support should be to provide sufficient amino acids to minimize muscle protein breakdown and maintain lean body mass. Whereas healthy animals that are deprived of food can adapt to conserve muscle mass and use stored fat for energy (simple starvation), critically ill animals that are malnourished may have accelerated muscle catabolism (stressed starvation) for generation of amino acids used for gluconeogenesis and synthesis of acute phase proteins. (Biolo et al., 1997; Chan, 2004). However, not all animals require increased protein during nutritional support; animals with protein intolerance (e.g., patients with hepatic encephalopathy, severe kidney failure) should be supported with reduced levels of protein (e.g., 3 g protein/100 kcal)

Carbohydrates

For provision of carbohydrate calories, dextrose solutions ranging from 5 to 50% are typically used for PN solutions. In CPN, 50% dextrose is the most commonly used concentration of dextrose, with an osmolarity of 2523 mOsm/L and providing 1.7 kcal/ml. For PPN the typical dextrose solution used is 5% dextrose, which corresponds to 0.17 kcal/ml and an osmolarity of 250 mOsm/L. The proportion of calories provided with carbohydrates depends on the patient's individual circumstances (e.g., protein, carbohydrate, lipid intolerance) but is typically half of the non-protein calories. The ratio of calories provided by carbohydrate and lipid can be adjusted as dictated by the patient's needs. As dextrose infusion rates exceeding 4 mg/kg/min have been associated with the development of hyperglycemia in non-diabetic human patients, the authors recommend limiting the amount of dextrose provided in PN to this amount (Rosmarin, Wardlaw and Mirtallo, 1996) When formulating PN for diabetic patients, a greater proportion of calories should be provided from amino acids and lipids. In some patients, insulin therapy may be necessary to control the degree of hyperglycemia.

Lipids

Lipid emulsions are used in PN to provide energy and essential fatty acids. The most commonly used lipid emulsion is a 20% solution, providing 2 kcal/ml with an osmolarity of 260 mOsm/L. Commercial lipid emulsions in the United States are usually based on soybean or safflower oil. They also include egg yolk phospholipids, glycerin and water. As the principal type of lipid used for PN is composed primarily of n-6 fatty acids, there are concerns on its affect on the inflammatory response. *In vivo* studies in people have shown an exaggerated inflammatory response to endotoxin following a long-chain triglyceride infusion (Krogh-Madsen et al., 2008). There have also been concerns raised with regards to possible effects of n-6 fatty acids on immune function, oxidative stress and negative hemodynamic effects, as well as an

increased risk for hyperlipidemia, lipid embolization and microbial contamination (Grimes and Abel, 1979; Wiernik, Jarstrand and Julander, 1983; Mirtallo et al., 2004; Kang and Yang, 2008; Calder et al., 2010; Kuwahara et al., 2010). In order to reduce these effects, different lipid emulsions containing n-3 fatty acids, n-9 fatty acids, medium-chain triglycerides or structured lipids have been developed but are not currently available in the United States (Wanten and Calder, 2007; Sala-Vila, Barbosa and Calder, 2007). Until these different types of lipids are evaluated in dogs and cats and demonstrated to have clinical benefits, the authors recommend limiting the typical n-6-based lipid emulsion dosage in dogs and cats to 2 g/kg/day (30–40% of total calories provided) to decrease the risk of lipemia and possible immunosuppression. Animals with pre-existing lipemia may also require lower doses of lipid or PN formulations without lipids. A recent study evaluated the use of a lipid-free PN formulation in dogs, and so this may be an option for some animals (Gajanayake and others 2013.

Electrolytes and trace minerals

Parenteral nutrition can be formulated with or without electrolytes depending on patient needs. The most commonly adjusted electrolyte in PN solution is potassium and most formulations contain 20 to 30 mmol/L (20 to 30 mEq/L) potassium. Potassium chloride and potassium phosphate can be used to adjust potassium content. In patients requiring additional phosphorus (e.g., patient with hypophosphatemia), the authors recommend supplementing phosphate as a separate infusion as requirements may change frequently and there may be an increased risk of mineral precipitation with addition of minerals to PN solutions. Adjusting electrolytes separately allows greater flexibility.

