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SAUNDERS

Nutrition in Critical Illness

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G reat advances have been made recently in the field of critical care nutrition. Although nutrition was once regarded as a supportive measure of low priority, it is increasingly being recognized as an important therapeutic intervention in the care of critically ill patients.

In human ICUs, nutrition not only provides supportive therapy but is also becoming a means to modulate even severe diseases. Although the developing applications are still years away from being standards in veterinary medicine, this trend highlights the possibilities of critical care nutrition in veterinary medicine. The current focus of veterinary critical care nutrition, and the major focus of this article, is on carefully selecting the patients most likely to benefit from nutritional support, deciding when to intervene, and optimizing nutritional support to individual patients.

RATIONALE FOR NUTRITIONAL SUPPORT IN CRITICAL ILLNESS
Critical illness induces unique metabolic changes in animals that put them at high risk for malnutrition and its deleterious effects. An important distinction in the body's response to inadequate nutritional intake occurs in disease (stressed starvation) compared with a healthy state (simple starvation). During acute fasting in the healthy state, use of glycogen stores is the primary source of energy. However, glycogen stores are quickly depleted, especially in strict carnivores such as the cat, and lead to the initial mobilization of amino acids from muscle stores. Within days, a metabolic shift occurs toward the preferential use of stored fat deposits, sparing catabolic effects on lean muscle tissue. In diseased states, the inflammatory response triggers alterations in cytokines and hormone concentrations and shifts metabolism toward a catabolic state. With a lack of food intake, the predominant energy source is derived from accelerated proteolysis, which in itself is an energy-consuming process. Thus, these animals may preserve fat deposits in the face of lean muscle tissue loss.

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These shifts in metabolism commonly result in significant negative nitrogen and energy balance. The consequences of continued lean body mass losses include negative effects on wound healing, immune function, strength (both skeletal and respiratory), and ultimately overall prognosis. Although the relationship between malnutrition and clinical outcome has not been proven definitively in companion animals, people experiencing malnutrition and critical illness have been documented to have poorer outcomes [1,2]. The immediate goal of providing nutritional support to hospitalized patients is not to achieve weight gain, per se, which mostly likely reflects shift in water balance, but rather to minimize further loss of lean body mass. Reversal of malnutrition hinges on resolution of the primary underlying disease. Nutritional support has the goal of restoring nutrient deficiencies, providing key substrate for healing and repair, and minimizing the development of malnutrition.

PATIENT SELECTION

As with any intervention in critically ill animals, nutritional support has some risk for complications and the potential to benefit. The risk for complications most likely increases with disease severity and the clinician must consider many factors in deciding to institute nutritional support. Of utmost importance, patients must be cardiovascularly stable before any nutritional support is initiated. In states of shock, perfusion of the gastrointestinal tract is often reduced in favor of maintaining adequate perfusion of heart, brain, and lungs. With reduced perfusion, processes such as gastrointestinal motility, digestion, and nutrient assimilation are altered, and feeding under these circumstances will probably result in more complications. An important goal of nutritional support for critically ill patients is to minimize risk for complications. Other factors that should be addressed before nutritional intervention include dehydration, electrolytes imbalances, and abnormalities in acid–base status.

In animals that have been stabilized, the appropriate time to start nutritional support should also be decided carefully. The number of days an animal has not consumed adequate calories before hospitalization must be determined from the history and added to the number of days during hospitalization that the animal has not consumed any significant amounts of food. Documentation of total days without adequate nutrition should be listed in the patient's daily progress notes to ensure that nutritional support remains an important therapeutic goal. The previous notion that nutritional support is unnecessary until 10 days of inadequate nutritional support have elapsed is certainly outdated and unjustified. Although commencing nutritional support within 3 days of hospitalization, even before diagnosing the underlying disease, is a more appropriate goal in most cases, other factors should be considered.

