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1. Introduction
Parenteral nutrition can be a valuable aid in supplying energy and nutrients to either critically ill horses or to those temporarily unable to ingest adequate feed to meet their caloric requirements. There are several conditions that make parenteral nutrition a viable treatment choice. Horses may be unable to eat because of neurologic dysfunction, pharyngeal or esophageal obstruction, trauma, or space-occupying masses. They may be able to eat, but be unable to tolerate food in the gastrointestinal tract. This would include cases of paralytic or adynamic ileus, anterior enteritis, post-operative colics, severe enterocolitis, or neonatal sepsis and gastrointestinal disease. Other patients, such as horses with inflammatory bowel disease or severe diarrhea, are unable to utilize feed. Some severely compromised patients are simply unwilling to eat.

The goal of parenteral nutrition is not to allow for growth but rather to supply calories and nutrients in order to prevent body catabolism and malnutrition. Parenteral nutrition should be considered a temporary measure to support the anorectic animal by sparing the body from destruction in order to allow energy for recovery [1,2]. In large-animal medicine, we often use it to supplement enteral feeding by providing additional calories not gained by enteral methods. Primarily because of the cost of the materials involved, parenteral nutrition is used much more often in foals than in adults. Anorectic foals rapidly lose energy and body condition, and if parenteral nutrition is an option, then it should be started before the foal enters a severely catabolic state (often after only 24 h of illness) [3,4]. The effects of malnutrition include abnormalities in energy metabolism, decreased immune function and wound healing [5,6]. These effects can be especially important in a critically ill patient. Because foals requiring parenteral nutrition are generally gravely ill or premature, clients must be thoroughly informed of the cost-benefit factors. Such foals have greater than average potential for complications and poor outcomes, and will certainly have an above-average bill. Their owners need to be informed as much as possible on the probable outcome and potential problems so that they are able to make the best treatment decisions for their resources. Total parenteral nutrition is not often used in adult horses, primarily because of the cost of the products, but even partial parenteral nutrition may be enough of an energy boost to start an anorectic, malnourished animal on the road to recovery.

Parenteral nutrition is avoided by many otherwise aggressive practitioners because of the perceived technical knowledge required, patient complications, and excessive cost. The purpose of this paper is to describe these factors so that veterinarians are better able to decide if parenteral therapy might be a service they can offer. Before implementing parenteral nutrition therapy in practice, it is imperative to have protocols in place that describe the details of aseptic mixing and the handling of lines and nutrition products, as well as intensive patient monitoring and record keeping to avoid as many complications as possible.

2. Methods of Preparation and Administration
Most patients given parenteral nutrition, either total or partial, are compromised neonates at high risk for sepsis, if not septic already. These cases require strict adherence to aseptic technique to prevent microbial inoculation of the nutrition solution. Ideally, a laminar flow hood should be used in the mixing process to prevent the introduction of normally contaminated room air into the solution containers and administration lines [4,7]. There are two general ways to approach the mixing of the nutrition solution. The ideal method involves running each component into a commercial administration bag, using a separate transfer line for each, and then using another intravenous line to administer the product to the patient. All mixing should be performed with aseptic techniques and wearing sterile gloves. A simpler method is often employed in adult horses that are receiving only partial nutrition supplementation. We administer the components directly into a 5-L bag of normal saline or lactated ringer's solution by adding the nutrition through the administration port via a regular fluid line, or through the
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3. Parenteral Nutrition Solutions