Trace minerals are sometimes added to PN solutions but the majority of veterinary patients receive PN without the addition of trace minerals. In patients that require prolonged PN support (e.g., >10 days) or are severely malnourished, the addition of zinc, copper, manganese and chromium may be considered. The authors have used a commercial trace element preparation[1] containing (per 5 mL) 4 mg zinc, 1 mg copper, 0.8 mg manganese and 10 µg chromium at a dosage of 0.2 to 0.3 ml/100 kcal of solution.

Vitamins

As many hospitalized animals requiring PN may already have a degree of malnutrition, supplementation of PN with B vitamins may be of benefit. As some B vitamins are light sensitive (e.g., riboflavin) it may be best to add B vitamins immediately before administration and dose it so that the dose is administered within the first 6 hours of infusion. Commercial vitamin B formulations[2] containing thiamine, niacin, pyridoxine, panthothenic acid, riboflavin and cyanocobalamin may be sufficient in most cases. The dosages that have been recommended for these B vitamins in PN formulation (per 1000 kcal of PN solution) include: 0.29 mg thiamine, 0.63 mg riboflavin, 3.3 mg niacin, 2.9 mg pantothenic acid, 0.29 mg pyridoxine and 6 µg cyanocobalamin (Perea, 2012).

Formulation of parenteral nutrition solutions

Using parenteral nutrient admixtures that include amino acids, dextrose and lipids in a single bag is preferred over single nutrient solutions. The authors use the calculations in Box 11.1 to formulate PN. The first step is to determine the animal's calorie requirements. As discussed in Chapter 2, a sensible starting point in estimating energy requirements of most hospitalized animals is to calculate the resting energy requirement (RER). The authors do not apply illness energy factors in determining the target calories to be administered due to concerns over overfeeding and its associated complications. It is worth noting that

Box 11.1 Worksheet for calculating parenteral nutrition using commonly available components.

1 Resting energy requirement (RER)

$70 \times (\text{current body weight in kg})^{0.75}$ = kcal/day or for animals 3–25 kg, can also use:
[30 × (current body weight in kg)] + 70 = kcal/day
RER = _____kcal/day. This caloric target can be adjusted down (e.g., 70% RER) if necessary.

2 Protein requirements

	Canine (g/100 kcal)	Feline (g/100 kcal)
Standard	4–5	6
Decreased requirements (hepatic/renal failure)	2–3	4–5
Increased requirements (protein-losing conditions)	5–6	6–8

(RER ÷ 100) × _____g/100 kcal = _____g protein required/day (protein required)

3 Volumes of nutrient solutions required each day

a. 8.5% amino acid solution = 0.085 g protein/mL
_____g protein required/day ÷ 0.085 g/mL = _____mL of amino acids/day

b. Nonprotein calories:
The calories supplied by protein (4 kcal/g) are subtracted from the RER to get total nonprotein calories needed:
_____g protein required/day × 4 kcal/g = _____kcal provided by protein
RER – kcal provided by protein = _____nonprotein kcal needed/day

c. Nonprotein calories are usually provided as a 50:50 mixture of lipid and dextrose. However, if the patient has a preexisting condition (e.g., diabetes, hypertriglyceridemia), this ratio may need to be adjusted:
*20% lipid solution = 2 kcal/mL
To supply 50% of nonprotein kcal:
_____lipid kcal required ÷ 2 kcal/mL = _____mL of lipid
*50% dextrose solution = 1.7 kcal/mL
To supply 50% of nonprotein kcal:
_____dextrose kcal required ÷ 1.7 kcal/mL = _____mL dextrose