NUTRITIONAL ASSESSMENT

Because objective measures of nutritional status (eg, anthropometry, bioelectrical impedance, dual energy x-ray absorptiometry, serum indicators of malnutrition) have limited availability in clinical veterinary medicine, subjective

assessment of malnutrition is important in identifying patients needing nutritional support. Proposed indicators of malnutrition include unintentional weight loss (typically greater than 10%), poor haircoat quality, muscle wasting, signs of inadequate wound healing, hypoalbuminemia, lymphopenia, and coagulopathy. These abnormalities are not specific to malnutrition and often occur late in the disease process. Evaluating overall body condition is emphasized rather than simply noting body weight. Fluid shifts may significantly impact body weight, whereas body condition scores (BCSs) are not influenced by these changes. BCSs, discussed elsewhere in this issue, have been shown to be reproducible, reliable, and clinically useful measures in nutritional assessment [3]. However, body condition scoring schemes were designed and validated to assess body fat and do not incorporate loss of lean body tissue. A muscle condition score has been proposed to enhance nutritional assessment, but further studies are needed to show its clinical usefulness [4].

Because of the limitations in assessing nutritional status, early risk factors must be identified that may predispose patients to malnutrition, such as anorexia lasting more than 5 days, serious underlying disease (eg, severe trauma, sepsis, peritonitis, acute pancreatitis, major gastrointestinal surgery), and large protein losses (eg, protracted vomiting, diarrhea, protein-losing nephropathies, draining wounds, burns). Nutritional assessment also identifies factors that can impact the nutritional plan, such as specific electrolyte abnormalities, hyperglycemia, hypertriglyceridemia, hyperammonemia, or comorbid illnesses, such as renal, cardiac, or hepatic disease. In the presence of these abnormalities, the nutritional plan should be adjusted accordingly to limit acute exacerbations of any pre-existing condition.

Finally, because many techniques required for nutritional support necessitate anesthesia, (eg, placement of most feedings tubes, intravenous catheters for parenteral nutrition), patients must be properly evaluated and stabilized before undergoing anesthesia, regardless of the urgency to implement nutritional support. When patients are deemed too unstable to undergo general anesthesia, temporary measures of nutritional support that do not require anesthesia (eg, nasoesophageal tube placement, placement of peripheral catheters for partial parenteral nutrition) should be considered. Once patients are deemed stable enough to undergo general anesthesia, more effective means of nutritional support can be implemented.

NUTRITIONAL PLAN

Successful nutritional management of critically ill patients relies on the proper diagnosis and treatment of the underlying disease, although nutritional support should not be delayed until a diagnosis is made. Nutrition should be provided as soon as it is feasible. After the need for support is established, the appropriate route of nutritional support should be determined. Providing nutrition through a functional digestive system is the preferred route of feeding, and the patient's tolerance to enteral feeding routes should be evaluated carefully.

Even if patients can only tolerate small amounts of enteral nutrition, this route of feeding should be pursued and supplemented with parenteral nutrition (PN) as necessary to meet nutritional needs. However, if an animal shows complete intolerance to enteral feeding, some form of PN should be provided. Based on the nutritional and medical assessment, the anticipated duration of nutritional support, and the route of delivery (ie, enteral or parenteral), a nutritional plan is formulated to meet nutritional needs and support healing or recovery from the disease process. The nutritional plan should be instituted gradually with the goal of reaching target level of nutrient delivery in 48 to 72 hours. The nutritional plan is adjusted based on reassessment and the changing medical status.

CALCULATING NUTRITIONAL REQUIREMENTS

Ideally, nutritional support should provide ample substrates for gluconeogenesis, protein synthesis, and energy necessary to maintain homeostasis without causing complications. Sufficient calories should be provided to sustain critical physiologic processes, such as immune function, wound repair, and cell division and growth. Total energy expenditure must be measured to precisely determine caloric needs. Although a few studies have used indirect calorimetry to estimate energy expenditure in select populations of veterinary patients, the use of mathematical formulas remains the only practical means of estimating the patient's daily caloric requirement.

Results of indirect calorimetry studies in dogs support the recent trend of formulating nutritional support to meet resting energy requirements (RER) rather than more generous illness energy requirements [5,6]. Until recently, many clinicians multiplied the RER by an illness factor between 1.1 and 2.0 to account for a presumed increase in metabolism associated with different diseases and injuries. More conservative energy estimates (ie, starting with the animal's RER) are currently recommended to avoid overfeeding and its associated complications [7,8]. A recent study showed an association between the use of illness factors and the development of hyperglycemia in cats administered total parenteral nutrition (TPN) [9], whereas another found a negative association between the development of hyperglycemia and poor outcome [10]. Furthermore, overfeeding energy can result in gastrointestinal complications, hepatic dysfunction, and increased carbon dioxide production [11].