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sterile saline before and after medications are delivered. It is not ideal, but has worked for us on several occasions when cost to polyionic fluids. If using only a single-lumen catheter, then we turn off the nutrition and flush approximately 100 ml of dedicated line for the nutrition product to prevent any precipitation or other chemical reactions with medications or additives. Initially, the mixing of the solution components needs to be in an aseptic fashion. Most practices do not have a laminar flow hood, but they will have a lab or other small, dust-free room that will suffice. A local hospital, diagnostic laboratory, or pharmacy may be willing to assist you by allowing the use of their hood. Use sterile gloves and wipe down any ports through which you will insert a needle or attach a line with chlorhexidine and alcohol during the mixing stage. The administration lines through which the nutrition solution runs into the horse should be replaced every 24 h, and this too should be performed using sterile gloves. Any location where one line is attached to another, or where the line is attached to the bag or bottle of solution, should be covered lightly with antibiotic ointment. Catheters should be gently palpated twice a day to check for evidence of thrombophlebitis. At the first sign of such problems, the catheter should be removed and replaced. The removed catheter should have the indwelling tip cultured for evidence of bacterial colonization.

To maintain the sterility of the solution entering the horse's body, several protective steps should be taken to protect from contamination. Initially, the mixing of the solution components needs to be in an aseptic fashion. Most practices do not have a laminar flow hood, but they will have a lab or other small, dust-free room that will suffice. A local hospital, diagnostic laboratory, or pharmacy may be willing to assist you by allowing the use of their hood. Use sterile gloves and wipe down any ports through which you will insert a needle or attach a line with chlorhexidine and alcohol during the mixing stage. The administration lines through which the nutrition solution runs into the horse should be replaced every 24 h, and this too should be performed using sterile gloves. Any location where one line is attached to another, or where the line is attached to the bag or bottle of solution, should be covered lightly with antibiotic ointment. Catheters should be gently palpated twice a day to check for evidence of thrombophlebitis. At the first sign of such problems, the catheter should be removed and replaced. The removed catheter should have the indwelling tip cultured for evidence of bacterial colonization.

Most patients on parenteral nutrition will be those with septicemia or other severe infections, some degree of malnutrition, and perhaps an inadequate immune response. All of these factors will increase their thrombogenic potential [4,8]. It is imperative that the least thrombogenic catheter material be selected. Studies have shown a definite increase in bacterial adherence to polyvinyl chloride catheters in comparison to those made of Teflon and silicone [8]. In other studies, it has been observed that the softer the catheter, the less irritating to the vein, and least thrombogenic, even among catheters composed of different materials [4]. Any catheter material, however, will incite an inflammatory response if not maintained properly. Silastic catheters are very soft, and are among the least reactive and best materials for long-term use [4,10]. Central catheters are recommended in foals because they are very soft, have a lower chance of becoming dislodged or kinked, and deliver the solution into a larger vessel, where it will be more rapidly disbursed and less likely to cause venous irritation. Double-lumen catheters are central lines in which a single catheter in the vein divides into two external extensions for two different administration sets. They allow the infusion of medications and fluids without interruption of the parenteral nutrition. In foals especially, it is helpful to run the nutrition solution and polyionic fluids separately in order to make appropriate adjustments to either without changing the rate of the other. These central catheters are very soft over-the-wire types and marketed by companies such as Arrow, Mila, and Cook. The use of fluid pumps is necessary in order to insure the calculated drip rate. Even in the best circumstances, the desired administration rate and the actual delivered volume may be quite different. In a foal, where it is important to accurately deliver a specific amount of calories and fluids, and to avoid an inadvertent bolus of nutrition solution, a functional fluid pump is an invaluable aid to the proper use of parenteral nutrition.

Basic, unfiltered fluid-administration lines are used for delivery of parenteral nutrition to the patient. It is important to have a dedicated line for the nutrition product to prevent any precipitation or other chemical reactions with medications or additives to polyionic fluids. If using only a single-lumen catheter, then we turn off the nutrition and flush approximately 100 ml of sterile saline before and after medications are delivered. It is not ideal, but has worked for us on several occasions when cost was a factor. It is not advisable to draw blood through catheters used for nutrition solutions [2].

3. Parenteral Nutrition Solutions

There are three primary solutions commonly used for parenteral nutrition in the equine patient: 50% dextrose, 10% amino acids, and 20% lipids.