4 Total daily requirements

_____mL 8.5% amino acid solution
_____mL 20% lipid solution
_____mL 50% dextrose solution
_____mL total volume of PN solution

the method of calculating the distribution of energy from carbohydrate, amino acids and lipids used in this chapter includes the contribution of energy provided by the amino acid solution. Some authors meet the target energy requirement with only the carbohydrate and lipid component, arguing that this results in a "protein sparring effect," whereby the amino acids are solely used for protein synthesis when all the energy needs are met by the other components. However, this strategy risks overfeeding so the authors and the calculations used in the worksheet do account for the calories provided by the amino acids (i.e., protein calories). As a final check, the estimated osmolarity of the final solution can be determined by the following formula: final osmolarity = [(mL of amino acids × osmolarity of solution) + (mL of dextrose × osmolarity of solution) + (mL of dextrose x osmolarity of solution) + (mL of additional fluids × osmolarity of solution)]/ total volume of parenteral admixture.

Compounding

To compound the PN admixtures aseptic conditions are required. Ideally, only individuals with the expertise and facilities who can ensure accurate and sterile preparation should compound PN solutions. This usually entails the use of automated compounders (Figure 11.1) within sterile environments (Figure 11.2). However, these compounders are not widely available, are expensive and usually

Figure 11.1 An automated parenteral nutrition compounder can facilitate accurate and safe compounding of admixtures.

Figure 11.2 In situations where manual parenteral nutrition compounding is required, sterile environments such as a positive air-pressure hood is required.

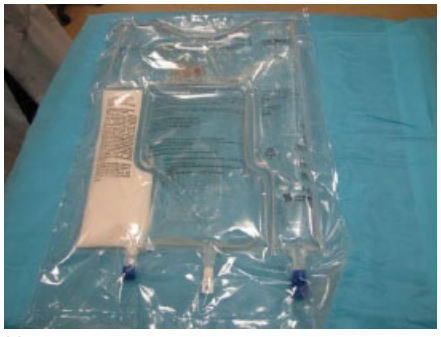
are not cost-effective unless PN is used frequently. For this reason, it may be preferable for veterinary practices that infrequently use PN to obtain solutions from hospitals or home-care companies that can compound PN to the required specifications for the patient. If this is not feasible, a less ideal option is to manually compound solutions using a "3-in-1" bag system. These bags have three attached leads that can be connected using an aseptic technique to bags of dextrose, amino acids and lipids, respectively. The components then are added to the recipient bag in a closed system by gravity. To make this system more accurate, the recipient bag should be weighed to ensure that an accurate amount of each solution is added, especially in very small animals. Many hospitals that do not use PN frequently do not find this method to be time- or cost-effective. The sequence for mixing the PN admixture should be to mix the amino acid solution with the dextrose solution, followed by any crystalloid fluid if required and finally, the lipid emulsion. If any other additive is required e.g., potassium, trace mineral, this is done last. The reason for this sequence is that lipids may destabilize if mixed with the amino acid solution.

Alternatives to compounding parenteral nutrition admixtures

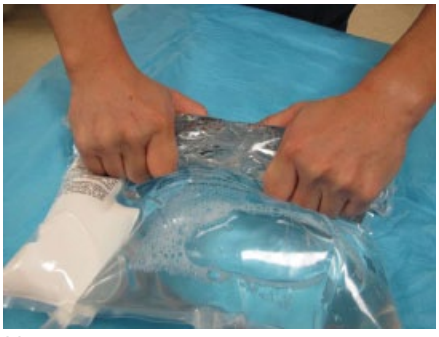
In practices that do not have compounding capabilities or access to facilties that can provide PN, there are a number of combination products commercially available that could be used in practice. Some products have multi-chambered sealed bags that keep the components (e.g., amino acids, dextrose, lipids) separate until the seals are broken by squeezing the bag and mixing the contents. (Figure 11.3a–c). There are also products that have premixed amino acids and a carbohydrate source. The advantages of these commercial combination products are their availability and the fact that they require no special compounding. There are several different formulations of the dextrose/amino acid solutions. Box 11.2 provides calculations for the use of a commonly used product (ProcalAmine)[3] available in the United States. There are two retrospective studies reporting the use of these combination products and findings are not dissimilar to studies reporting the use of partial PN (Gajanayake et al., 2013; Olan and Prittie, 2015). The major disadvantage of these products is that they do not allow the proportions of different components to be adjusted to suit the needs of the patient. The use of these ready-made products is a compromise that enables some form of nutritional support for patients requiring PN in practices that cannot provide individualized PN formulation.