Although several formulas have been proposed to calculate the RER, a widely used allometric formula can be applied to both dogs and cats of all weights. This formula, most commonly used by the authors, is:

$$RER = 70 \times (\text{current body weight in kg})^{0.75}$$

Alternatively, for animals weighing between 3 and 25 kg, the following may be used:

$$RER = (30 \times \text{current body weight in kg}) + 70$$

Other veterinary nutritionists recommend using the animal's ideal body weight in these equations, which differs from the authors' recommendations, particularly in critically ill animals for which the authors believe using ideal body weight is inappropriate. To avoid overfeeding underweight animals, the authors recommend using the animal's current weight for the RER calculation. Animals that are overweight should be fed the appropriate number of calories to avoid weight loss, because seriously ill or injured animals lose more lean body mass than fat. Nutritional requirements in significantly overweight animals (ie, >25% above ideal body weight) can be calculated in several ways. One is to use the animal's current body weight for the RER calculation and adjust to maintain weight. Another option assumes that 25% of excess weight is lean tissue and the remaining 75% is metabolically inactive fat (ie, if a dog's ideal weight is 20 kg and he weighs 30 kg, he has 10 kg of excess weight, 2.5 kg of which is lean tissue and 7.5 kg of which is fat). Therefore, the ideal weight plus 25% of the excess weight (to account for the extra lean body mass) can be used to calculate RER. Using the 30-kg dog whose ideal weight is 20 kg, the adjusted body weight to use to calculate RER would be 20 kg + (25% × 10 kg) or 20 kg + 2.5 kg = 22.5 kg. Thus, the RER for this overweight dog would be 723 kcal/d.

Although nitrogen balance is often used to determine the protein requirements of critically ill people, this is not commonly measured in critically ill animals. One method of estimating the extent of amino acid catabolism is to measure 24-hour urinary urea nitrogen content. Although measuring urinary urea nitrogen in critically ill dogs has been shown to be a feasible tool in assessing nitrogen balance, further studies are warranted to better characterize the protein requirements of critically ill animals [12]. Experts currently recommend that hospitalized dogs be supported with 4 to 6 g of protein per 100 kcal (15%–25% of total energy requirements), whereas cats are usually supported with 6 or more grams of protein per 100 kcal (25%–35% of total energy requirements) [8]. Protein requirements are usually estimated based on clinical judgment and the recognition that protein requirements are markedly increased during certain diseases (eg, peritonitis, draining wounds). Further studies are clearly needed to better characterize the protein requirements of critically ill animals.

PARENTERAL NUTRITIONAL SUPPORT

PN can be delivered through a central vein (total parenteral nutrition) or a peripheral vein (peripheral or partial parenteral nutrition). TPN, as defined in this article, is the provision of all of the animal's calorie and protein requirements. Partial parenteral nutrition (PPN) only supplies part of the animal's energy, protein, and other nutrient requirements [7], which can be administered through either a peripheral or central vein.

Because TPN supplies all calorie and protein requirements, it is often the preferred modality for an animal requiring PN. The disadvantages are that it requires a jugular venous catheter, is slightly more expensive (with solutions costing typically approximately 10%–20% more than a PPN solution for the

same sized animal), and may be associated with more metabolic complications. PPN may be an alternative to TPN in selected cases, but clinicians must be aware that it will not provide all of the animal's requirements. Both TPN and PPN are typically a combination of dextrose, an amino acid solution, and a lipid solution. The concentration of some components (eg, dextrose, lipid) varies depending on the disease state and whether TPN or PPN is chosen.

Crystalline amino acid solutions are essential components of PN. The importance of supplying amino acids relates to the maintenance of positive nitrogen balance and repletion of lean body tissue, which may be vital in the recovery of critically ill patients. Supplementation of amino acids may support protein synthesis and spare tissue proteins from being catabolized through gluconeogenesis. The most commonly used amino acid solutions contain most essential amino acids for dogs and cats, except taurine. However, because PN is typically not used beyond 10 days, the lack of taurine does not become a problem in most circumstances. Amino acid solutions are available in different concentrations from 3.5% to 15%, but the most commonly used concentration is 8.5%. Amino acid solutions are also available with and without electrolytes. Animals that have normal serum electrolytes typically receive amino acid solutions with electrolytes, whereas patients who have electrolyte disturbances may benefit from amino acid solutions without electrolytes so that they can be individually corrected.