Carbohydrate in the form of dextrose is the least expensive and least calorie-dense portion of the diet. Each milliliter of 50% dextrose contains 0.5 g of dextrose, and supplies 3.4 kcal of energy per gram. The commonly used 50% dextrose solution is extremely hypertonic with an osmolality of 2,522 mOsm/L, and cannot be used without dilution because of its thrombogenic potential (normal plasma has an osmolality of 300 mOsm/L). It has been suggested that 50% dextrose solution should not
exceed 60% of the total parenteral nutrition volume because of its high tonicity. The pH of this dextrose solution is 4.2, which is high enough to cause separation of the lipid components if improperly mixed. Carbohydrates should always be the primary energy source, because they have a protein-sparing effect not shared by lipids.

The 10% amino acid solution supplies 0.1 g of crystalline amino acids per milliliter, and 4 kcals of energy per gram. It also is hypertonic at 800 mOsm/L, and not suitable for undiluted intravenous administration. The pH is high and is damaging to the lipid emulsion if not mixed correctly. This fluid is a combination of both essential and nonessential amino acids at various concentrations, according to accepted bodily needs (formulated on human ratios). Amino acid solutions are also made by using protein hydrolysates that may have a higher ammonia level and cause some immune reactions [3]. [The described chemical information is from the package inserts of the products made by Abbott Laboratories (Chicago, IL, USA): 50% dextrose, 10% amino acid solution, and 20% lipid emulsion].

Lipid solution, or emulsion, is usually derived from a combination of safflower and soybean oils, using egg-yolk phospholipids and glycerin as emulsifying agents. "Lipid" is a term describing a characteristic of substances that can be extracted from cells by fat solvents. An "emulsion" is a type of fluid that contains two immiscible liquids in which one is suspended in the form of tiny globules throughout the other, such as the water and oil in mayonnaise. Lipid is the most calorie-dense component of parenteral nutrition at 9 kcal/g. In contrast to the other two components, lipid emulsions are isotonic. Lipids should not make up more than 50% of the total calories because they have been associated with decreased immune function and the development of hyperlipidemia in animals predisposed to it by genetics (ponies and miniature horses specifically) or disease process (liver disease or endotoxemia). In the mixing of the calculated parenteral nutrition solution, it is important that the dextrose and amino acids be combined first, and then the lipid component added to them. This method prevents the emulsion from being disrupted by extremes of pH [7].

Additional components can be added to the nutrition solution, but only those approved for such additions. There are specific total parenteral nutrition electrolyte additions and multiple vitamins for infusions on the market. If an animal requires parenteral nutrition for more than 4 - 5 d, then add vitamins and minerals, but not before. It is not uncommon, however, to add B-complex at a dose of 1 mL/L in anorectic animals that we are attempting to interest in feed. Although essential amino acids are already in the solution, there has been research interest in the past few years into what are being called "conditionally essential" amino acids. These are essential during times of major body stress such as that endured in severe disease states [2,12]. One of the most pursued conditionally essential amino acids is glutamine, and it is often added to total parenteral nutrition of small animals. Glutamine has been shown to have strong trophic effects on enterocytes, enhancing their normal function, as well as being necessary in the turnover of healthy mucosa [6,11,12]. The majority of equine parenteral nutrition cases are neonates with gastrointestinal disease in which glutamine supplementation may be beneficial. Unfortunately, even in small-animal medicine, doses have been extrapolated from the human literature and experiments have not yet been performed directly on the horse. Additions to parenteral nutrition not approved for this use may cause precipitations, bind vitamins, affect vitamin function, or disrupt the lipid emulsion [9]. In general, it is not necessary to add vitamins and extra amino acids to parenteral nutrition solutions for animals who only need it for a few days [3,7].