Administering parenteral nutrition

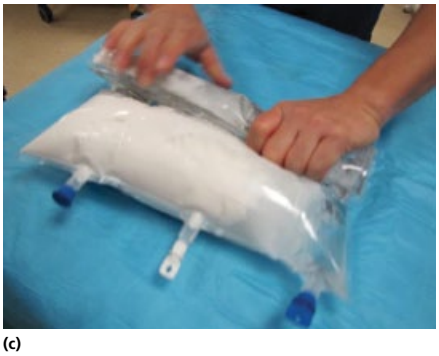
The procedure described for formulation of PN in this chapter yields an admixture that is intended to last 24 hours when administered as a constant-rate infusion. Current recommendations are that bags of PN admixtures should not be at room temperature for more than 24 hours. The bag should be administered



(a)



(b)



(c)

Figure 11.3 **a**) Commercially available 3-in-1 parenteral nutrition products are available which allow fixed-formulation admixtures to be used in facilities unable to compound parenteral nutrition. Components (dextrose, amino acids, lipids) are held in separate compartments until solution is prepared for administration. **b**) For mixing the various components, the bag is rolled from the top and the pressure opens the internal seals, first between the dextrose and amino acids and then the lipid compartment. **c**) After all the internal seals are opened, the bag is gently inverted to ensure complete mixing. The bag is now ready for set up and administration.

during the 24-hour period via a fluid infusion pump (Figure 11.4). During this time, the lines should not be disconnected from the bag or the patient (i.e., it should remain a closed system). At the end of each 24-hour period, the infusion should be complete, and the empty bag, along with the lines, can be changed using an aseptic technique and a new bag and lines substituted (Figure 11.5). Some studies have reported the use of PN administered for only part of the day (i.e., 10–12 hour infusions), which is termed "cyclic PN" (Zentek et al., 2003; Chandler and Payne-Jones, 2006). Although this may be appealing for practices without 24 hour care, this increases the risk of cathether contamination and is not recommended by the authors. All PN should be administered through a 1.2-μm in-line filter. The filter can help to prevent lipid globules or precipitates (particularly calcium phosphate) from being introduced to the patient.

Parenteral nutrition should be instituted gradually over 48 to 72 hours. Most animals tolerate receiving 50% of total requirements on the first day and 100%

Box 11.2 Worksheet for calculating parenteral nutrition using ProcalAmine®

1 Calculate resting energy requirement (RER):

RER = 70 × (current body weight in kg)$^{0.75}$
or for animals weighing between 2 and 30 kg:
RER = (30 × current body weight in kg) + 70
RER = _____kcal/day

2 Calculate protein requirement:

	Canine (g/100 kcal)	Feline (g/100 kcal)
*Standard	4	6
*Reduced (hepatic/renal disease)	2–3	3–4
*Increased (excessive protein losses)	6	7–8

(RER÷100) × _____ g/100 kcal protein requirement = _____ g protein required/day

3 Calculate rate of administration for *ProcalAmine*®:

ProcalAmine® is a 3 % amino acid solution thus it has 0.03 g protein /mL
Rate of administration required = _____ g of protein/day ÷ 0.03 g prot /mL ÷ 24 h
= _____ mL/h of ProcalAmine®

Make sure this rate of infusion is acceptable for this patient.

4 Calculate proportion of RER provided at this rate:

ProcalAmine® has 0.25 kcal/mL of energy
Energy provided = 0.25 kcal/mL × _____ mL/h × 24 h = _____ kcal/d
Proportion of energy met = _____ PPN energy ÷ _____ RER x 100 = _____ %

5 Calculate rate of glucose infusion at calculated PPN rate:

ProcalAmine® has 3% glycerol (dextrose equivalent) i.e. 30 mg/ml
Glucose infusion rate = _____ ml/hr PPN ÷ 60 mins × 30 mg/ml ÷ kg body weight.
= _____ mg/kg/min glucose.