Lipid emulsions are the calorically dense component of PN and a source of essential fatty acids. Lipid emulsions are isotonic and are available in 10% to 30% solutions. These commercially available lipid emulsions are made primarily of soybean and safflower oil and provide predominantly long-chain polyunsaturated fatty acids, including linoleic, oleic, palmitic, and stearic acids. These solutions are emulsified with egg yolk phospholipids and their tonicity is adjusted with glycerol. The emulsified fat particles are comparable in size to chylomicrons and are removed from the circulation through the action of peripheral lipoprotein lipase.

A common misconception exists regarding the use of lipids in pancreatitis. Although hypertriglyceridemia may be risk factor for pancreatitis, infusions of lipids have not been shown to increase pancreatic secretion or worsen pancreatitis and are therefore considered safe [13], The one exception, however, is in cases where serum triglycerides are elevated, indicating a clear failure of triglyceride clearance. According to the most recent guidelines provided by the American Society for Parenteral and Enteral Nutrition, human patients with serum triglycerides exceeding 400 mg/dL should have the lipid proportion in PN markedly reduced or eliminated altogether [13]. Although specific data on the maximal safe level of lipid administration in veterinary patients are not available, maintaining normal serum triglycerides levels in patients undergoing PN seems prudent. Another concern about using lipids in PN is their purported immunosuppressive effects from impairing the reticuloendothelial system, particularly in PN solutions containing a high percentage of lipid. Despite in vitro

evidence supporting the notion that lipid infusions can also suppress neutrophil and lymphocyte function, studies have not correlated lipid use and increased rates of infectious complications.

Electrolytes, vitamins, and trace elements also may be added to the PN formulation. Depending on the hospital and the individual patient, electrolytes can be added individually to the admixture, added as an electrolyte mixture, included as part of the amino acid solution, or left out altogether and managed separately through the animal's other fluids. Amino acids with or without electrolytes can be included, based on clinician preference. Because most animals undergo PN for only a short duration, fat-soluble vitamins usually are not limiting and therefore supplementing human TPN with vitamin preparations is usually not indicated. The exception is obviously malnourished animals in which supplementation may be desirable.

However, because B vitamins are water soluble, they are more likely to become deficient, particularly in anorectic animals and those with high-volume diuresis (eg, renal failure, diabetes). Therefore, supplementing B vitamins in the PN admixture may be appropriate in certain animals. Some authors recommend vitamin K supplements for animals undergoing PN because PN is believed to be low in vitamin K (it is generally administered subcutaneously on day 1 of TPN and then once weekly). Because vitamin K deficiency is unlikely to occur, particularly when a lipid emulsion is used, the authors do not routinely supplement vitamin K unless the animal's underlying disease indicates the need. Trace elements serve as cofactors in various enzyme systems and can become deficient in malnourished animals or those undergoing long-term PN. In people undergoing PN, zinc, copper, manganese, and chromium are routinely included in the PN admixture. These nutrients are sometimes added to PN for malnourished animals, but the authors do not routinely include them. Nonetheless, because zinc and vitamin B status may be important for normal smell, taste, and appetite, supplementing these nutrients could be considered.

Although adding other parenteral medications to the PN admixture is possible, their compatibility must be verified first. Drugs that are known to be compatible and are sometimes added to PN include heparin, insulin, potassium chloride, and metoclopramide. Although the addition of insulin to PN is often required in people undergoing PN, the hyperglycemia seen in veterinary patients undergoing PN does not usually require insulin administration, except in those with diabetes who will require adjustments to their insulin regimen.

PARENTERAL NUTRITION COMPOUNDING

Based on the nutritional assessment and plan, PN can be formulated according to the worksheets found in Appendices 1 and 2. For TPN (see Appendix 1), the first step is calculating the patient's energy needs or RER. Protein requirements (grams of protein required per day) are then determined, taking into consideration factors such as excessive protein losses or severe hepatic or renal disease. Although some nutritionists believe that the energy requirements are supplied

by the dextrose and lipid portion of the PN, the authors apply the energy provided by amino acids to the energy calculations, subtracting it from the daily RER to establish the total nonprotein calories required. The nonprotein calories are then usually provided as a 50:50 mixture of lipids and dextrose, although this ratio can be adjusted in cases of persistent hyperglycemia or hypertriglyceridemia (eg, a higher proportion of calories would be provided by lipids in an animal with hyperglycemia). The calories provided by each component (amino acids, lipids, and dextrose) are then divided by their respective caloric densities and the exact amounts of each component are added to the PN bags in an aseptic fashion. The amount of TPN delivered often provides less than the patient's daily fluid requirement. Additional fluids can be either added to the PN bag at compounding or provided as a separate infusion.