4. Calculations

Calculating the composition and volume of parenteral nutrition required per day can be daunting when one considers the many formulae available in the literature. One important rule is that the patient should be gradually adjusted to receiving total caloric requirements parenterally over 2 - 3 d [3,6,15]. Parenteral nutrition is not physiologic, so adjustment time is crucial to prevent hyperglycemia. The patient should be discontinued gradually over 2 - 3 d as it becomes more able to utilize enteral feeding [4,6]. It would take much more than the scope of this paper to describe all of the available methods, so I will simply describe the method we use.

The concentration and energy of solutions: dextrose 50% provides 3.4 kcal/g, amino acids 10% provides 4 kcal/g, and lipids 20% provide 9 kcal/g.

Your desired g/kg/d of each component changes for 3 d to allow for a gradual increase in calories as well as volume. Past Day 3, continue to use the third-day calculations. The g/kg/d factors are given in the formula.

Example - A 50-kg foal requires total parenteral nutrition:

For each day, use the formula shown in the table as demonstrated:

**Day 1:**

Dextrose = 10 g (50 kg body weight [BW])/0.5 because this is a 50% solution = 1,000 ml/d
Amino acids = 2 g (50 kg)/0.1 because this is a 10% solution = 1,000 ml/d
Lipids = 1 g (50 kg)/0.2 because this is a 20% solution = 250 ml/d
Total volume on Day 1 = 2,250 ml

**Day 2:**

Dextrose = 12 (50 kg BW)/0.5 = 1,200 ml
Amino acids = 3 (50 kg BW)/0.1 = 1,500 ml
Lipids = 2 (50 kg BW)/0.2 = 500 ml
Total volume on Day 2 = 3,200 ml

**Day 3+:**
Dextrose = 15 (50 kg BW)/0.5 = 1,500 ml
Amino acids = 3 (50 kg BW)/0.1 = 1,500 ml
Lipids = 3 (50 kg BW)/0.2 = 750 ml
Total volume on Day 3 and further = 3,750 ml

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Dextrose</th>
<th>10 g/kg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amino Acids</td>
<td>1 g/kg/d</td>
</tr>
<tr>
<td></td>
<td>Lipids</td>
<td>1 g/kg/d</td>
</tr>
<tr>
<td>Day 2</td>
<td>Dextrose</td>
<td>12 g/kg/d</td>
</tr>
<tr>
<td></td>
<td>Amino Acids</td>
<td>3 g/kg/d</td>
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<tr>
<td></td>
<td>Lipids</td>
<td>2 g/kg/d</td>
</tr>
<tr>
<td>Day 3</td>
<td>Dextrose</td>
<td>15 g/kg/d</td>
</tr>
<tr>
<td></td>
<td>Amino Acids</td>
<td>3 g/kg/d</td>
</tr>
<tr>
<td></td>
<td>Lipids</td>
<td>3 g/kg/d</td>
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</tbody>
</table>

**Check ratio of non-protein nitrogen (NPN) to nitrogen (N):**

NPN calories/g N = dextrose cals + lipid cals/(g amino acid/6.35)

The factor 6.35 is from the fact that 6.35 g protein typically provides 1 g N

To prevent protein catabolism, this ratio should be from 100 - 200.

**Day 1:** calories provided:
Dext 3.4 kcal/g = 3.4 (1,000 ml of 50%) = 1,700 kcal
Amino 4 kcal/g = 4 (1,000 ml of 10%) = 400 kcal
Lipids 9 kcal/g = 9 (250 cc of 20%) = 450 kcal
Plug into formula from box: kcal dextrose + kcal lipid/(g amino acid/6.35)
(400) + (1,700)/(100/6.35) = 2,150/15.75 = 136.5 ratio of non-protein nitrogen (NPN) to nitrogen (N), which is within the optimal range.

Check ratio in this manner for each day. Once the math is done, combine the solutions in the described manner and you have your total parenteral nutrition for this foal.