Glucose infusion rate should not exceed 4 mg/kg/min as it may cause hyperglycemia. May need to decrease infusion rate and recalculate.

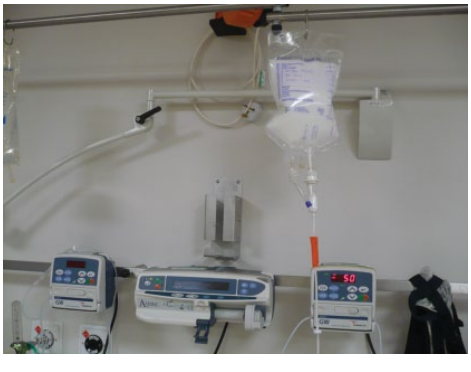


Figure 11.4 It is recommended that parenteral nutrition admixtures should be administered continuously over 24 hours with automated fluid infusion pumps and that the system remain closed until infusion is complete.

on the second day. Animals that have been without food for long periods may require slower introduction (i.e., 33% on the first day, 66% on the second day, and 100% on the third day). It is important to adjust the animal's other intravenous fluids when initiating PN support to avoid fluid volume overload.

Figure 11.5 Set up of parenteral nutrition requires strict adherence to an aseptic technique which includes use of disposable protective clothing, sterile gloves and new infusion sets.

Monitoring

The other critical aspect in reducing the risk of complications is vigilant monitoring. Checking the catheter site daily can identify malpositioning of the catheter and phlebitis or cellulitis early, before serious problems develop. Body weight should be monitored daily in animals receiving PN. Fluid shifts can also explain rapid changes in weight during hospitalization, emphasizing the need for continued nutritional assessment. Use of the RER as the patient's caloric requirement is merely a starting point. The number of calories provided may need to be increased to prevent weight loss or to keep up with the patient's changing needs. To avoid complications with PN, the patient should be monitored carefully and frequently. General attitude, body weight, temperature, blood glucose concentration, total plasma protein (also checking the serum for presence of gross lipemia or hemolysis) and serum electrolyte concentrations should be assessed daily, or more frequently if indicated. Pulse and respiratory rates should be recorded several times a day. Metabolic complications can occur frequently in animals receiving PN and monitoring is crucial to detect and address them early, if necessary. The clinical situation should dictate the frequency and spectrum of monitoring required because some patients will need more intensive monitoring. The development of metabolic abnormalities usually does not require discontinuation of PN but may require reformulation (e.g., a reduction in the lipid content for animals that develop hypertriglyceridemia). Other parameters to monitor include gastrointestinal signs and appetite so that enteral nutrition or oral intake can be initiated as soon as possible. Finally, the overall nutritional plan should be reassessed on a regular basis so that it can be adjusted to meet the animal's changing needs.

Complications

Metabolic complications

A number of possible complications can be associated with PN and these generally are grouped into one of three categories. Metabolic complications are the most common, with hyperglycemia typically seen most frequently (Lippert,

Fulton and Parr, 1993; Reuter et al., 1998: Chan et al., 2002; Pyle et al., 2004; Crabb et al., 2006; Queau et al., 2011). Despite being the most commonly encountered complication, hyperglycemia was only associated with a poorer survival in cats in the Pyle study (2004). In that study, cats that developed hyperglycemia after the first 24 hours of PN had a fivefold increase in mortality risk. It is worth noting that many of the cats in that study were fed in excess of RER. Although the development of hyperglycemia following PN administration may not necessarily worsen outcome, it may still be prudent to avoid this complication. Using conservative energy targets (i.e., initial target of RER), slowly increasing PN infusion rates during first day, close monitoring of patients receiving PN are recommended for minimizing the risks for development of hyperglycemia.