Appendix 2 provides a step-by-step protocol for formulating PPN, in which patients of various sizes can receive 70% of their RER and approximately meet their daily maintenance fluid requirement. In very small animals (≤3 kg), the amount of PPN will exceed the maintenance fluid requirement and increase the risk for fluid overload, so adjustments may be necessary. Furthermore, in animals requiring conservative fluid administration (eg, those with congestive heart failure), these calculations for PPN may provide more fluid then would be safe. In this formulation, the proportion of each PN component depends on the weight of the patient, so that a smaller animal (between 3 and 5 kg) receives proportionally more calories from lipids than a large dog (>30 kg), which would receive more calories in the form of carbohydrates. Therefore, the resulting formulation approximates the patient's daily fluid requirement.

Ideally, PN should be compounded aseptically under a laminar flow hood using a semiautomated, closed-system, PN compounder (eg, Automix compounder, Clintec Nutrition, Deerfield, Illinois). If an automated compounder is not available, manual compounding can be performed in a clean, low-traffic area with strict adherence to aseptic technique using a 3-in-1 bag (eg, All-In-One EVA container, Clintec Nutrition, Deerfield, Illinois). Because of these ideal conditions, having a local human hospital, compounding pharmacies, or a human home health care company compound PN solutions is often easier and more cost-effective. Alternatively, commercial ready-to-use preparations of glucose or glycerol and amino acids suitable for (peripheral) intravenous administration are available. Although ready-to-use preparations are convenient, they provide only 30% to 50% of caloric requirements when administered at maintenance fluid rates and therefore should only be used for interim nutritional support or to supplement low-dose enteral feedings.

PARENTERAL NUTRITION ADMINISTRATION

Administering any PN requires a dedicated catheter used solely for PN administration that is placed using aseptic technique. In most cases, additional catheters are required because PN should not be administered through existing catheters that were placed for reasons other than PN. Long catheters composed of silicone, polyurethane, or tetrafluoroethylene are recommended for any type

of PN to reduce the risk for thrombophlebitis. Multilumen catheters are often recommended for TPN because they can remain in place for long periods, and separate ports can be used for blood sampling and administering additional fluids and intravenous medications without needing separate catheters at other sites. Although placement of multilumen catheters requires more technical skills than conventional jugular catheters, they can be effective in treating critically ill patients. Because of the high osmolarity of TPN solutions (often 1200 mOsm/L), they must be administered through a central venous (jugular) catheter, whereas PPN solutions can be administered through either a jugular catheter or catheters placed in peripheral veins. High osmolarity is a concern because it may increase the incidence of thrombophlebitis, although this has not been well characterized in veterinary patients.

Because of the various metabolic derangements associated with critical illness, TPN should be instituted gradually over 48 hours. In the authors' respective institutions, TPN is typically initiated at 50% of the RER on the first day and then increased to the targeted amount by the second day. In most cases, PPN can be started without gradual increase. Adjusting the rates of other fluids being administered concurrently is also important. For TPN and PPN, the animal's catheter and infusion lines must always be handled aseptically to reduce the risk for PN-related infections. Even with aseptic technique, injections into the PN catheter infusion port or administration lines should be strictly prohibited because many drugs and solutions are incompatible with PN solutions. Drug incompatibilities can result in precipitates, alter the lipid emulsion, and possibly lead to pulmonary embolism and patient death.

PN should be administered as continuous rate infusions over 24 hours through fluid infusion pumps. Inadvertent delivery of massive amounts of PN can result if administration is not properly regulated. Once a bag of PN is set up for administration, it is not disconnected from the patient even for walks or diagnostic procedures; the drip regulator is decreased to a slow drip and accompanies the patient throughout the hospital. Administering PN through an 1.2-μm in-line filter is also recommended and is attached at setup. This setup process is performed daily with each new bag of PN. Each bag should only hold a day's worth of PN, and the accompanying fluid administration sets and in-line filter are also changed using aseptic technique. PN should discontinue when the animal resumes consuming an adequate amount of calories of at least 50% of RER. TPN should be gradually discontinued over 6 to 12 hours. Abrupt discontinuation can cause hypoglycemia when the concentrated dextrose solution is discontinued in the face of high endogenous insulin secretion by the patient. PPN can be discontinued without weaning.