**5. Complications**

By its very nature, parenteral nutrition is not physiologically normal. Some complications are associated with the physical means of delivering the solution to the patient; i.e., intravenous catheters, lines, and attachment points. These are handled in routine fashion, but with special attention to aseptic technique, as previously described. One mechanical complication not generally a problem with the use of crystalline fluids is the potential for bacterial growth in the solution and in the lines through which it runs. A patient receiving parenteral nutrition with unexplained fevers should be evaluated for a contaminated solution or delivery system [10].

Other complications are physiologic responses to the solution itself. The most common physiologic complications are hyperglycemia and hyperlipidemia [5,6]. It is important to closely monitor blood glucose concentrations in patients (especially foals) receiving parenteral nutrition. We generally check glucose every 3 - 4 h. If there is a trend toward increasing glucose that reaches a high of 200 mg/dL, then we temporarily decrease the nutrition administration rate. Hyperglycemia is not unusual during the initial 24 - 48 h transition period as the body adapts to the infused glucose. Once this adaptation has passed, continuing intermittent hyperglycemia may have other causes, the most likely being sepsis or endotoxemia [4,6,16]. It may be necessary to reformulate a solution with less carbohydrate, or even to add an insulin infusion in refractory animals that are also glucosuric. Continuous infusion of insulin prevents the acute hypoglycemia that may follow an insulin bolus.
6. Enteral Feeding

Although the parenteral route has definite benefits in the care of critically ill animals, the benefits of enteral feeding are well known and should not be overlooked, especially in the neonate. Enteral feeding promotes gut maturation, feeds the enterocytes themselves, and promotes epithelial integrity [13]. Luminal nutrients are important in maintaining the epithelial barrier to bacteria and toxins. An intact epithelial barrier prevents these substances from being translocated across the gut wall, and maintains local immune function and normal flora [2,13]. Food in the lumen also aids in mucosal shedding, which helps mechanically remove bacteria from the mucosa. Food also promotes the secretion of the mucus barrier, again preventing bacterial adherence. Ingesta in the gut enhances intestinal motility, which also moves bacteria out of the body. If the patient is able to tolerate a small amount of enteral nutrition, then it is best to supply it [5,6,13,14]. Enteral nutrition in the critically ill horse can range from milk, electrolyte (Pedialyte®), or elemental solutions in foals to grain slurries or elemental diets in adults. A reported adverse effect of liquid diets in adult horses is laminitis [6,10].

7. Cost

A large part of the cost of parenteral nutrition support is lab work and nursing care. The lab work must be performed in order to minimize the occurrence of complications. The three-solution components are available in 500-cc volumes. Hospital cost of a bottle of 50% dextrose is approximately $3.50. The 10% amino acid solution is approximately $12, and the 20% lipid emulsion is around $13. (These numbers are based on our distributor's prices in March 2003). In our hospital, 24 hour of total parenteral nutrition for a 45-kg foal costs approximately $300. This is for the solution only. Keep in mind the costs of administration sets, gloves, etc. The cost for adults can reach $900 per day. An important factor in the decision whether to offer parenteral nutrition will be cost. It may be helpful to add all the costs you would need to bill for 3 d of parenteral nutrition solutions, fluid sets, lab work, etc. so the number will be available in discussions with clients.

8. Results

There is much written on parenteral nutrition in veterinary practice, and this paper merely skims the surface in order to provide enough information to help practitioners decide if it is a therapy they wish to offer their clients. The average duration of parenteral nutrition required in equine cases over the past 2 years at Mississippi State University has been 4 d. An average duration of 5 d was found in the review of 79 cases at the Equine Medical Center in Leesburg [6]. The decision to use parenteral nutrition in your practice should be made before a patient is in dire need of it. Taking into account the previously mentioned logistical factors, there must be written operating procedures and personnel trained in the necessary techniques, record keeping, and charting and analysis of data. The hardest thing to supply may be a doctor with time to evaluate the patient and its collected data several times a day. Last but not least, parenteral nutrition therapy requires an owner who understands and accepts the cost of such treatment.
References


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