Hyperlipidemia is also a commonly reported metabolic complication in dogs and cats receiving PN (Lippert et al., 1993; Chan et al., 2002; Crabb et al., 2006), although in two studies some animals experienced a resolution of hyperlipidemia following initiation of PN (Reuter et al., 1998; Pyle et al., 2004). The rates of hyperlipidemia appear to be decreasing from almost 70% in the Lippert study reported in 1993, to <20% in more recent studies (Reuter et al., 1998; Chan et al., 2002; Pyle et al., 2004, Crabb et al., 2006). A decrease in overall energy targets and decrease in the proportion of energy provided via lipids in more recent studies are likely reasons for improvement for this complication.

Electrolyte disturbances can develop either after instituting nutritional support or may worsen in animals with preexisting abnormalities. Hyponatremia, hypokalemia, hypocalcemia, hypophosphatemia and hypochloremia have been reported in various studies although these complications were not associated with non-survival, (Lippert et al., 1993; Reuter et al., 1998; Chan et al., 2002; Pyle et al., 2004; Crabb et al., 2006; Queau et al., 2011). In contrast, a recent report, Gajanayaje et al., (2013) reported that hyperkalemia occurred in approximately 24% of dogs receiving a commercially available amino acid and dextrose solution and that this complication was associated with a decrease in survival.

Refeeding syndrome (see Chapter 16) is rarely reported in companion animals but can be difficult to manage when it occurs (Armitage-Chan, O'Toole and Chan, 2006; Brenner, KuKanich and Smee, 2011). Refeeding syndrome refers to a potentially fatal complication secondary to reintroduction of feeding in severely malnourished patients (Solomon and Kirby, 1990; Crook, Hally and Pantelli, 2001). It includes the development of hypophosphatemia with or without hypokalemia, hypomagnesemia, thiamine deficiency, and fluid shifts (Solomon and Kirby, 1990; Crook et al., 2001). It can develop when nutritional support, either parenteral or enteral, is initiated in a severely malnourished animal (particularly those that have not eaten for a prolonged period). The glucose provided stimulates insulin secretion that drives extracellular ions (e.g., phosphorus, potassium, magnesium) intracellularly and stimulates protein synthesis. The result may be clinically significant hypophosphatemia, hypokalemia, and hypomagnesemia. The shift to carbohydrate metabolism increases demands for important cofactors such as thiamine, which may already be depleted in malnourished patients, and neurological manifestations of thiamine deficiency

may occur (Solomon and Kirby, 1990; Crook et al., 2001; Armitage-Chan et al., 2006; Brenner et al., 2011). Congestive heart failure also can occur secondary to fluid shifts. It is important, particularly in animals with prolonged anorexia, to initiate parenteral nutrition slowly, to supplement vitamins (particularly thiamine), and to monitor serum electrolytes for the first 3 to 4 days after initiation.

Other metabolic complications that have been reported in association with PN in animals include hyperbilirubinemia and azotemia. Hyperbilirubenemia is a more significant complication in infants as cholestasis and fatty infiltration of the liver are of particular concern. It is unknown if the development of hyperbilirubinemia in animals following PN administration is due to similar liver pathology. The rates of azotemia reported in dogs receiving PN range from 1 to 17% (Lippert et al., 1993; Reuter et al., 1998; Chan et al., 2002; Queau et al., 2011). The development of azotemia associated with PN administration may be due to increased turnover of amino acids due to influx of amino acids in the PN admixture, progression of endogenous muscle catabolism or onset of acute kidney injury. In the study by Queau et al. (2011), azotemia was the only metabolic complication associated with mortality.

Mechanical complications

The most commonly reported mechanical complications reported in association with PN include catheter dislodgement, catheter disconnection, catheter occlusion, chewed lines, occluded lines and thrombophlebitis. Mechanical complications appear to be more common in dogs compared with cats, with chewed lines and catheter disconnection occuring more frequently. (Lippert et al., 1993; Reuter et al. 1998; Chan et al., 2002). In the study by Gajanayake et al. (2013) there was a particularly high rate of catheter dislodgement (40%) and this was mostly encountered in peripherally inserted catheters. As most other studies of PN in animals had predominantly used central catheters, it is difficult to draw conclusions whether the high rate of complication was related to PN administration, the formulation of PN (dextrose/amino acid combination) or no different if compared to peripheral catheters where PN was not used.