ENTERAL NUTRITIONAL SUPPORT

Feeding tubes are the standard mode of nutritional support in critically ill animals that have a functional gastrointestinal tract. Nasoesophageal, esophagostomy, gastrostomy, and jejunostomy feeding tubes are the most commonly used. In animals undergoing laparotomy, placing gastrotomy or jejunostomy

feeding tubes should particularly be considered. Newer techniques that incorporate an intraluminal jejunal tube through a gastrostomy tube were also developed. The decision to use one tube over another is based on the anticipated duration of nutritional support (eg, days vs. months), the need to circumvent certain segments of the gastrointestinal tract (eg, oropharnyx, esophagitis, pancreatitis), clinician experience, and the patient's ability to withstand anesthesia (very critical animals may only tolerate placement of nasoesophageal feeding tubes). In-depth instructions for placing feeding tubes have been provided in the literature [14–19].

The major advantages of nasoesophageal feeding tubes are that they are simple to place; require minimal, if any, sedation; and require no special equipment. Because this procedure is largely blind, verifying placement of the tube within the esophagus using radiography or an end-tidal carbon dioxide monitor is recommended [20]. Tubes placed within the gastrointestinal tract should yield no carbon dioxide when checked [20]. Disadvantages of nasoesophageal tubes include patient discomfort and the exclusive use of liquid diets because tubes typically measure 3.5 to 5 Fr.

Esophageal feeding tubes are an excellent choice for many critically ill animals and have completely supplanted the need for pharyngostomy tubes. They are also easy to place, require only brief anesthesia, and can accommodate more calorically-dense diets (ie, >1 kcal/mL), making them ideal for patients that have feeding-volume limitations. Tubes ranging from 12 to 19 Fr are commonly used and patient discomfort is usually not an issue. The most common problems associated with this tube are tube obstruction and cellulitis at the stoma site. Intermittent bolus feeding is usually used with these tubes, but low-rate continuous infusions can be used for animals that cannot tolerate bolus feeding.

Surgically placed and percutaneous-guided gastrostomy tubes (PEG) are good options for patients undergoing laparotomy and endoscopy, respectively. These tubes can be used for long-term nutritional support (ie, months) and feeding is usually performed through bolus feeding. Gastrostomy feeding tubes are the largest feeding tubes (16–32 Fr) and can deliver most diets after blenderizing. Placing PEG tubes requires special equipment and considerable experience, but can be effective. Complications associated with these tubes range from mild cellulitis around the stoma site to more serious life-threatening peritonitis. Premature tube dislodgement (before 14 days) should be immediately evaluated for the need for possible surgery.

Animals requiring laparotomy and deemed to require bypass of the stomach or pancreas (eg, significant stomach wall resection, severe pancreatitis, pancreatectomy) should have a jejunostomy feeding tube placed. These tubes are similar in size to nasoesophageal tubes and therefore can only accommodate liquid diets. Feeding through these tubes should also be performed through continuous infusions (eg, 1 mL/kg/h initially and slowly increased) rather than bolus feeding. Complications associated with these feeding tubes include tube occlusion, diarrhea, and dislodgement resulting in peritonitis [21]. Placing jejunal tubes through gastrostomy tubes offers a certain degree of versatility in that

the nutrients can be administered to the mid-distal jejunum without the need for a jejunostomy [15,19]. However, this technique has limited experience and possible complications have not been adequately described.

A common misconception is that animals fed through feeding tubes will not eat voluntarily, and therefore feedings are withheld to evaluate the animal's appetite. However, the main purpose of nutritional support is to provide nutrients and calories that the animal needs, and therefore less emphasis should be placed on appetite per se. Anorexia should be corrected once the primary disease is addressed. Weaning animals from tube feedings while they are still hospitalized is discouraged; this is more appropriate after discharge while the animal is recovering in its own environment. Because feeding regimens should have been reduced to three or four times daily by discharge, owners can be instructed to offer oral feeding before each tube feeding so they can monitor for the return of adequate spontaneous feeding. Based on reassessment by the clinician, tube feedings can then be reduced or discontinued depending on progress made.

MONITORING FOR COMPLICATIONS

Because the development of complications in critically ill animals can have serious consequences, it is an important aspect of nutritional support that involves close monitoring. With implementation of enteral nutrition, possible complications include vomiting, diarrhea, fluid overload, electrolyte imbalances, feeding tube malfunction, and infectious complications associated with insertion sites of feeding tubes. Metabolic complications are more common with PN and include the development of hyperglycemia, lipemia, azotemia, hyperammonemia, cholestasis, and electrolyte abnormalities. Rarely, nutritional support can be associated with severe abnormalities that are sometimes referred to as the *refeeding syndrome* [22,23]. Strategies to reduce risk for complications include using aseptic techniques when placing feeding tubes and intravenous catheters, using conservative estimates of energy requirements (ie, RER), and paying careful attention to nutritional assessment. Frequent monitoring and adjusting the nutritional plan if complications arise are important aspects of reassessment. Parameters that should be monitored during nutritional support include body temperature, respiratory rate and effort, signs of fluid overload (eg, chemosis, increased body weight), and serum concentrations of glucose, triglyceride, electrolytes, packed cell volume, total protein, and blood urea nitrogen/creatinine.

PHARMACOLOGIC AGENTS IN NUTRITIONAL SUPPORT

Because critically ill animals are often anorexic, the temptation exists to use appetite stimulants to increase food intake. Unfortunately, appetite stimulants are generally unreliable and seldom result in adequate food intake in critically ill animals. Pharmacologic stimulation of appetite is often short-lived and only delays true nutritional support. The authors do not believe appetite stimulants should be used to manage hospitalized animals when more effective measures of nutritional support, such as placement of feeding tubes, are more appropriate. Appetite stimulants may be considered in recovering animals once they are

home in their own environment, because the primary reason for loss of appetite should ideally be reversed by discharge. As with many drugs, appetite stimulants also have negative side effects, such as behavioral changes associated with cyproheptadine and sedation associated with diazepam, and therefore should be used with caution.

Other agents commonly used in critically ill animals that have gastrointestinal dysfunction include antiemetics, H_2 blockers, and prokinetics. Similar to appetite stimulants, these drugs have not been formally evaluated in critically ill animals. A recent prospective study in dogs with parvoenteritis and early enteral nutrition incorporated the use of metoclopramide (an antiemetic and prokinetic agent) in the treatment of all dogs enrolled [24]. Tolerance to enteral feeding was remarkably good considering the usual clinical course of parvoenteritis [24]. A more recent retrospective study of parvoenteritis in dogs proposed that metoclopramide was associated with increased hospitalization and did not show a benefit [25]. Although phenothiazine derivatives, such as prochlorperazine and chlorpromazine, also have antiemetic properties, the risk for hypotension precludes their use in many critically ill animals. A more potent class of antiemetics, the $5HT_3$ antagonists, is increasingly being used despite a lack of formal evaluation in animals. Drugs in this class include ondansetron and dolasetron, which were first used to treat chemotherapy-induced nausea in people and then animals and are now used routinely to treat critically ill animals. Although antiemetics and prokinetic agents probably have a place in veterinary critical care, further studies are needed to define their role and optimal use.

FUTURE DIRECTIONS IN CRITICAL CARE NUTRITION

The current state of veterinary critical care nutrition revolves around proper recognition of animals requiring nutritional support and implementing strategies to best provide nutritional therapies. Important areas needing further evaluation in critically ill animals include the optimal composition and caloric target of nutritional support and strategies to minimize complications and optimize outcome. Recent studies implicating poor clinical outcome in the development of hyperglycemia in critically ill people have led to more vigilant monitoring and stricter control of blood glucose, with obvious implications for nutritional support [26–29]. Evidence of a similar relationship in dogs and cats is mounting, and ongoing studies are focusing on the possible consequences of hyperglycemia for clinical outcome in the veterinary ICU [9,10,30–32]. Until further studies suggest otherwise, efforts to reduce the incidence of hyperglycemia in critically ill animals, especially those undergoing nutritional support, should be strongly pursued.