Septic complications

Although potentially the most devastating, septic complications appear to be uncommon in animals receiving PN. In all studies to date, septic complication has been described in < 7% of animals receiving PN (Lippert et al., 1993; Reuter et al., 1998; Chan et al., 2002; Pyle et al., 2004; Crabb et al., 2006; Queau et al., 2011; Gajanayake et al., 2013). Catheter-related infections are the main concern in this patient population and many patients respond with removal of the intravenous catheter. Although contamination of PN admixture is said to pose a particular risk, especially if the admixture contains lipids, to date, there are no reports of a positive bacterial culture of PN admixture in any of the studies in animals. The low rates of septic complications may be due to insistance on strict aseptic techniques during catheter placement, PN compounding and handling of PN bags and infusing sets.

Preventative measures

The most important factor in reducing the risk of complications is institution of preventative measures and protocols. Careful attention to catheter placement and catheter and line care will reduce the risk of problems. Placement of catheters by experienced personnel has been shown to reduce mechanical and septic complications (O'Grady et al., 2002). Elizabethan collars should be used for any animal that shows a propensity to chew lines. Protocols for catheter placement, handling catheters and line with an aseptic technique and maintaining dedicated catheters also are beneficial in minimizing the incidence of sepsis. If there is a suspicion of the development of a septic complication, the catheter must be investigated or removed. Submission of the catheter tip or of any discharge from around the catheter site, a sample of the PN admixture, or a blood culture for bacteriological cultures should be considered in all patients that develop pyrexia or an unexplained left-shifted neutrophilia following institution of PN, especially if this is not believed to be directly related to underlying disease.

Transitioning to enteral nutrition

Animals receiving PN should be transitioned to enteral feeding as soon as it is feasible. Unless there are specific contraindications to enteral feeding (e.g., intractable vomiting or regurgitation) animals receiving PN should be offered food and water on a daily basis. Some authors have recommended reducing the rate of PN infusion when tempting animals to eat voluntarily as there is some thought that PN administration in itself can suppress appetite via peptide YY and neuropeptide Y receptor-mediated events (Lee et al., 1997; Perea, 2012). The effectiveness of this technique has not been further evaluated but can be trialed and PN administration can be restored to the previous infusion rate if the animal continues to be intolerant of enteral feeding. The use of antiemetic and prokinetic therapy may be of further benefit in such patients.

Summary

The provision of nutritional support in patients intolerant of enteral nutrition can be challenging due to technical, logistical and management issues. As many hospitalized animals may already have a degree of malnutrition present or are at high risk of becoming malnourished, being able to implement PN support is an important technique in such cases. Proper identification of patients that will benefit from PN as well as the ability to formulate and compound PN safely are critical for successful management of these cases. As the patient population that requires PN support is usually afflicted with serious conditions, avoiding and minimizing complications is also important. Despite some of the technical challenges associated with the compounding and administration of PN in animals, this form of nutritional support can be successfully adopted in many practice settings and play an important role in the recovery of critically ill animals.

KEY POINTS

- Parenteral nutrition may be an important mode of nutritional support for hospitalized patients intolerant of enteral nutrition.
- Before initiation of PN support, nutritional assessment should be carried out to assess the need for PN, identify complicating factors and devise a plan for commencing PN.
- Formulation of PN requires calculation of energy and protein needs and facilities for safe compounding techniques.
- The safe provision of PN requires special attention to the placement and maintenance of intravenous catheters, the aseptic technique in compounding and handling of PN and vigilant patient monitoring.
- Potential complications associated with PN include metabolic, mechanical and septic complications.
- With appropriate protocols and safeguards in place, the use of PN can be successfully incorporated in the care of critically ill patients in many practice settings.
- Transitioning to enteral nutrition should occur as soon as it is feasible.

Notes

1 4 Trace Elements, Abbott Laboratories, North Chicago, Ill.
2 B vitamin complex, Veterinary Laboratories, Lenexa, KS.
3 ProcalAmine. B. Braun Medical Inc, Irvine, CA.

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