Other exciting areas of clinical nutrition in critical care include the use of special nutrients that possess immunomodulatory properties, such as glutamine, arginine, n-3 fatty acids, and antioxidants. In specific patient populations, these nutrients, used singly or in combination, have shown promising results [33–35]. However, the response has not been consistent, and ongoing trials continue to evaluate their efficacy [36–38]. Limited information is available on using these

nutrients to specifically modulate disease in clinically affected animals. Two studies using enteral glutamine have not shown any benefit [39,40]. A recent study did not show a depletion of glutamine in critically ill dogs that had several illnesses, but showed a marked decrease in arginine compared with healthy controls [41]. Future studies should focus on whether manipulating these nutrients offers any benefit in animals. Further development of veterinary critical care nutrition may transition nutrition from a strictly supportive measure to one designed to modulate disease and outcome.

APPENDIX 1. WORKSHEET FOR CALCULATING A TOTAL PARENTERAL NUTRITION FORMULATION

1. Resting energy requirement (RER):
   $70 \times$ (current body weight in kg)$^{0.75}$ = kcal/d
      or for animals 3–25 kg, can also use:
   $30 \times$ (current body weight in kg) + 70 = kcal/d
   RER = _____kcal/d

2. Protein requirements:

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

   (RER ÷ 100) × _____g/100 kcal = _____g protein required/d
   Protein requirement:_____

3. Volumes of nutrient solutions required each day:

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

   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/d × 4 kcal/g = _____kcal provided by protein
   RER − kcals provided by protein = _____nonprotein kcal needed/d

   c. Nonprotein calories are usually provided as a 50:50 mixture of lipid to dextrose. However, if the patient has a pre-existing condition (eg, 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 non-protein 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 TPN solution[a]

5. Administration rate:

   Day 1: _____mL/h

   Day 2: _____mL/h

   Day 3: _____mL/h

[a]Be sure to adjust the patient's other fluids accordingly!

APPENDIX 2. WORKSHEET FOR CALCULATING A PARTIAL PARENTERAL NUTRITION FORMULATION

1. Resting energy requirement (RER):

   $70 \times$ (current body weight in kg)$^{0.75}$ = kcal/d

   or for animals 3–25 kg, can also use:

   $30 \times$ (current body weight in kg) + 70 = kcal/d

   RER = _____kcal/d

2. Partial energy requirement (PER):

   Plan to supply 70% of the animal's RER with PPN:

   PER = RER $\times$ 0.70 = _____kcal/d

3. Nutrient composition:

   (Note: For animals ≤3 kg, the formulation will provide a fluid rate higher than maintenance fluid requirements. Be sure that the animal can tolerate this volume of fluids.)

   a. Cats and dogs 3–5 kg:

      PER $\times$ 0.20 =_____kcal/d from carbohydrate

      PER $\times$ 0.20 =_____kcal/d from protein

      PER $\times$ 0.60 =_____kcal/d from lipid

   b. Cats and dogs 6–10 kg:

      PER $\times$ 0.25 =_____kcal/d from carbohydrate

      PER $\times$ 0.25 =_____kcal/d from protein

      PER $\times$ 0.50 =_____ kcal/d from lipid

   c. Dogs 11–30 kg:

      PER $\times$ 0.33 =_____kcal/d from carbohydrate

      PER $\times$ 0.33 =_____kcal/d from protein

      PER $\times$ 0.33 =_____kcal/d from lipid

   d. Dogs >30 kg:

      PER $\times$ 0.50 =_____kcal/d from carbohydrate

      PER $\times$ 0.25 =_____kcal/d from protein

      PER $\times$ 0.25 =_____kcal/d from lipid

4. Volumes of nutrient solutions required each day:

   a. 5% dextrose solution = 0.17 kcal/mL
      _____kcal from carbohydrate ÷ 0.17 kcal/mL =_____mL
      dextrose/d

   b. 8.5% amino acid solution = 0.085 g/mL = 0.34 kcal/mL
      _____kcal from protein ÷ 0.34 kcal/mL = _____mL amino acids/d

   c. 20% lipid solution = 2 kcal/mL
      _____kcal from lipid ÷ 2 kcal/mL = _____mL lipid/d

5. Total daily requirements:
   _____mL 5% dextrose solution
   _____mL 8.5% amino acid solution
   _____mL 20% lipid solution
   _____mL total volume of PPN solution[a]

6. Administration rate:
   This formulation provides approximately a maintenance fluid rate.
   _____mL/hr PPN solution

[a]Be sure to adjust the patient's other fluids accordingly!

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